Intravenous immunoglobulin (IVIg) overtreatment in chronic inflammatory demyelinating polyneuropathy (CIDP)

Published: 18-03-2014
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The primary objective is to determine whether subjects with CIDP are overtreated with maintenance IVIg treatment and to reduce overtreatment-associated subjects* burden and health care costs.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Peripheral neuropathies
Study type	Interventional

Summary

ID

NL-OMON45047

Source
ToetsingOnline

Brief title
IVIg overtreatment in CIDP: IOC trial

Condition

- Peripheral neuropathies

Synonym
inflammation of nerves, Inflammatory neuropathy

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMW,Sanquin Bloedvoorziening

Intervention

Keyword: Chronic inflammatory demyelinating polyneuropathy, Intravenous immunoglobulin, Overtreatment

Outcome measures

Primary outcome

For the primary outcome we will use the Rasch-Overall Disability Scale (R-ODS), a patient self-report linearly weighted scale that measures activity and social participation limitations.

Secondary outcome

1) The proportion of subjects remaining stable on their individual R-ODS score and completing the follow-period. A subject will be considered stable if he/she does not reach the individual predefined limits of a clinically important deterioration on the R-ODS during follow-up.

2) Muscle strength using the Medical Research Council (MRC) sum score of 12 predefined muscle groups (range 0 to 60, including shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension and foot dorsiflexion).

3) Grip strength, measured in kPa by a Martin-Vigorimeter.

4) Sensory impairment using the modified INCAT Sensory Sum Score (INCAT*SS, range 0-20).

5) Subject*s perception of clinical deterioration on a 5-point Likert scale.

6) Disase-non-specific disability using the AMC Linear Disability Scale (ALDS, range 0 [dead] to 100 [fully able]).

7) Quality of life using Short Form-36 (SF-36).

8) Pain using the Pain-Intensity Numerical Rating Scale (PI-NRS, a 11-point

scale).

9) Fatigue using a 7-item linear modified Rasch-built fatigue scale.

10) Costs of health care use, costs of production loss, and out-of-pocket

expenses.

11) Difference between serum IgG levels before and after last IVIg infusion

prior to first study treatment.

Study description

Background summary

IVIg is an efficacious treatment for CIDP but there is no evidence on how long maintenance treatment should be administered. CIDP runs different disease courses including monophasic, relapsing-remitting and chronic courses. In some patients treated with IVIg, there is no disease activity making ongoing maintenance treatment unnecessary. The only way to assess whether treatment is needed is to try and stop treatment. There is however reluctance to perform IVIg withdrawal attempts because there is a chance of temporary deterioration in IVIg-dependent patients. Several recent studies have showed that there is overtreatment with IVIg in patients with CIDP. This can lead to unnecessary adverse events, discomfort of frequent infusions and very high health care cost.

Study objective

The primary objective is to determine whether subjects with CIDP are overtreated with maintenance IVIg treatment and to reduce overtreatment-associated subjects* burden and health care costs.

Study design

A multicentre, randomized, double-blind, standard treatment-controlled non-inferiority trial.

Intervention

1) IVIg withdrawal (tapering consists of 3 infusions (75%, 50% and respectively 25% of the subjects* prestudy IVIg dose combined with placebo) which will be followed by 100% placebo infusions . Placebo will consist of sodium chloride

0.9% in comparable amounts and intervals as the previous IVIg treatment.
2) Comparative treatment will be the standard treatment in which subjects will be randomised to IVIg will receive the same IVIg infusions (dose and interval) as prior to the study.

Study burden and risks

The risk of this study is considered *negligible*. Upon IVIg withdrawal a certain number of patients will deteriorate. The exact number is unknown and this is one of the main research questions. Participation in this trial is not associated with an additional risk for increases of disability as withdrawal attempts are part of daily care. It is generally considered that deterioration during withdrawal is temporary and can be counteracted by re-instituting IVIg treatment. Most patients, if not all, are expected to reach their baseline level in less than 6 weeks.
The risks for participants will be minimized by close clinical monitoring, using patient-relevant outcomes to measure deterioration and immediate restarting of IVIg treatment when a confirmed worsening has occurred. We have developed a pragmatic restabilisation protocol allowing higher IVIg dosages if these are deemed necessary by the treating physician.
Participation in this trial has some other minor risks such as changing of individual home care nurse in some patients possibly leading to more difficult intravenous access. Measurements during the trial are not considered invasive, except for vena punctures.
Unknown risks to participants related to the study and aside of the risk of deterioration are not expected as patients would have normally continued maintenance treatment.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1) Probable or definite CIDP according to the EFNS/PNS criteria 2010
2) Stable disease for 6 months (e.g. no progression of disease in last 6 months)
3) IVIg treatment for at least 6 months
4) IVIg infusion interval of 2 to 6 weeks.
5) Age of at least 18 years

Exclusion criteria

1) Deterioration after IVIg withdrawal in the last 12 months
2) Changes in IVIg treatment dose/interval in last 6 months
3) Change of additional CIDP treatment, if any, in the last 3 months (e.g. corticosteroids or immunosuppressive treatment)
4) A prolonged period (> 6 weeks) of disability increase following an earlier IVIg withdrawal attempt
5) History of respiratory failure related to CIDP
6) Legally incompetent
7) Lack of written informed consent

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:	Recruitment stopped
Start date (anticipated):	09-04-2014
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Flebogamma
Generic name:	Intravenous immunoglobulin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Gammagard
Generic name:	Intravenous immunoglobulin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Kiovig
Generic name:	Intravenous immunoglobulin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Nanogram
Generic name:	Intravenous immunoglobulin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Privigen
Generic name:	Intravenous immunoglobulin

Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	18-03-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-09-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-09-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-08-2019
Application type:	Amendment
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	EUCTR2013-005363-52-NL
CCMO	NL47383.018.14