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

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

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON26011

Bron
NTR

Verkorte titel
MITOMS

Aandoening

Secondary progressive multiple sclerosis

Ondersteuning

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Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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 cardiotoxity 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-â, IFN-ã, IL-4, IL-17 will be measured.

A cross sectional study to explore the immunological respons 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 en 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 venapunctions 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.

Doel van het onderzoek

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

Onderzoeksopzet

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

Onderzoeksproduct en/of interventie

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

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Relapsing remitting multiple sclerosis;

2. Treatment with intravenous corticosteroids in the last 30 days;

3. Any prior use of cyclophophamide, cladribine, anthracenediones or recieved a total lymphoid irradiation or mediastinal radiotherpay;

4. Use of experimental drugs 1 year prior to screening.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	22-03-2010
Aantal proefpersonen:	10
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	19-03-2010
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2124
NTR-old	NTR2248
Ander register	METC : 10-N-13
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A