Trial of anti IgE in RA.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28491

Source
Nationaal Trial Register

Brief title
TIGER

Health condition

Rheumatoid arthritis

Sponsors and support

Primary sponsor: Leiden University Medical Center
Source(s) of monetary or material Support: university funds

Intervention

Outcome measures

Primary outcome

1. Clinical parameters for disease activity are measured by the DAS44 (Disease Activity Score on 44 joints) assessment. Responses are classified as follows:

A. Complete response is defined as a DAS44 improvement of > 1.2 and DAS<2.4;

B. Moderate response is defined as DAS44 improvement of 1.2 and DAS >2.4 or DAS 44 improvement of >0.6 en <=1.2 and DAS <=3.7;

C. Non-response is defined as DAS44 improvement of >0.6 en <=1.2 improvement and DAS >3.7 or improvement of <=0.6.

2. Immunological parameters in peripheral blood and synovium after treatment with anti-IgE antibodies (omalizumab) are:

A. Proportion of peripheral blood basophils, mast cells in synovium;

B. Functional presence of IgE-ACPA;

C. IgE , FcERI expression on basophils, mast cells, B cells and DC;

D. Synovial infiltration of B cells, plasmacells, mast cells and (IgE-)ACPA presence in synovial fluid.

3. Safety and toxicity parameters are evaluated according to WHO Common Toxicity Criteria.

Secondary outcome

N/A

Study description

Background summary

This investigation is a double blinded single-center placebo controlled randomized phase IIa study, administering subcutaneously monoclonal anti-IgE antibody (300mg/month) or placebo in IgE-ACPA positive RA patients, refractory to methotrexate. This study evaluates the safety and efficacy of anti-IgE therapy with respect to: Clinical (DAS), laboratory parameters and adverse events. In addition, this study investigates whether disease activity correlates with immunological parameters, including immunopathology and IgE-ACPA-autoantibodies.

Study objective

Recent data showed for the first time that IgE-ACPA antibodies have a direct biological immune response in mast cells of IgE-ACPA+ RA patients. Subsequently, mast cell targeting agents, such as anti-IgE therapy have rationale for application in RA patients.

Study design

Visits:

1. Day 0 = M0 baseline-visit 1;

2. Day 28 = M1 visit 2;

3. Day 56 = M2 visit 3;

4. Day 84 = M3 visit 4;

5. Day 112 = M4 visit 5;

6. day 140 = M5 visit 6;

7. Day 168 = M6 visit 7.

Intervention

This investigation is a placebo-controlled randomized double blinded single-center phase IIa study, administering subcutaneously every four weeks 300 mg of monoclonal anti-IgE antibody or placebo in patients with IgE-ACPA positive RA during 6 months.

Contacts

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Eligibility criteria

Inclusion criteria

1. Patients with refractory active rheumatoid arthritis (RA). Refractory disease is defined as persistent or relapsed disease activity despite conventional treatment, i.e. combination of disease modifying antirheumatic drugs including maximal tolerable doses of methotrexate. Active disease is defined as a DAS44 (Disease Activity Score of 44 joints) score of more than 3.6;

2. Presence of IgE-ACPA;

3. Age above 18 years;

4. WHO performance status 0, 1 or 2;

5. Informed consent according to rules and regulations of Leiden University Medical Center.

Exclusion criteria

1. History of allergic or anaphylactic reaction to any therapeutic agent or known hypersensitivity to any component of anti-IgE monoclonal antibodies or to murine proteins;

2. No previous therapy with corticosteroids or a biological agent during the last 3 months;

3. No previous therapy with rituximab, leflunomide;

4. Life expectation of less than 6 months;

5. History of severe CNS disturbances and psychiatric problems;

6. Severe uncontrolled infections including parasitosis;

7. Irreversible major organ dysfunction, defined by any of the following criteria:

A. Creatinine clearance < 40 ml/min;

B. Left ventricular ejection fraction < 40%;

C. Pericardial effusion with haemodynamic consequences;

D. Resting arterial oxygen tension (PaO2) < 8 kPa (<60 mmHg) and / or resting arterial carbon dioxide tension (PaCO2) > 6.7 kPa (>50 mmHg);

E. Sustained 3-fold increase in serum transaminase or bilirubin.

8. HIV positivity;

9. Positive pregnancy test or unwillingness to use adequate contraception for the duration of

the study;

10. History of cancer, including solid tumors, hematological malignancies and carcinoma in situ (except for basal cell and squamous cell carcinoma of the skin that have been treated and cured).

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2011
Enrollment:	80
Type:	Anticipated

Ethics review

Positive opinion

Date:	28-07-2010
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	NL2328
NTR-old	NTR2434
Other	EudraCT number : 2009-017306-36
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results

Schuerwegh AJM, Ioan A, Dorjée AL, Roos J, Bajema IM, van de Voort EIH, Huizinga TWJ, Toes REM. Evidence for a functional role of IgE anticitrullinated protein antibodies in rheumatoid arthritis. Proc Natl Acad Sci U S A. 2010 Feb 9;107(6):2586-91.

Schuerwegh AJM, Ioan A, Dorjée AL, van de Voort EIH, Huizinga TWJ, Toes REM. The Functional Role of IgE-Anti Citrullinated Peptide/Protein Antibodies in Rheumatoid Arthritis. Ann Rheum Dis 2009;68(suppl I):A18-A19. Oral presentation on European Workshop of Rheumatology Research (EWRR) February 26-28th, 2009, Warsaw, Poland.

Direct activation of IgE-ACPA positive cells in rheumatoid arthritis. Schuerwegh AJM, Ioan A, Dorjée AL, van de Voort EIH, Huizinga TWJ, Toes REM. Ann Rheum Dis 2009;68(supplIII):150. Oral presentation on European League of Arthritis and Rheumatism (EULAR) June 10t -13th, 2009, Copenhagen, Danmark.

Citrullinated Proteins Activate IgE-ACPA+ Cells in Rheumatoid Arthritis. Annemie JM Schuerwegh, Andreea Ioan-Facsinay, Annemarie L. Dorjée, Ellen IH van der Voort, Tom WJ Huizinga and René EM Toes. Annual Congres on Rheumatology ACR/AHRP Scientific Meeting October 2009, Philadelphia, USA.