A new dosing strategy of infliximab versus standard dosing in patients with severe sarcoidosis: optimization of treatment

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Objective: To determine whether serum concentration guided dosing of infliximab is not inferior to standard dosing based on bodyweight in patients with severe sarcoidosis in terms of FVC change at 26 weeks.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Immune disorders NEC
Study type	Interventional

Summary

ID

NL-OMON42033

Source
ToetsingOnline

Brief title
Concentration guided dosing of infliximab in sarcoidosis

Condition

- Immune disorders NEC
- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
Sarcoidosis

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Infliximab, Pharmacokinetics, Sarcoidosis

Outcome measures

Primary outcome

Lung function i.e. FVC at 26 weeks.

Secondary outcome

Symptoms, CRP-, ACE-, sIL2R-concentrations at week 0, 14, 26 and 50.

Lung function i.e. FVC and DLCO at week 0, 26 and 50.

Imaging: X-Thorax, HRCT and PET scanning at week 0, 26 and 50.

Endpoints in terms of Quality of Life are measurements obtained with EuroQol 5D

and SF36 questionnaires at week 0, 14, 26 and 50.

Endpoints in terms of fatigue are measurements obtained with Checklist

Individual Strength (CIS) at week 0, 14, 26 and 50.

Safety endpoints such as infusion reactions, infections.

Study description

Background summary

Rationale: Sarcoidosis is a granulomatous disease that primarily affects the lung. Severe cases are treated with infliximab. Problems met in daily clinical practice are that the optimal infliximab dose in sarcoidosis is not known and the very high drug cost. This study aims to improve cost effectiveness and safety.

Study objective

Objective: To determine whether serum concentration guided dosing of infliximab is not inferior to standard dosing based on bodyweight in patients with severe sarcoidosis in terms of FVC change at 26 weeks.

Study design

Study design: Randomized, controlled, double blind study with a follow up of one year.

Intervention

Intervention: The intervention group will receive infliximab 3 mg/kg, week 0 and 2. Based on measured serum concentrations, for every patient a dose, to be given at week 6, resulting in a concentration within the target window, will be calculated. Thereafter, patients will receive infliximab every 4 weeks. Additional dose adjustments will be made based on infliximab serum concentrations. The control group will receive infliximab at the standard dose of 5 mg/kg at week 0, 2, 6 and thereafter every 4 weeks.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The burden and risks are minimal and consists of several venipunctures, patients have to fill out questionnaires at 4 timepoints. Patients in the intervention arm will receive lower infliximab dosages. However, at any time during the study the treating pulmonologist can indicate that an individual patient must receive the maximal dose of 5 mg/kg e.g. in case of rapid progression of the disease.
Revenues: It is expected that drug cost will decrease by approximately 2 million Euro*s per year in The Netherlands and drug safety might improve.

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

patients diagnosed with sarcoidosis being treated with infliximab or with an indication for infliximab;capability of giving informed consent

Exclusion criteria

vaccination with live viral or bacterial vaccines within the previous 3 months, or with the last dose within the previous 3 months;active or untreated latent tuberculosis (by mantoux-Elispot/TBC-IGRA);serious infections within the last 2 months;serious right ventricular heart failure or cor polmunale;Active hepatitis B;history of allergic reactions to monocolonal antibodies or their fragments;oppotunistic infections with the last 6 months;HIV;transplantation;known malignancy;pregnancy or breastfeeding

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	70
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO Date:	20-01-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-05-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
Other	9999
EudraCT	EUCTR2014-002224-26-NL
CCMO	NL49562.100.14