COBRA treat-to-target trial

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON19866

Source
Nationaal Trial Register

Brief title
COBRA T2T

Health condition

Patients with early rheumatoid arthritis

Sponsors and support

Primary sponsor: VU University Medical Center
Source(s) of monetary or material Support: Pfizer BV

Intervention

Outcome measures

Primary outcome

The primary outcome is the difference in disease activity in the two randomisation arms of both groups, measured by the percentage of patients that reach an EULAR good response at 26 weeks. EULAR good response is reached when the DAS44-score is ≤2.4 and has improved ≥1.2 points compared to baseline.

Secondary outcome

The secondary outcomes are functional ability, remission, radiological progression, and patient reported outcomes. Clinical lab, bone mineral density, body composition, social demographic parameters, and lifestyle factors are tertiary parameters.

Study description

Background summary

The objective of this study is twofold. First, we want to investigate the effectiveness of a COBRA-plus therapy after incomplete response on COBRA-light therapy after 13 weeks to improve the percentage of RA-patients with a high disease activity and/or unfavourable prognostic factors that reach a good response to treatment. Second, we want to investigate the effectiveness of adding prednisone to MTX monotherapy in RA-patients with initial low disease activity failing MTX monotherapy after 13 weeks. By using treat-to-target strategies, this study aims a high percentage of all early RA patients with a good response to treatment at 26 weeks. A secondary objective of this study is to study the psychometric properties of patient reported outcomes in low disease activity and remission and investigate the validity of the outcomes that have been shown to be important to patients in defining remission.

This is a multicenter study containing a randomisation step after incomplete response at 13 weeks and with two strategy arms: one arm of patients with unfavourable prognostic factors, the so-called ‘high risk group’ (group 1), and in the other study arm patients without unfavourable prognostic factors, the ‘low risk group’ (group 2). This study includes early RA patients of 18 years and above, who enter one of the two study arms based on disease activity and the presence or absence of prognostic factors. Group 1 (‘high risk group’) consists of patients with moderate to high disease activity (based on the disease activity score (DAS44) >3.7); or DAS44 ≤3.7 combined with an unfavourable prognosis (presence of at least two out of the four following factors: CRP≥35 mg/l OR ESR≥50 mm/h; IgM-rheumatoid factor positive; aCCP positive; at least one erosion). Group 2 (‘low risk group’) consists of patients with low to moderate disease activity (DAS44 ≤3.7 and a maximum of one out of the four following factors: CRP≥35 mg/l OR ESR≥50 mm/h; IgM-rheumatoid factor positive; aCCP positive; at least one erosion).

Patients are treated according to a treat-to-target protocol, using mono- and combination therapy commonly used in clinical practice. In case of suboptimal response after 13 weeks, patients are randomised to continue initial therapy or intensified therapy. Treatment is protocolised for 26 weeks and patients are followed for 52 weeks. After 26 weeks, the treating rheumatologist is at liberty to make an own treatment decision.

The primary outcome is the difference in disease activity in the two randomisation arms of both groups, measured by the percentage of patients that reach an EULAR good response at 26 weeks. EULAR good response is reached when the DAS44-score is ≤2.4 and has improved ≥1.2 points compared to baseline.

Study design

At baseline, and after 4, 13, 17, 26, 39, and 52 weeks, patients will visit their treating rheumatologist where usual measurements will take place (i.e. number of tender and swollen joints, lab tests, x-rays of hand and feet, patient reported outcomes in the form of questionnaires on perceived pain, global wellbeing, and physical functioning). In addition, research questionnaires will be collected on additional patient reported outcomes including fatigue, sleep, stiffness, and employment.

Intervention

This is a multicenter study containing a randomisation step after incomplete response at 13 weeks and with two strategy arms: one arm of patients with unfavourable prognostic factors, the so-called ‘high risk group’ (group 1), and in the other study arm patients without unfavourable prognostic factors, the ‘low risk group’ (group 2). Patients are treated according to a treat-to-target protocol, using mono- and combination therapy commonly used in clinical practice. In case of a moderate or non response according to European response criteria (EULAR criteria) after 13 weeks, treatment is randomised to continue initial therapy or to intensification of the therapy. At baseline, the high risk group starts with COBRA-light therapy (a combination of MTX 25 mg per week and initially 30 mg prednisolone per day tapered to 7.5 mg prednisone per day in eight weeks). If EULAR response after 13 weeks is good, COBRA-light therapy will be continued. If EULAR response is moderate or none, patients will be randomised to continue COBRA-light therapy or to intensification to COBRA-plus therapy (a combination of MTX 25 mg per week, initially 60 mg prednisolone per day tapered to 7.5 mg prednisone per day in seven weeks, sulfasalazine 2000 mg per day, and hydroxychloroquine 400 mg per day). The low risk group starts with MTX monotherapy (started with 10 mg MTX per week increased to 25 mg per week in eight weeks). After 13 weeks, EULAR response will be determined. If EULAR response is good, initial medication will be continued. If EULAR response is moderate or none, patients will be randomised to continue MTX mono-therapy or to intensification to COBRA-light therapy. Treatment is protocolised for 26 weeks and patients are followed for 52 weeks. After 26 weeks, the treating rheumatologist is at liberty to make an own treatment decision.

Contacts

Public
VU Medical Center
depatment of rheumatology 4a-42
Boelelaan 1117

W.F. Lems
Amsterdam 1081 HV
The Netherlands
+31 20-4443432
Scientific
VU Medical Center
depatment of rheumatology 4a-42
Boelelaan 1117
W.F. Lems
Amsterdam 1081 HV
The Netherlands
+31 20-4443432

Eligibility criteria

Inclusion criteria

1) RA according to the 2010 classification criteria of the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR)

2) Age of 18 years and older

3) Early RA: disease activity of less than 2 years

4) Active RA, the patient must meet at least one of the following unfavourable prognostic markers: DAS44 score >3.7 OR presence of at least two of the four following features (CRP≥35 mg/l OR ESR≥50 mm/h; IgM-RF positive; aCCP positive; at least 1 erosion) Patients meeting the first three criteria, but not the criteria for active RA, can participate in the group of patients with a high probability of a mild disease course (low risk group). Patients meeting all four inclusion criteria, including the active RA criterion, can participate in the group of patients with a potentially severe course of the disease (high risk group).

Exclusion criteria

- Prior treatment DMARDs (except hydroxychloroquine)

- Insulin-dependent Diabetes mellitus

- Uncontrollable non-insuline dependent diabetes mellitus

- Heart failure NYHA class 3-4

- Uncontrollable hypertension

- ALAT/ASAT >3 times normal values

- Reduced renal function

- Contra-indications for methotrexate, sulphasalazine or prednisolone

- Indications of probable tuberculosis

- Increased risk of harm due to contraindications to the study drugs

- Language problems

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	15-05-2014
Enrollment:	190
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 44989
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL4393
NTR-old	NTR4524
CCMO	NL45991.029.13
OMON	NL-OMON44989

Study results