

Intravenous treatment with Mitoxantrone in active secondary progressive multiple sclerosis: effects on adaptive immune system.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON26011

Source

NTR

Brief title

MITOMS

Health condition

Secondary progressive multiple sclerosis

Sponsors and support

Primary sponsor: R. Hupperts

Orbis Medical Center

Department of Neurology

Postbus 5500

6130 MB Sittard-Geleen

Source(s) of monetary or material Support: R. Hupperts

Orbis Medical Center

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Intervention

Outcome measures

Primary outcome

1. T cell compartment;
2. B-cell compartment;
3. Vitamin D.

Secondary outcome

Expanded disability status scale score.

Study description

Background summary

Multiple sclerosis (MS) is an inflammatory disease of the central nervous system causing severe inflammation in the central nervous system (CNS). This inflammation and scar formation, probably due to autoimmunity, is thought to damage both oligodendrocytes and axons resulting in demyelination and neuronal dysfunction, even in a early stage of the disease. Clinically, this damage causes a large variety of neurological symptoms including problems with muscle weakness, muscle paralysis, vision problems and even cognitive impairment. The majority of patients start with a relapsing remitting form of the disease that in general becomes progressive overtime with patients becoming more severe disabled in time. Given the complex pathogenesis, MS is hard to treat. The consensus is that MS is mainly a T-cell mediated disease. T-cells follows different steps in MS, which can be used as targets in the treatment of MS. These steps involve peripheral T-cell activation, migration into the CNS, reactivation of macrophages and B-cells in CNS and demyelination, axonal damage and remyelination. Current treatment of MS comprises acute treatment of relapses with intravenous corticosteroids and maintenance therapy with first line immunomodulatory drugs as Interferon W (IFN-W) and Glatiramer Acetate (GA). Non-responders to these drugs need a more aggressive therapy in order to prevent increasing disability. Treatment options for nonresponders are second-line therapies as Mitoxantrone and Natalizumab. Mitoxantrone is a good treatment option, however, due to its cardiotoxicity and small risk of secondary acute myelogenous leukemia (AML), it's often not first choice of the physician. The risk of AML has been calculated on 0.25% and is not correlated with dosage, cumulative dosage and time onset after Mitoxantrone administration. Adverse effects can be limited if Mitoxantrone is restricted to patients who will have a good clinical response to it. Therefore a good understanding of its mechanism of action in MS is necessary.

To determine the immunological reaction of SPMS patients treated with Mitoxantrone. T-cell and B-cell compartment will be taken into account, B-cell stimulating factor BAFF and a proliferation inducing ligand (APRIL) serum levels and cytokine profile IL-10, TGF- β , IFN- γ , IL-4, IL-17 will be measured.

A cross sectional study to explore the immunological response of intravenous mitoxantrone treatment in 10 SPMS patients.

A total of 10 subjects will be included in this study. Dropouts will not be replaced. Ten SPMS patients will be included, which will be treated with Mitoxantrone according to normal neurological practice. Subjects must meet all inclusion criteria in order to be eligible for the study:

1. Age between 18 years and 65 years;
2. MS clinically determined by the McDonald criteria;
3. Subtypes: SPMS;
4. Subjects must be relapse free and in a stable neurological condition at least 30 days prior to start of the therapy;
5. Patients with a deterioration of 1 point of the expanded disability status scale (EDSS) score who will receive mitoxantrone according to normal practical care;
6. Subjects must be willing to give a written informed consent prior to the study.

T-cell compartment, B-cell compartment, Cytokine profile produced by B-cells and T-cells, IgG and IgM antibodies, BAFF and APRIL (stimulating factors for B-cells) will be measured.

Neurological clinical outcomes as EDSS and relapses will be recorded in patients' record.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

Participating patients will have to donate blood 4 times. This is as less often as possible; the venapunctures will be combined with the regular blood controls. The risks of a blood donation are a temporary vasovagal reaction or a local haematoma at the puncture spot. At long-term this could be of advantage for all MS patients, since MS is a chronic disorder, all patients will need adequate therapy to prevent disability. This helps us to better understand the

immunology in MS and one of the treatments used in MS.

Study objective

Mitoxantrone depletes mainly pro-inflammatory T- and B- cells. Anti-inflammatory cells are spared.

Study design

0, 4 20 and 54 weeks after starting Mitoxantrone treatment.

Intervention

Patients are treated according to normal neurological practice with mitoxantrone. During the planned blood controls 2 extra tubes will be taken.

Contacts

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Eligibility criteria

Inclusion criteria

1. Secondary progressive MS patients who are treated with mitoxantrone according to normal neurological practice;
2. Age 18-65;
3. Relapse free for 30 days;

4. Willing to give informed consent.

Exclusion criteria

1. Relapsing remitting multiple sclerosis;
2. Treatment with intravenous corticosteroids in the last 30 days;
3. Any prior use of cyclophosphamide, cladribine, anthracyclines or received a total lymphoid irradiation or mediastinal radiotherapy;
4. Use of experimental drugs 1 year prior to screening.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL	
Recruitment status:	Pending
Start date (anticipated):	22-03-2010
Enrollment:	10
Type:	Anticipated

Ethics review

Positive opinion	
Date:	19-03-2010
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	NL2124
NTR-old	NTR2248
Other	METC : 10-N-13
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results

N/A