Efficacy and safety of adalimumab in patients with peripheral spondyloarthritis without ankylosing spondylitis or psoriatic arthritis.

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

Summary

ID

NL-OMON32839

Source
ToetsingOnline

Brief title
Adalimumab in peripheral spondyloarthritis without AS or PsA

Condition

- Autoimmune disorders
- Joint disorders

Synonym
spondyloarthritis - spondyloarthropathy

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Abbott,Dana Foundation

Intervention

Keyword: adalimumab, efficacy, peripheral spondyloarthritis, safety

Outcome measures

Primary outcome

Efficacy: Patient*s Global Assessment of Disease at week 12

Safety: detailled questionaire for adverse events, clinical examination,

laboratory evaluation (hematology, chemistry, urine analysis)

Secondary outcome

Efficacy: Patient's Global Assessment of Disease at week 24, Physician*s Global

Assessment of Disease, BASDAI, number of swollen and tender joints, CRP and ESR

Serum biomarkers: MMP3, MRP8/14, cartilage and bone biomarkers, autoantibodies

Synovial biomarkers: celinfiltration, cytokine expression, MMP expression,

vascularisation

Function and quality of life: Health Assessment Questionnaire; AMC Linear

Disability Score; HUI-3

Study description

Background summary

Spondyloarthritis is a frequent form of chronic, inflammatory arthritis and is divided in different subtypes: ankylosing spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis, arthritis with inflammatory bowel diseases and undifferentiated spondyloarthritis. Both clinical and pathophysiological data show that the different subtypes belong to one concept. Almost all

therapeutical trials with TNFalpha blockers are conducted in patients with AS or PsA. Peripheral spondyloarthritis without AS or PsA counts for almost 20 % of all patients with spondyloarthritis. This important group has no entrance tot treatment with TNFalpha blockers, whereas the standard treatment (local injections with corticosteroids, NSAID of sulphasalazine) is not efficient enough in 25-50% of the patients. Furthermore, there are now (preliminary) data that TNFalpha blockers are effective in this patient group.

Study objective

The aim of the study is to assess the efficacy and safety of treatment with adalimumab in patients with peripheral spondyloarthritis (without AS of PsA). Furthermore, the effect of adalimumab will be investigated on systemic and local disease activity (serum and synovial biomarkers), function and quality of life.

Study design

After screening, patients with active peripheral spondyloarthritis (without AS of PsA) will be enrolled in a 12-week, randomised, double-blind, placebo-controlled trial, followed by a 12-week open label extension trial. Study medication = adalimumab (Humira); dosage = 40 mg every 2 weeks, subcutaneous injection. The study is conducted in the department of Clinical Immunology and Rheumatology, AMC, Amsterdam. In total, there are 6 visits: screening, baseline, and week 6, 12, 18 and 24. At every visit, there is a clinical evaluation of the disease activity and safety (according the guidelines of *Good Clinical Practise*) and a laboratory evaluation. If a large peripheral joint is affected, the patient undergoes a needle-arthroscopy at baseline, week 12 and week 24, in order to obtain synovial tissue.

Intervention

Therapeutical intervention:
The first 12 weeks the patients are treated with adalimumab (40 mg every 2 weeks, subcutaneous injection) or placebo. The last 12 weeks all patients are treated with adalimumab (40 mg every 2 weeks, subcutaneous injection).

Procedure:
Venous blood punction at every study visit (40 ml per visit, in total 240 ml)
Arthroscopy at baseline, week 12 and week 24

Study burden and risks

Adalimumab is used worldwide in thousands of patients with chronic arthritis (rheumatoid arthritis, AS, PsA) and is extensively investigated in clinical trials. The most reported adverse events are: local skin reaction on the site

of the injection, infections of the upper airways, headache and nausea. Some of the rare adverse events are: opportunistic infections and reactivation of tuberculosis, neurological disorders caused by demyelinisation, and allergic reactions. During treatment with adalimumab, the patient should not receive vaccinations with living viruses. On the moment, there are not sufficient data on the effect of adalimumab on the foetus. The therapy can be harmful. Pregnant women or during lactation are therefore not allowed to participate in the study.
Beside the risks related to the treatment with adalimumab, there are also risks related to the procedures. The venous blood punction (40 ml blood at each visit) and the arthroscopy can cause a vagal reaction. This adverse event is rarely seen. At the arthroscopy, there is a very small risk (< 0,3%) on a complication, such as an infection of the joint. Careful disinfection of the skin and the use of sterile gloves diminish that risk. Reactions on the local anaesthesia (nausea, nervositas, skin reactions) are rarely seen and disappear quickly.
In general, the therapeutic effects of treatment with adalimumab are superior to the extent of the burden and risks associated with participation in the trial.

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. Prior to any study procedure, voluntary written informed consent must be obtained, after the nature and purpose of this study are explained
2. Patients should be between 18 and 70 years of age
3. Patients must have a diagnosis of peripheral spondyloarthritis not fulfilling the classification criteria for ankylosing spondylitis or psoriatic arthritis for at least 3 months. The disease must be moderate to severely active as defined by at least 1 swollen and at least 1 tender or painful joints
4. If female, patient should either be of not-childbearing potential (i.e. postmenopausal or surgically sterile) or practice a reliable method of birth control until 150 days post-study (e.g. use of condom, IUD, oral contraceptives) or have a vasectomized partner
5. Patients should have inadequate response to NSAID therapy (non-steroidal, anti-inflammatory drugs)
6. The use of concomitant NSAIDs and corticosteroids is allowed. The dose of corticosteroids should not exceed a prednisone equivalent * 10 mg/day and must be stable for at least 4 weeks prior to baseline
7. The use of concomitant DMARDs (disease modifying anti-rheumatic drugs, Methotrexaat or Sulphasalazine) is allowed. If using DMARDs, patients must have received a minimum of 3 months of therapy and be on a stable dose for at least 4 weeks prior to baseline
8. Patients are considered to be in generally good health based upon the result of a medical history, physical examination, laboratory profile, chest X-ray and ECG

Exclusion criteria

1. Patient has previously received anti-TNF therapy or another investigational drug in the past 2 months
2. Patient has received an intra-articular injection with corticosteroids within 4 weeks prior to baseline
3. Patient has an active articular disease (other than peripheral spondyloarthritis not fulfilling the classification criteria for ankylosing spondylitis or psoriatic arthritis) that could interfere with the assessment of arthritis
4. Patient has a history of active tuberculosis. A PPD test and chest X-ray done at screening should be negative (in case of latent tuberculosis, a patient may enter the study if prophylaxis with isoniazide is begun prior to administration of adalimumab)
5. Patients has a recent history of (or persistent) infection requiring hospitalization or antibiotic treatment within 4 weeks of baseline

6. Patient has a significant history of cardiac, renal, neurological, metabolic or any other disease that may affect his/her participation in this study
7. Patient has a history of malignancy (other than basal cell carcinoma of the skin) in the past 10 years
8. If female, patient should not be pregnant or breast-feeding. A serum pregnancy-test will be performed at screening has to be negative
9. Patient is, in the opinion of the investigator, unable to comply with the requirements of the study protocol or is unsuitable for the study for any reason

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	15-11-2008
Enrollment:	40
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Humira
Generic name:	Adalimumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	21-04-2009
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	EUCTR2008-006885-27-NL
CCMO	NL25563.018.08