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Treatment intensification based on disease activity parameters or on cartilage breakdown markers in early rheumatoid arthritis

Submission date	Recruitment status	[ ] Prospectively registered
12/09/2005	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
12/09/2005	Completed	[X] Results
Last Edited	**Condition category**	[ ] Individual participant data
23/08/2011	Musculoskeletal Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
P03627; NTR80

Study information

Scientific Title

Study objectives
In early rheumatoid arthritis (RA), does treatment intensification (by conventional and biological means) aimed at keeping urine CTX-2 levels below 150 nmol/µmol creatinine lead to a lower radiological progression than treatment intensification aimed at keeping DAS28 at or below 3.2?

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Ethics Review board of the Vrije University Medical Center has approved this protocol (reference number 2003-186).

Primary study design
Interventional

Study design
Double blinded randomised controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Rheumatoid arthritis

Interventions
The study design randomises to two monitoring strategies that lead to subsequent steps in the treatment schedule: either clinical monitoring by DAS28 to achieve and keep the DAS below 2.6 (clinical remission); or: lab monitoring by CTX-2 to achieve and keep the urinary level of CTX-2 below 150 ng/µmol creatinine.

All patients will receive 'traditional' combination DMARD therapy for a minimum of 22 weeks: step 1 is evaluated at week 8, and step 2 at week 22. Patients will receive treatment intensification according to achieved levels of DAS28 (DAS group) or according to achieved levels of CTX-2 (CTX group).

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)
1. DAS28: Disease activity score calculated from swollen and tender joint counts, erythrocyte sedimentation rate (ESR), patient global assessment of disease activity (10 cm Visual Analogue Scale [VAS])
2. CTX-2: measured in spot urine (delivered 1 week before visit) together with creatinine (method Garnero, Lyon)

Key secondary outcome(s)

1. WHO/ILAR core set; DAS remission, EULAR improvement; ACR remission, ACR20,etc; EuroQoL
2. Efficacy self assessment: RADAI joint score, fatigue VAS
3. Bone Mass: DEXA lumbar spine; Right hip (neck)

Completion date
30/09/2006

Eligibility

Key inclusion criteria
Patients must have:
1. Rheumatoid arthritis (American College of Rheumatology [ACR] criteria met cumulatively)
2. Requiring treatment: 28-item Disease Activity Score (DAS28) greater than 3.2
3. Propensity for radiographic progression: urinary CTX-2 greater than 150 ng/µmol creatinine

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Unwillingness to participate in the study and comply with its procedures by signing a written informed consent

More chance of harm:
2. Contraindication to study drugs:
2.1. Previous serious adverse reaction or documented allergy to any of the trial drugs or their constituents
2.2. Previous inability to tolerate sulphasalazine (minimum 1 g/d), hydroxychloroquine (minimum 200 mg/d) methotrexate (minimum 7.5 mg/week) or oral prednisolone
3. Active infection or those at high risk of infection:
3.1. Abnormal chest X-ray or positive tuberculin test suggestive of previous TB that has not been adequately treated
3.2. Chronic leg ulcers
3.3. Septic arthritis of a native joint within the last 12 months
3.4. Previous prosthetic joint sepsis within the last 12 months, indefinitely if prosthesis remains in situ
3.5. Bronchiectasis, indwelling urinary catheter and other situation deemed high risk by treating physician
4. Malignancy, excluding basal cell carcinoma and malignancies diagnosed and treated more than 10 years previously, in whom there is a high probability of cure in the opinion of the treating physician
5. Pregnancy, planned pregnancy or lactation. Women of childbearing age (includes women who are less than 1 year postmenopausal and women who become sexually active) must be using an

acceptable method of birth control (e.g., hormonal contraceptive, medically prescribed intrauterine device [IUD], condom in combination with spermicide) or be surgically sterilised (e. g., hysterectomy or tubal ligation)
6. Current signs or symptoms of severe, progressive, or uncontrolled renal, haematological, hepatic, respiratory, gastrointestinal, endocrine, cardiac, neurological or cerebral disease. Specifically, this includes cardiac failure (New York Heart Association [NYHA] class 3 or 4)
7. Screening blood tests at baseline which show haemoglobin less than 8 g/l, total white blood cell count (WBC) less than 3.5 or neutrophils less than 1.5, platelets less than 100. Patients will also be excluded if serum alanine aminotransferase (ALT) or alkaline phosphatase are more than twice the upper limit of normal, or impaired renal function: creatinine greater than 100 mumol/L AND Cockroft creatinine clearance less than 40 ml/min
8. Subjects who have used any investigational product within 30 days prior to enrolment
9. Aged less than 18 years

Less chance of benefit:
10. Disease duration greater than 36 months (date of diagnosis by rheumatologist
11. Previous treatment of RA with more than two disease modifying anti-rheumatic drugs (DMARDs). Systemic glucocorticoids are counted as DMARDs. Treatment is defined as a cumulative period of 8 weeks or more.

Measurement difficulties:
12. Insufficient command of local language
13. Illiteracy
14. Inability to comply with the protocol (opinion of treating physician)

Date of first enrolment
01/10/2004

Date of final enrolment
30/09/2006

Locations

Countries of recruitment
Netherlands

Study participating centre
VU University Medical Center
Amsterdam
Netherlands
1007 MB

Sponsor information

Organisation
Vrije University Medical Centre (VUMC) (The Netherlands)

ROR
https://ror.org/00q6h8f30

Funder(s)

Funder type
Industry

Funder Name
Schering-Plough (The Netherlands)

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Funder Name
Vrije University Medical Centre (VUMC) (The Netherlands)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Results	01/11/2008		Yes	No