A Double Blind, Randomized, Placebo Controlled, Multi-Center Trial of Anti-TNF alfa Chimeric Monoclonal Antibody (Infliximab, Remicade) and Azathioprine in Patients Suffering from Systemic Lupus Erythematosus (SLE) with WHO Class V Glomerulonephritis.

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Primary: To prove that infliximab in combination with azathioprine is superior to azathioprine alone in rapidly inducing a meaningful renal improvement, defined as a reduction in preoteinuria of at least 50%, in patients with membranous SLE...

Ethical review	Approved WMO
Status	Pending
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON30091

Source
ToetsingOnline

Brief title
Trial V

Condition

- Autoimmune disorders
- Nephropathies

Synonym

Lupus

Research involving
Human

Sponsors and support

Primary sponsor: Medical University of Vienna AKH, Department of Rheumatology, Internal Medicine III, Josef Smolen, MD
Source(s) of monetary or material Support: Centocor,Centocor B.V. Einsteinweg 101, 2333 CB Leiden

Intervention

Keyword: Azathioprine, Glomerulonephritis, Infliximab, SLE

Outcome measures

Primary outcome

Comparison of time needed to reduce proteinuria 1.5 g/day or less between the

infliximab plus azathioprine and the azathioprine only group.

Secondary outcome

-Percentage of patients reaching reduction in proteinuria to <= 1.5 g/day, at

week 12 and week 52.

-Percent reduction in proteinuria at 6 weeks, 12 weeks, 20 weeks, 36 weeks, and

52 weeks after the first infusion.

-Absolute reduction in proteinuria at 6 weeks, 12 weeks, 20 weeks, 36 weeks,

and 52 weeks after the first infusion.

-Percent reduction in SLE disease activity

-Absolute reduction in SLE disease activity

-Changes in Quality of life

-Changes in Fatigue

Study description

Background summary

Systemic Lupus Erythematosus (SLE) is a prototypical autoimmune disease in which a variety of autoantibodies, and the consecutive formation of immune complexes ultimately inflict injury on a variety of organ systems. The classical severe lupus organ manifestation is immune-complex glomerulonephritis. Standard treatment for WHO class V glomerulonephritis has yet to be defined. Some patients respond favourably to ACE inhibitors with or without glucocorticoids, but for those not responding sufficiently, the overall risk of renal failure, cardiovascular complications and death is considerable. In the limited experience with infliximab therapy in SLE patients, infliximab in combination with azathioprine was safe and led to rapid improvement in proteinuria in all patients treated so far, including patients with class V glomerulonephritis.

Study objective

Primary: To prove that infliximab in combination with azathioprine is superior to azathioprine alone in rapidly inducing a meaningful renal improvement, defined as a reduction in preoteinuria of at least 50%, in patients with membranous SLE glomerulonephritis not adequately responding to ACE inhibitors and glucocorticoids.

Secundary: Lab studies on renal markers, disease activity measurements, safety evalutation of infliximab for this population, general quality of life and fatigue.

Study design

This is a double-blind, randomized, placebo-controlled trial in which treatment of the combination of infliximab and azathioprine will eb compared to azathioprine alone in patients with SLE and WHO class V glomerulonephritis.

Intervention

Subjects will be randomly assigned to one of the 2 groups. Subjects in both groups will receive azathioprine on a daily basis, administered orally. The dose build up should be done in 50 mg steps every two weeks, up to a total daily dose of 2 mg/kg. Subjects in the experimental group will receive , next to azathioprine, Infliximab infusions at weeks 0, 2, 6 and 10. The total dose (5 mg/kg) will be administered over a period of 2 hours. Subjects in the control group will receive a placebo-infusion (saline solution 0.9%) at these

times.

Study burden and risks

After informed consent has been obtained, subjects that meet all eligibility criteria will be screened and randomized. 3 Days prior to the first infusion of the blinded infliximab/placebo infusion, treatment with azathioprine will be started.
There will be 12 visits to the site in total en the following procedures will be peformed at various visits throughout the study: Medical and medication history, physical exam, vital signs, blood pressure, heart rate, ECG, TBC skin test, chest x-ray, pregnancy test, Hepatitis B and C tests, ESR, haematology and serum chemistry, serum samples, urine analysis, recording concomitant medication, receive study medication. Adverse events will be recorded throughout the study.
The most frequently reported adverse events are infections and infusion reactions and these are the most important reason for discontinuing of the treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-SLE with biopsy-proven membranous glomerulonephritis (WHO class V)
-Proteinuria >3g/day despite adequate therapy with ACE inhibitors
-Individuals (>18 years) who have the capacity to understand and sign an informed consent
-No evidence of current active TB or old inactive TB

Exclusion criteria

-Active WHO class IV SLE nephritis
-Treatment with azathioprine / cyclophosphamide within the previous 12 months, or with cyclosporine within the previous 6 weeks
-Active cerebral SLE
-Active infection, malignancy

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Pending

Start date (anticipated):	01-05-2006
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Azathioprine
Generic name:	Imuran
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Remicade
Generic name:	Infliximab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	11-05-2006
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-08-2006
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2005-004067-30-NL
CCMO	NL11519.042.06