

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

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<b>Registration date</b> 01/02/2007	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 01/08/2011	<b>Condition category</b> Musculoskeletal Diseases	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

Not provided at time of registration

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

### Protocol serial number

N/A

# Study information

## Scientific Title

## Study objectives

Can predictors of response 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

## Study type(s)

Treatment

## 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(s)

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

## Key secondary outcome(s)

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

**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

**Healthy volunteers allowed**

No

**Age group**

Not Specified

**Sex**

All

**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  $3.5 \times 10^9/l$
- 17. Platelet count less than  $100 \times 10^9/l$
- 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)

## 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

## 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?
<a href="#">Results article</a>	results	01/02/2011		Yes	No
<a href="#">Results article</a>	exploratory study results	01/08/2011		Yes	No