TrEatment Targets in Rheumatoid Arthritis: a randomized multi-centre, treat to target strategy trial: TETRA study

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We aim to estimate the difference in effectiveness of DAS28CRP low disease activity and SDAI remission as treatment targets in RA treat to target strategies with regard to RA outcome.

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

Summary

ID

NL-OMON53234

Source
ToetsingOnline

Brief title
TETRA

Condition

- Autoimmune disorders
- Joint disorders

Synonym
joint inflammation, rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Sint Maartenskliniek
Source(s) of monetary or material Support: AbbVie B.V.,Galapagos,RSMK;AbbVie;Galapagos

Intervention

Keyword: DAS28CRP, rheumatoid arthritis, SDAI, treat-to-target

Outcome measures

Primary outcome

The main outcome of this trial is the proportion of patients that score positive for the dichotomous composite outcome for clinical and radiological remission. This composite measure includes:

- radiographic progression <= 1 SENS score point

- <=1 swollen joints detected during joint count

- Positive patient acceptable symptom state (PASS)

Secondary outcome

Secondary outcomes in this study are defined as:

1. All individual parts of the composite primary endpoint including radiographic progression, number of swollen joints and proportion of patients being in PASS at 18 months follow-up

2. The proportion of patients who reach the predefined target for each treatment arm (DAS28CRP-LDA or SDAI remission)

3. Percentage of patients that reach LDA or remission, using DAS28CRP- and SDAI-based definitions, in each treatment arm

4. Number of flares that occur in each treatment arm over 18-months follow-up

5. Daily functioning, measured by HAQ DI

6. Physician T2T/Ta2T protocol adherence

7. Drug use of the patients, consisting of the type and volume of antirheumatic drugs (GC, DMARDS, NSAIDs) used over the 18 months period, and at 18 months visit

8. Safety ((serious) adverse events, according to CTCAE criteria version 5.0)

9. Quality of life (QoL) as defined by the EQ5-D-5L questionnaire

10. Costs: volumes of medical costs and productivity loss

Study description

Background summary

Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by inflammation of synovial joints. RA patients present with pain, stiffness and swelling of the affected joints. Due to high direct and indirect medical costs, RA is associated with a great economic burden for both patients and society. There is currently no cure for RA, but many treatment options are available. The central aim of RA treatment is lowering disease activity. The proactive treatment strategy called treat to target (T2T) includes measuring disease activity, setting a target and adjusting treatment accordingly until the goal is reached. Additionally, the strategy can be implied in the phase when stable disease or remission is reached to taper the drug, also called *taper to target* (Ta2T). T2T has proven to be superior to usual care, but there is much debate regarding the most optimal treatment measure and target. The Disease Activity Score with 28-joint counts and c-reactive protein (DAS28CRP) low-disease activity (LDA) target and the more stringent Simplified Disease Activity Index (SDAI) remission target are the best validated targets. Especially the DAS28CPR is the most commonly used in research and practice, whereas the SDAI remission target is most recommended. The EULAR recommends to strive for remission, whereas the ACR recommends to strive for LDA.
In patients with new and established RA, the (cost)effectiveness of aiming for remission compared to LDA when starting and tapering antirheumatic drugs has not been directly compared. This study therefore aims to directly compare two T2T strategies, aiming at DAS28CRP-LDA and SDAI remission, in patients with established RA.

Study objective

We aim to estimate the difference in effectiveness of DAS28CRP low disease activity and SDAI remission as treatment targets in RA treat to target strategies with regard to RA outcome.

Study design

A multi-centre, randomized strategy trial in 340 patients with an existing diagnosis of RA. Patients are randomised towards a treatment target of :
1. Disease Activity Score with 28-joint counts and c-reactive protein (DAS28CRP), low-disease activity target
2. Simplified Disease Activity Index (SDAI), remission target

A follow-up period of 18 months is chosen to facilitate assessment of the full difference between the two arms, as some time is needed in T2T for each drug to show its effect (3-6 months). Several iterative cycles might be necessary to arrive at the desired effect, with another six months until any changes in radiological progression can be seen. Both strategies are already implemented in clinical practice and all drugs used are already authorised for RA.

Intervention

Patients are randomised towards a treatment target of :
1. Disease Activity Score with 28-joint counts and c-reactive protein (DAS28CRP), low-disease activity target
2. Simplified Disease Activity Index (SDAI), remission target

Study burden and risks

During the trial period, patients are asked to fill in different questionnaires at different points in time. It is estimated that the questionnaires take less than 30 minutes to complete. The remainder of the data will be measured and collected by a trained nurse at different points in time during the trial.

In the literature, it has been established that T2T strategies are more effective compared to usual care in newly diagnosed RA. There is a risk for the patients that one of the T2T strategies might be less effective than the other. However, it is thought to still be more effective than usual care. Therefore, there is limited additional risk for the patients that participate in this study.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Diagnosis of RA (according to the 2010 ACR/ EULAR classification criteria and/or clinical diagnosis)
- Aged 16 years or older
- At most low disease activity, operationalised as DAS28-CRP <3.5 (DAS28 CRP 2.9 cut off for low disease activity with measurement error 0.6) or SDAI < 19 (SDAI 11 cut off for low disease activity with measurement error 8) or the rheumatologist*s opinion. A state of low disease activity is required at inclusion, as for RA patients in moderate or high disease activity there is no equipoise on the best course of action (treatment needs to be escalated, both in case of aiming for remission or LDA).
- Fluency of Dutch or English, both written and verbally; able to fill in questionnaires
- Provided informed consent

Exclusion criteria

- Clinical deep remission, operationalised as SDAI <3.3 or DAS28-CRP

<2.4, AND a taper attempt in the past 2 years that was discontinued due to occurrence of flare.
- Fewer than 3 DMARD treatment options left for this patient (severe difficult-to-treat or refractory RA)
- Current severe comorbidity or other serious life-shortening conditions hampering trial participation
- Inability to comply with the study protocol or to provide informed consent with regard to intervention control and measuring outcomes

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-12-2023
Enrollment:	280
Type:	Actual

Ethics review

Approved WMO Date:	06-11-2023
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-05-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	02-10-2024
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

No registrations found.

In other registers

Register	ID
Other	clinicaltrial.gov nummer volgt
CCMO	NL84995.091.23