Towards personalized dosing of natalizumab in multiple sclerosis

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Our main objective is to prove that extending dose intervals guided by serum concentrations of natalizumab, will not result in radiological or clinical disease activity.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Demyelinating disorders
Study type	Interventional

Summary

ID

NL-OMON43550

Source
ToetsingOnline

Brief title
Personalised Dosing of Natalizumab in Multiple Sclerosis (The PDNMS trial)

Condition

- Demyelinating disorders

Synonym
MS, multiple sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: De Hersenstichting

Intervention

Keyword: dose, extending, MS, natalizumab

Outcome measures

Primary outcome

The primary endpoint is the number of patients developing gadolinium (Gd+)

enhancing lesions on brain MRI.

Secondary outcome

The secondary endpoints are new or enlarging T2 lesions on brain MRI,

progression on the expanded disability status scale (EDSS) and clinical

relapses and measurements of the quality of life by the SF-36.

Study description

Background summary

Natalizumab is an efficacious second line treatment for relapsing remitting multiple sclerosis (RRMS). Despite the knowledge of a large variation in pharmacokinetics
and patient characteristics, treatment with natalizumab in MS is the same for every patient with a 300mg infusion every four weeks. We believe that most patients have natalizumab concentrations largely exceeding the threshold of optimal efficacy just before a new infusion of natalizumab.

Study objective

Our main objective is to prove that extending dose intervals guided by serum concentrations of natalizumab, will not result in radiological or clinical disease activity.

Study design

A prospective multi-center, single arm trial.

Intervention

Before subsequent natalizumab infusions, serum concentrations will be evaluated. If the concentration exceeds 15µg/ml the dose interval will be extended with a week to a maximum of eight weeks. If serum concentration is

between 10-15µg/ml patients will remain on their current schedule. If serum concentration drops below 10µg/ml the infusion schedule will be put back with one week with a minimum of a four week interval between infusions.

Study burden and risks

Patients will be exposed to 3-monthly hospital visits for clinical follow-up brain MRI scans. Patients will receive two additional MRI-scans (the normal frequency of brain MRI is one yearly) during the study period. JC-virus positive patients (who have chance of developing progressive mulifocal leukoencephalopathy) are already used to this frequency of MRI-scans.
We expect that patients will receive less natalizumab infusions based on serum concentrations. The risk of extending intervals between natalizumab infusion is disease activity, clinically or radiologically. The risks of disease activity is minimized by the frequent measurements of the concentration of natalizumab. Patients will be monitored thoroughly. In case of any sign of disease activity the dose interval will be reset to 4 weeks for the remaining study period

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

- 18 years or older.
- Relapsing-remitting multiple sclerosis (RRMS) according to the McDonald criteria, revised by Polman 2010.
- Natalizumab treatment for 12 months or longer at inclusion.
- An expanded disability status scale (EDSS) score of 0.0-6.0 at baseline.
- Natalizumab level more than 15 µg/ml just prior natalizumab infusions for 2 consecutive months.
- Written informed consent.

Exclusion criteria

- Any MS disease activity (radiologically or clinically) during natalizumab treatment, with exclusion of the first three months of treatment.
- Unable to undergo frequent MRI.
- The use of other immunomodulatory medication other than natalizumab.

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	03-11-2016
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tysabri
Generic name:	Natalizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	11-04-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-09-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	EUCTR2016-000345-31-NL
CCMO	NL56584.029.16