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Identification of predictive factors in synovial samples for the clinical response to tumour necrosis factor-alpha blockade in rheumatoid arthritis

Submission date
01/02/2007

Recruitment status
No longer recruiting

Registration date
01/02/2007

Overall study status
Completed

Last Edited
01/08/2011

Condition category
Musculoskeletal Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title

Study objectives
Can predictors of reponse to anti-Tumour Necrosis Factor (TNF) therapy be identified by immunohistochemical analysis of synovial tissue obtained before initiation of treatment?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval received from the Medical ethical committee of the Academic Medical Center /University of Amsterdam on the 14th February 2001 (ref: MEC 01/003).

Study design
Multicentre phase IV prospective study

Primary study design
Interventional

Secondary study design
Multi-centre

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

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

Interventions
Infliximab therapy (3 mg/kg intravenous [i.v.]) at week zero, two, six, 14 and every eight weeks.

Clinical efficacy assessments are performed at baseline and subsequently every four weeks up to week 24. Serum samples are drawn on these visits. At baseline synovial biopsies are obtained from a maximally inflamed joint.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Infliximab

Primary outcome measure
1. Primary immunohistological outcome: TNF-alpha expression in synovial tissue as shown by immunohistochemistry and quantified by digital image analysis
2. Primary clinical outcome: clinical response at week 16 assessed using the DAS 28

Secondary outcome measures
Secondary immunohistological outcome: analysis of the synovial cell infiltrate, and cytokines other than TNFalpha.

Overall study start date
01/04/2001

Completion date
01/05/2004

Eligibility

Key inclusion criteria
1. Men/women suffering from rheumatoid arthritis, based on the American Rheumatism Association (ARA) 1987 criteria, who failed at least one Disease Modifying Anti-Rheumatic Drug (DMARD) including methotrexate, will be included in the study
2. Patients in ARA functional classes I, II, and III may be included
3. In addition the patients must fulfill the following criteria at baseline:
a. Disease Activity Score (DAS 28) more than 3.2
b. patients global evaluation of his/her rheumatoid condition assessed as fair, poor or very poor and
investigators global evaluation of patients rheumatoid condition assessed as fair, poor or very poor
c. more than 18 years of age and less than or equal to 85 years
d. 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 of less than or equal to 10 mg/day provided that the dosage has been stable for at least two months prior to entry

Participant type(s)
Patient

Age group
Not Specified

Sex
Both

Target number of participants
143

Key exclusion criteria
1. Pregnancy
2. Breastfeeding
3. A history of or 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. Previous therapy at any time with: TNF-alpha directed monoclonal antibodies or p75 TNF receptor fusion protein
6. Therapy within the previous 60 days with:
a. any experimental drug
b. alkylating agents, e.g. cyclophosphamide, chlorambucil
c. antimetabolites
d. monoclonal antibodies
e. growth factors
f. other cytokines
7. Therapy within the previous 28 days with:
a. parenteral or intra-articular corticoid injections
b. oral corticosteroid therapy exceeding a prednisone equivalent of 10 mg daily
c. present use of DMARDs other than methotrexate
8. A history of hypersensitivity to the study medication or to drugs with similar chemical structure
9. Fever (orally measured as more than 38°C), chronic infections or infections requiring anti-microbial therapy
10. Known positive reaction to hepatitis B surface antigen
11. Other active medical conditions such as inflammatory bowel disease, bleeding diathesis, or severe unstable diabetes mellitus
12. Manifest cardiac failure (stage III or IV according to New York Heart Association [NYHA] classification)
13. Progressive fatal disease/terminal illness
14. Impaired coagulation
15. A congenital or acquired (known Human Immunodeficiency Virus [HIV]-positive status) immunodeficiency, a history of cancer or lymphoproliferative disease or treatment with total lymphoid irradiation (the known HIV-positive status may be defined either by a positive blood test or clinical diagnosis), or a haematopoietic disease
16. A white cell count less than 3.5 x 10^9/l
17. Platelet count less than 100 x 10^9/l
18. Haemoglobin of less than 5.3 mmol/l
19. Body weight of less than 45 kg
20. History of drug or alcohol abuse
21. Any concomitant medical condition which would, in the investigators opinion, compromise the patients ability to tolerate, absorb, metabolise or excrete the study medication
22. Inability to give informed consent
23. Mental condition rendering the patient unable to understand the nature, scope and possible consequences of the study and/or evidence of an uncooperative attitude

Date of first enrolment
01/04/2001

Date of final enrolment
01/05/2004

Locations

Countries of recruitment
Netherlands

Study participating centre
Academic Medical Center (AMC)
Amsterdam
Netherlands
1100 DD

Sponsor information

Organisation
Academic Medical Centre (AMC) (The Netherlands)

Sponsor details
Division of Clinical Immunology and Rheumatology
P.O. Box 22660
Amsterdam
Netherlands
1100 DD

Sponsor type
Hospital/treatment centre

Website
http://www.amc.uva.nl/

ROR
https://ror.org/03t4gr691

Funder(s)

Funder type
Research organisation

Funder Name
Dutch Arthritis Association (Reumafonds) (The Netherlands)

Funder Name
The Netherlands Organisation for Health Research and Development (ZonMw) (The Netherlands)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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	01/02/2011		Yes	No
Results article	exploratory study results	01/08/2011		Yes	No