Difficult-to-treat RA: a study to obtain insight into the occurrence and nature of potential problems underlying the disease state and into its clinical burden

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To obtain insight into the occurrence and nature of potential problems underlying difficult-to-treat RA and into its clinical burden, that will eventually be used to improve the management approach for difficult-to-treat RA.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Synovial and bursal disorders
Study type	Observational invasive

Summary

ID

NL-OMON49002

Source
ToetsingOnline

Brief title
D2T RA

Condition

- Synovial and bursal disorders

Synonym
Arthritis, RA

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Difficult-to-treat, Rheumatoid arthritis, Treatment, Underlying factors

Outcome measures

Primary outcome

- Clinical RA activity

- Objectively assessed inflammation

- Potential problems underlying difficult-to-treat RA:

* Causes of persistent inflammation

* Non-inflammatory causes of complaints

* Factors which hamper proper grading

Sub study: Qualitative research about non-adherence to DMARDs

- Reasons for being (non-)adherent: Gathered through face-to-face interviews and thereafter sorted using a card sorting task

- Facilitators and barriers of treatment adherence: Gathered through face-to-face interviews and thereafter sorted using a card sorting task

- Differences between patients and rheumatologists regarding the level of applicability of reasons, facilitators and barriers to themselves and the general population of RA patients, respectively

Secondary outcome

Clinical burden:

- Patient burden:

* Quality of Life using EuroQol 5 dimensions (EQ-5D)

* Functional ability using Health assessment questionnaire (HAQ)

- Socioeconomic burden: Health care utilization and work participation costs

Serum biomarkers levels:

- Serum biomarker levels, including but not limited to IL-6

Study description

Background summary

Difficult-to-treat rheumatoid arthritis (RA) is defined by signs of active/progressive RA, which is perceived as problematic by rheumatologist and/or patient, despite treatment according to European League Against Rheumatism (EULAR) recommendations and failure of *2 biologic (b-) or targeted synthetic (ts) disease modifying anti-rheumatic drugs (DMARDs)(with different mechanism of action. ~5-20% of RA patients can be characterized as difficult-to-treat. The treatment of difficult-to-treat RA patients may be challenged by several problems underlying the disease state, e.g. immunologic mechanisms, adverse drug reactions, treatment non-adherence, and comorbidities. However, the importance of these individual problems is unknown, which shows the unmet need for this patient population.

Study objective

To obtain insight into the occurrence and nature of potential problems underlying difficult-to-treat RA and into its clinical burden, that will eventually be used to improve the management approach for difficult-to-treat RA.

Study design

Exploratory, single centre, cross-sectional, observational.

Study burden and risks

Patients will have one study visit, at which an interview, joint examination and blood sampling will be performed. In addition, patients are requested to fill in 11 questionnaires. These can be filled in at home. The total amount of blood drawn in the study is 5 ml. Patients may develop a hematoma at the site of venepuncture.

Some parameters (viz., medical history, demographic data, height/weight, smoking status, alcohol use, disease duration, usage of anti-rheumatic drugs and painkillers and clinical disease parameters) are recorded or performed in regular care depending on the clinical situation. In that case the data will be retrieved from the electronic patient record. However, as regular care does not follow a strict protocol, these data may not be available for each patient. In that case, these assessments will be collected specifically for the purpose of this study.
In patients without evident arthritis but with some suspicion of synovitis, ultrasound (US) will be performed in regular care in (a) suspect joint(s) to exclude or demonstrate synovitis. In patients with (a) swollen joint(s) but with some suspicion of having only secondary osteoarthritis, in these joints (in addition to ultrasound) an X-ray will be performed in regular care to exclude or demonstrate secondary osteoarthritis. For both US and X-ray, an ipsi- or contralateral joint will be chosen as a control joint, these will be study procedures.
The total study visit (including filling in the questionnaires) will take approximately 2 hours.

Sub study: Qualitative research about non-adherence to DMARDs
Participants will be invited for a second study visit for a sub study to explore reasons of DMARD non-adherence. A minimum of 10 patients will be interviewed face-to-face to find out the reasons of non-adherence for DMARDs and to examine facilitators and barriers for optimal adherence. These face-to-face interviews will be carried out until data saturation is reached during two successive interviews (expected number of interviews in between 10 and 15). The reasons, facilitators and barriers respectively, that have been discussed during the face-to-face interviews will serve as a base for conducting the card soring task. They will be reduced to a maximum of 60 for each category by the project group.
Another 40 patients will be asked to perform a card sorting task to sort the reasons, facilitators, and barriers, respectively, based on similarity and, thereafter, to sort these into five categories of applicability to themselves. 20 rheumatologists (in training) will sort these into five categories in terms of applicability to the general population of patients with RA.

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

* Age * 18 years
* Patient can speak and read Dutch
* Fulfilling 2010 American College of Rheumatology (ACR)/EULAR classification criteria for RA
* Treatment according to the current standard of care/EULAR recommendations for at least one year, Additional criteria for difficult-to-treat RA group:
* Failure of *2 b/tsDMARDs (with different mechanism of action) after failing csDMARD therapy (unless contraindicated)
* Signs of active/progressive disease, defined as *1 of:
o At least moderate disease activity (according to validated composite measures including joint counts e.g. DAS28-ESR > 3.2 or CDAI >10)
o Signs (including inflammatory markers and imaging) and/or symptoms suggestive of active disease (joint related or other)
o Rapid radiographic progression (with or without signs of active disease)
o Inability to taper glucocorticoid treatment (below 7.5 mg/day prednisone or equivalent)
o Well-controlled disease according to above standards, but still having RA symptoms that are causing a reduction in Quality of Life
* The management of signs and/or symptoms is perceived as problematic by the rheumatologist and/or the patient. , Additional criteria for control group:

* not fulfilling the definition of difficult-to-treat RA.

Exclusion criteria

NA

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-02-2019
Enrollment:	300
Type:	Actual

Ethics review

Approved WMO Date:	19-12-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	11-04-2019
Application type:	Amendment
Review commission:	METC NedMec

Approved WMO Date:	29-08-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-03-2020
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

No registrations found.

In other registers

Register	ID
CCMO	NL66141.041.18