Dose response trial of IV immunoglobulin in chronic inflammatory demyelinating polyradiculoneuropathy

Published: 23-07-2014
Last updated: 20-04-2024

The primary objective is:1. To investigate whether high frequency low dosage IVIg treatment is more effective than low frequency high dosage as maintenance treatment for CIDP. Secondary objectives are:2. To investigate whether high frequency low…

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

Summary

ID

NL-OMON41611

Source
ToetsingOnline

Brief title
Dose Response of IVIg in CIDP (DRIP-study)

Condition

- Autoimmune disorders
- Peripheral neuropathies

Synonym
peripheral nerve disorder, polyneuropathy

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Baxter

Intervention

Keyword: Chronic Inflammatory Demyelinating [MeSH], Immunoglobulins, Intravenous [MeSH], Polyradiculoneuropathy

Outcome measures

Primary outcome

Hand grip strength (Vigorimeter) will be used as the primary outcome measure. A difference in the (mean of the 4) Vigorimeter changes from baseline between the two groups of > 8 kPa (mean of both hands) is considered clinically relevant. A difference of > 8 kPa in Vigorimeter change from baseline in favour of the group treated with half the dosage and interval as compared with the other treatment group will be considered a clinical relevant improvement.

Secondary outcome

Changes in the R-ODSS, R-FSS, and SF-36 will be used as secondary outcome measures. The secondary objective will be to record the occurrence of side-effects.

Study description

Background summary

In clinical practice CIDP patients are being treated with different dosages and different infusion intervals of IVIg. The optimum dosage and intreval has not been investigated IgG is the major component of IVIg and is probably responsible for most of the immune-modulating effects.
It is unknown how IVIg should be administered for optimal immunomodulation; whether keeping the plasma level of IgG high for prolonged periods is better than spiking the immune system intermittently with high doses of IVIg. The purpose of maintenance IVIg treatment in CIDP is to maintain a constant serum IgG level. A high peak dose may result in greater catabolism of IgG which might

be avoided by giving smaller doses more often. Shortening the interval between IVIg infusions results in a higher IgG trough level which appears to correspond to clinical efficacy. The pharmacokinetics of IgG differ when lower dosages are given more frequently resulting in lower peaks and higher troughs which may be preferable to a lower frequency high dosage regimen. It is known that the treatment frequency cannot be lowered in CIDP patients. More frequent dosing leads to more stable IgG levels without high peak levels which have been held responsible for the systemic side effects.

Study objective

The primary objective is:
1. To investigate whether high frequency low dosage IVIg treatment is more effective than low frequency high dosage as maintenance treatment for CIDP.
Secondary objectives are:
2. To investigate whether high frequency low dosage of IVIg results in less adverse events compared to low frequency high dosage.
3. To prove that high frequency low dosage of IVIg results in higher IgG trough levels than low frequency high dosage.

Study design

Randomised double-blind controlled crossover study. Two dosing schedules of the same drug are being compared. Placebo will be only added to maintain the blind.

Intervention

intervention group/arm:
4 infusions of IVIg of half the normal dosage (with placebo added to maintain the total volume) and half the interval (double the frequency).

Control group/arm:
2 infusion of IVIg according to the normal; dose and intreval as well as two sham (placebo) infusions.

The total amount of IVIg given during the whole double-blind phase will remain the same in both groups. As this is a crossover study all pateints will receive both treatment schedules once.

Study burden and risks

Due to the fact that patients are treated in the trial with the same drug as before start of the trial and the fact that the total amount (grams) of IVIg over time will be the same as before start of the trial there are no risks to be expected from participation of this trial. A burden for the patients is that

patients receive four extra infusions during the trial. Before and after very infusion a blood sample will be drawn. this blood sample will be taken from the infusion needle therefore no extra venapunction is needed. when pateints give additional permission once a blood sample will be drawn from the infusion needle for DNA examination and 2 days after every infusion a blood sample will be drwan (venapunction) which can be done at the patients home. Furthermore patients will be asked to complete some questionnaires before every infusion.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

's gravendijkwal 230
Rotterdam 3000 CA
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

's gravendijkwal 230
Rotterdam 3000 CA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1.Diagnosis of CIDP or acute-onset CIDP made by a consultant neurologist, fulfilling the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) clinical diagnostic criteria. ;2. Age 18 years or older. ;3. Significant improvement following the first

use of IVIg, defined as a decrease of * 1 grade on the modified Rankin disability scale. ;4. To indicate that the patient is still IVIg dependent and has active CIDP, he/she must have shown either an objective deterioration (decrease in muscle strength measured with the vigorimeter and/or MRC sum score) following reduction of IVIg dose or lengthening of the IVIg interval or an objective improvement (measured with the vigorimeter and/or MRC sum score) following an increase in IVIg dose or shortening of the IVIg interval at some time during the 9 months before randomisation. ;5. Ongoing intermittent treatment with 10% liquid IVIg (Kiovig) for at least 2 infusions. The dose must have been not changed within the 8 weeks prior to the study.;6. EMG findings compatible with CIDP showing peripheral nerve demyelination at least once during their illness.;7. Signed informed consent by the patient.

Exclusion criteria

1. Known IgA deficiency or known allergic reaction to IVIg.;2. Hand grip strength measured by the Martin Vigorimeter equal or more than the median value (kPa) for an age and sex matched healthy control.;3. Maintenance dose less than 15 gram of IVIg every infusion or an infusion interval less than 14 days.;4. Known hereditary neuropathy or severe concomitant diseases such as HIV infection, Lyme disease, chronic active hepatitis, congestive heart failure, systemic lupus erythematosus, drug or toxin induced neuropathy, vasculitis, and malignancies. ;5. Multifocal motor neuropathy (MMN), fulfilling the European Federation of Neurological Societies /Peripheral Nerve Society criteria. ;6. IgM paraprotein with anti-myelin-associated glycoprotein (MAG) antibodies. ;7. Atypical CIDP with pure sensory or persistent unifocal impairment or significant central nervous system involvement.;8. Participation in a controlled trial of an investigational medicinal product within the past 12 weeks. ;9. Severe known abnormalities in liver, kidney function or serum glucose level.;10. Treatment with more than 20 milligrams of prednisone a day.;11. Treatment with other immunosuppressives (e.g. methotrexate, azathioprine, prednisone) if the dosage has been changed within 8 weeks prior to start of the study.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-04-2015
Enrollment:	17
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Kiovig
Generic name:	Immunoglobulin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	23-07-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	18-11-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	09-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	16-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	01-02-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-02-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2012-005150-34-NL
CCMO	NL42671.078.14