Hypothesis generating study to identify the changes in synovial tissue early after initiation of infliximab therapy

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20080

Source
NTR

Brief title
N/A

Health condition

Rheumatoid arthritis

Sponsors and support

Primary sponsor: Principal investigator: Prof. Dr. P.P. Tak
Academic Medical Center (AMC), Division of Clinical Immunology and Rheumatology
Source(s) of monetary or material Support: Supported by Centocor

Intervention

Outcome measures

Primary outcome

1. Primary immunohistologic outcome: detection of apoptosis in synovial tissue within 1 or 24 hours after initiation of treatment. Analysis by immunohistochemical staining and

electronmicroscopy.

2. Primairy serological outcome: To determine whether TNF targeted therapy with infliximab results in apoptosis of peripheral blood mononuclear cells within 1 or 24 hours after initiation of treatment.

Secondary outcome

To determine whether TNF targeted therapy with infliximab results in decreased synovial cellularity.

Study description

Background summary

To provide more insight into the mechanism of action of anti-TNF therapy in RA, we investigated whether early apoptosis induction is an important mechanism of action of infliximab therapy. This was studied in both peripheral blood and the inflamed knee joint before 1 or 24 hours after infusion in patients with active RA.

Study objective

Exploratory study to investigate the effects of TNF targeted therapy with infliximab on the synovial cell infiltrate, and the induction of apoptosis.

Study design

N/A

Intervention

Infliximab therapy (3mg/kg i.v.) according to the normal regimen. At baseline and 1 (n=5) hour or 24 hours (n=5) after the first infliximab infusion synovial biopsies were obtained from an inflamed knee joint. Peripheral blood mononuclear cells were obtained before and 1 and 24 hours after infliximab infusion in 20 patients (10 only blood, 10 with paired synovial biopsies). Serum was drawn at similar timepoints.

Contacts

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Eligibility criteria

Inclusion criteria

1. RA patients with active disease at baseline assessed by the DAS28;

2. Be =>18 years of age;

3. Use concurrent methotrexate treatment (7.5-30 mg/week; stable since =>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 <=10 mg/day provided that the dosage has been stable for at least a months prior to entry.

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 spondyloarthropathy, 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:

a. TNF-directed monoclonal antibodies
p75 TNF receptor fusion protein;

6. Therapy within the previous 45 days with:

a. any experimental drug;

b. alkylating agents, e.g. cyclophosphamide, chlorambucil;

c. anti metabolites;

d. monoclonal antibodies;

e. growth factors;

f. other cytokines;

7. Therapy within the previous 28 days with:

a. parenteral or intraarticular corticoid injections;

b. oral corticosteroid therapy exceeding a prednisone equivalent of 10 mg daily;

c. present use of DMARDs other than methotrexate;

8. Fever (orally measured > 38 ¡ãC), chronic infections or infections requiring anti-microbial therapy;

9. Manifest cardiac failure (stage III or IV according to NYHA classification);

10. Progressive fatal disease/terminal illness;

11. A hematopoietic disease;

12. Body weight of less than 45 kg.

Study design

Design

Study type: Interventional

Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-10-2003
Enrollment:	20
Type:	Actual

Ethics review

Positive opinion

Date:	02-07-2007
Application type:	First submission

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
NTR-new	NL983
NTR-old	NTR1011
Other	:
ISRCTN	ISRCTN20710193

Study results

Summary results
Manuscripts in progress.

