Detailed and consistent clinical and immunological monitoring of patients with Rheumatoid Arthritis who are treated with biological agents.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Joint disorders
Study type	Observational invasive

Summary

ID

NL-OMON39129

Source
ToetsingOnline

Brief title
Clinical and immunological monitoring of rheumatoid arthritis patients.

Condition

- Joint disorders

Synonym
rheuma, rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht

Source(s) of monetary or material Support: Ministerie van OC&W,ZonMw,Schering-Plough,UCB Pharma

Intervention

Keyword: biologicals, immunological profile, prediction, reumatoid arthritis

Outcome measures

Primary outcome

(short-term) Eular response to a specific biological agent

Secondary outcome

Side effects

Long-term outcome based on radiographic joint damage

Quality of life

Effectiveness and cost-effectiveness of use of the developed prediction rule

Fatigue and depressed mood

Differences in response to therapy with biologicals between RA patients with a

"Cold" or "Heat" type of symptom profile.

Study description

Background summary

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammation of joints leading to joint destruction. The onset, course of inflammation, rate of progression of joint damage is different for each patient. As thus far no curative therapy is available, the therapeutic possibilities range from conventional disease modifying anti-rheumatic drugs (DMARDs), to the more recent biological agents (such as anti-TNFalfa and anti-B cell therapy). These drugs have been proven to effectively suppress inflammation whereas "biologicals" might even result in retardation of joint destruction.
Like the variability in the process of the disease, there is a significant variability in the response to different "biologicals". Not all patients

respond (to the same extent) to the treatment they get first, second, or in combination. Patients might thus be subject to potential delay in treatment efficacy and thereby unnecessary irreversible joint destruction, unnecessary side effects, and high costs. This in the light of the generally accepted concept that tight control of these patients early in the disease process, aimed at remission of disease, provides the best window of opportunity to limit joint destruction and co-morbidity with major social-economic impact. It is therefore of major importance to characterise patients with rheumatoid arthritis in a consistent and detailed way by immunological and clinical parameters, before, during, and upon change of "biologicals", to identify subpopulations with specific characteristics, enabling more patient tailored treatment in the future, preventing delay of treatment efficacy, unnecessary side effects, and high costs.

With the help of state-of-the-art technologies patients can be characterized in much more detail than clinical practice allows.
• Gene (mRNA) profiling makes it possible to evaluate a great number of genes simultaneously, thus avoiding the cost- and time-consuming analysis of single factors.
• Protein profiling by multicytokine analysis (e.g. Luminex) or specific targets (such as biomarkers of cartilage and bone turnover) will be performed on serum, plasma and/or urine samples used to characterize the patients. Molecules include, but are not restricted to, pro- and anti-inflammatory cytokines, proteases, and biomarkers of cartilage and bone turnover.
• Phenotypic characterization of sub populations of mononuclear cells will provide differentiation between patients at the level of immunological constitution and activity.
• Multiple clinical parameters are gathered and filed in a consistent way.
• Symtom profiling based on Chinese diagnosis can indicate differences in response to biologicals.

Altogether this study contributes to the emergence of a more customized treatment for patients with rheumatoid arthritis, preventing unnecessary delay of treatment efficacy, side effects, and costs.

Proinflammatory cytokines are considered of key importance as initiating and maintaining factors of fatigue and depressed mood. In rheumatoid arthritis, the treatment with biologicals reduces disease activity by blocking specific proinflammatory cytokines. This treatment offers a unique opportunity to clarify this role of cytokines as a maintaining factor of fatigue and depressed mood. Two-hundred patients will fill out short diaries daily to assess fatigue and depressed mood.

Study objective

The proposed study aims to develop a prediction rule for response to biological treatment in RA (i.e. effectiveness and adverse events). Guidelines for treating the disease with biologicals using the (derived) prediction rules will be defined.
To develop a prediction rule we aim to identify immunological, clinical, and symptom based characteristics that are predictive of the effectiveness of different biological agents currently on the market for RA (i.e. anti-TNFa agents, anti CD20, anti-T-cell activation, and anti-IL6R therapy) and the characteristics that are predictive of side effects.
The aim of the diary part of the study is to examine whether and to what extent a decrease of fatigue and depressed mood in rheumatoid arthritis after treatment with biologicals is a direct effect of cytokine blockade or an indirect effect of a reduction in disease activity.

Study design

Rheumatoid arthritis patients within the SRU (Stichting Reumaonderzoek Utrecht) study group who start treatment with "biologicals" are asked to participate in this immunological and clinical monitoring programme. Patient characteristics and biomaterials are consistently gathered and stored (directly) in electronic databases and biobanks.
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To evaluate clinical efficacy clinical parameters are evaluated at baseline (before start with treatment with a new biological), at 3 and 6 months after start of biological treatment, subsequently yearly and if treatment is stopped due to inefficacy or side-effects. Questionnaires on "quality of life" and radiographs of hand and feet are gathered at baseline and yearly. Additionally patients are asked to fill in a questionnaire related to symptoms based on Chinese diagnosis. These symptoms are used to find patterns of symptoms that are predictive for a response on thearpy with biologicals.
To find predictive factors for respons on biologicals, urine and blood are gathered to evaluate immunological characteristics, together with clinical parameters.

Two-hundred patients will fill out short diaries during 28 consecutive days with questions on their fatigue, mood state and disease-activity.

Study burden and risks

Not applicable

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Rheumatoid Arthritis according to ACR criteria (criteria van American College of Rheumatology) who start with biological treatment
Age >18 years

Exclusion criteria

Patients who understand the Dutch language insufficiently to appreciate the informed consent and to complete the Dutch questionnaires.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-06-2009
Enrollment:	880
Type:	Actual

Ethics review

Approved WMO Date:	24-03-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-10-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-11-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-10-2013
Application type:	Amendment

Review commission: METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL23830.041.08