INFLUENCE OF B CELL DEPLETION BY MONOCLONAL ANTI-CD20 ANTIBODIES IN SYSTEMIC SCLERODERMA

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24091

Source
NTR

Brief title
RITIS

Health condition

To evaluate the safety and efficacy of anti-CD20 therapy with respect to:
- Clinical and laboratory adverse events, as measured every three months.
- Survival and prevention of major organ failure (referred to as ¡¥event-free survival¡¦ which is considered the primary endpoint).
- Impact on skin thickening, visceral involvement, functional status, and quality of life

Sponsors and support

Primary sponsor: ROCHE
Source(s) of monetary or material Support: ROCHE
Universitiy funds

Intervention

Outcome measures

Primary outcome

1. Treatment related mortality is defined as any death during the study period that cannot be attributed to progression of the disease according to the consensus opinion.

2. Treatment toxicity will be assessed using WHO toxicity parameters (expressed as maximum grade toxicity per organ system) (Appendix) in consecutive 3-month periods following randomization.

3. Efficacy will be assessed as progression-free survival, defined as the time in days since the day of randomization until any of the following changes from baseline has been documented at two consecutive 3-month evaluations:

- death

- „d 10% drop in (F)VC and/or „d 15% drop in DLCO (of predicted values)

- „d 15% drop in LVEF by MUGA

- „d 15% drop in body weight

- „d 30% drop in creatinine clearance

- „d 30% increase in Modified Rodnan skin score

- „d 0.5 increase in SHAQ

Changes during the study period (from baseline until completion of 2 years follow-up) in the following parameters :

- Modified Rodnan Skin score

- (F)VC and DLCO

- LVEF

- Weight (Kg)

- SF-36

- EuroQol (EQ-5D)

- gas (pO2, pCO2, p(A-a)O2) at room air

Secondary outcome

- To evaluate whether disease activity correlates with immunological parameters, including immunopathology of skin, immune reconstitution, and autoantibodies.

- To search for predictive factors (clinical and immunological) of response.

Study description

Study objective

In view of the poor prognosis of SSc, the presumed autoimmune origin, and the lack of available therapies, this disease is considered suitable for initial investigation of the tolerability and efficacy of anti B-cell therapy. In literature, there is evidence for a role for B cells in the pathogenesis of scleroderma.

The need remains for other safe alternative treatment strategies in systemic scleroderma and the need for information to test whether a novel approach (B cell depletion) is suitable for treatment.

Study design

Protocol august 2008

MEC submission 11/2009

Anticipated start recruitement 01/2009

Anticipated end enrolment 01/2011

Anticipated analysis primary endpoint 01/2013

Anticipated analysis longterm follow-up 5 years 01/2016

Intervention

This investigation is a placebo-controlled randomized double blinded single-center phase II study, administering intravaneously monoclonal anti-CD20 antibody or placebo together with a corticosteroid regimen consisting of methylprednisolone 100 mg IV 30 minutes prior to study drug infusion in patients with systemic sclerosis.

Contacts

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Eligibility criteria

Inclusion criteria

1. Age between 18 and 70 years.

2. Established diagnosis of systemic sclerosis according to ARA-criteria (appendix).

3. Informed consent.

Exclusion criteria

1. Pregnancy or unwillingness to use adequate contraception during study.

2. Previous treatments with biological agents, cell depleting therapies including investigational
agents.

3. Significant exposure to bleomycin, tainted rapeseed oil, vinyl chloride, trichlorethylene or silica; eosinophilic myalgia syndrome; eosinophilic fasciitis.

4. History of allergic or anaphylactic reaction to a biological agent or known hypersensitivity to any component of anti-CD20 monoclonal antibodies or to murine proteins.

5. History of deep tissue infection (e.g. Fasciitis, abscess, osteomyelitis) within 1 year prior to baseline.

6. History of serious chronic or recurrent infection within 12 weeks prior to baseline, including HIV, HTLV-1,2 positivity.

7. 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).

8. Concurrent liver failure as defined by a sustained 3-fold increase in serum transaminase or bilirubin.

9. Active drug or alcohol abuse or persistent psychiatric disorders that prevent inclusion.

10. Uncontrolled hypertension.

11. Poor compliance of the patient as assessed by the referring physicians.

12. Receipt of any vaccine 28 days prior to baseline.

13. Intolerance or contraindications to IV glucocorticoids.

14. Positive tests for HbsAg, Hepatitis core antibody or hepatitis C serology.

15. Concentrations of serum IgG and /or IgM below 5.0 and 0.40 mg/ mL.

16. Absolute neutrophil count of less than 1.0x 109/L.

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):	01-01-2009
Enrollment:	20
Type:	Anticipated

Ethics review

Not applicable
Application type: Not applicable

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	NL676
NTR-old	NTR1521
Other	:
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results
N/A