Prospective study on the effects of etanercept treatment in patients with rheumatoid arthritis who are naive for TNF-alpha blocking therapy or are non-responders to prior treatment with other anti-TNF-alpha medication

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To evaluate the response to etanercept treatment in TNF-alpha blockade naïve patients and patients who failed prior other anti-TNF-alpha treatment and to understand the mechanisms underlying the clinical response to TNF-alpha blockade

Ethical review	Approved WMO
Status	Pending
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON32681

Source
ToetsingOnline

Brief title
Not applicable

Condition

- Autoimmune disorders
- Joint disorders

Synonym
rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Etanercept treatment, rheumatoid arthritis

Outcome measures

Primary outcome

The primary outcomes are:

1) factors distinguishing responding patients from non responding patients on etanercept treatment Differences in cytokine profiles or other serological markers, RA activity driven by other mediators than TNF-alpha)

2)percentage of patients (TNF-alpha blockade naïve versus failures on prior anti-TNF-alpha treatment) respond after 16 weeks of etanercept treatment

Secondary outcome

The secundary outcomes are:

1) the clinical efficacy of etanercept after 1 year treatment (Eular response criteria (DAS 28), ACR response, RADAI, SF 36, HAQ, and radiological progession)

2) genetic markers, e.g. genetic polymorphisms in the TNF-alpha genes, that may predict diagnosis, efficacy and side-effects of treatment in the individual

patient

3) periferal blood (mRNA) micro-array analysis identifying new markers that

distinguish responders from non-responders to etanercept treatment

Study description

Background summary

Previous randomised trials have shown the efficacy of etanercept in RA patients. In this study we will evaluate the respons of etanercept in anti-TNF naive patients compared to patients who have failed other anti-TNF. We will look for clinical parameters and serological markers that may differentiate responders from non-responders on etanercept.

Study objective

To evaluate the response to etanercept treatment in TNF-alpha blockade naïve patients and patients who failed prior other anti-TNF-alpha treatment and to understand the mechanisms underlying the clinical response to TNF-alpha blockade

Study design

A monocenter prospective, exploratory study with a 2 to 4-week screening period and a 52-week follow-up period

Study burden and risks

Patients will visits our outpatient clinic seven times during this study. They will get a physical exam and blood test each time they come. During visits 2 till 7 they have to fill out a questionnary (ACR Radai, HAQ, VAS, morning stiffness, SF36) and give urine for tests. The objects will get a X-chest at the screening and during this study there will be two X-hands and X-foots made.

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

1) Patients with the diagnosis rheumatoid arthritis according to the American Rheumatism Association (ARA) 1987 criteria and in ACR 1991 functional classes I, II, and III (see appendix)
2) The patient is naive for anti-TNF-alpha therapy or has failed other prior TNF-alpha blockers
3) DAS 28 > or <= 3.2
4) Failure on two previously used DMARDs
5) Age > 18 and < or <= 85 years old
6) Use concurrent methotrexate treatment (5 - 30 mg/week; stable since at least 28 days before initiation) during the study. Subjects may be taking nonsteroidal anti-inflammatory drugs, provided the dose and frequency have been stable for at least 28 days. Subjects may be receiving prednisone therapy < or <= 10 mg/day provided that the dosage has been stable for at least 28 days prior to entry.

Exclusion criteria

1) Pregnancy

2) Breastfeeding
3) A history of or current acute inflammatory joint disease of different origin e.g. mixed connective tissue disease, seronegative spondylarthropathy, psoriatic arthritis, Reiter*s syndrome, systemic lupus erythematosus or any arthritis with onset prior to age 16 years
4) Acute major trauma
5) Therapy within the previous 60 days with:
* any experimental drug
* alkylating agents, e.g. cyclophosphamide, chlorambucil
* antimetabolites
* monoclonal antibodies (including infliximab and adalimumab)
* growth factors
* other cytokines
6) Therapy within the previous 28 days with:
* parenteral or intraarticular corticoid injections
* oral corticosteroid therapy exceeding a prednisone equivalent of 10 mg daily
* present use of DMARDs other than methotrexate
7) Receipt of any live (attenuated) vaccines within 4 weeks prior to baseline
8) Fever (orally measured > 38 °C), chronic infections or infections requiring anti-microbial therapy
9) Other active medical conditions such as inflammatory bowel disease, bleeding diathesis, or severe unstable diabetes mellitus
10) Manifest cardiac failure (stage III or IV according to NYHA classification)
11) Progressive fatal disease/terminal illness
12) a history of lymphoproliferative disease or treatment with total lymphoid irradiation.
13) A white cell count less than 3.5 x 10^9/l
14) Platelet count less than 100 x 10^9/l
15) Haemoglobin of less than 5.3 mmol/l
16) Body weight of less than 45 kg
17) History of drug or alcohol abuse
18) Any concomitant medical condition which would in the investigator*s opinion compromise the patient*s ability to tolerate, absorb, metabolize or excrete the study medication.
19) Inability to give informed consent
20) Mental condition rendering the patient unable to understand the nature, scope and possible consequences of the study and/or evidence of an uncooperative attitude.

Study design

Design

Study phase:	4
Study type:	Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2010
Enrollment:	200
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Enbrel
Generic name:	Etanercept
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	08-03-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC

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
EudraCT	EUCTR2009-015653-20-NL
CCMO	NL29616.018.09
Other	Not applicable