Intravenous immunoglobulin and intravenous methylprednisolone as optimal induction treatment in CIDP (OPTIC trial)

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

Summary

ID

NL-OMON50340

Source
ToetsingOnline

Brief title
OPTIC trial

Condition

- Peripheral neuropathies

Synonym
Chronic Inflammatory Demyelinating Polyneuropathy, CIDP

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W,ZonMW,Prinses Beatrix Spierfonds,Sanquin Bloedbank

Intervention

Keyword: CIDP, induction treatment, intravenous immunoglobulin, methylprednisolone

Outcome measures

Primary outcome

Primary outcome is the number of patients in remission at 1 year after start of an 18 weeks treatment period. Remission is defined as sustained improvement without the need for further treatment. Improvement is defined as improvement by at least the minimal clinical important difference (MCID) on the I-RODS and/or improvement of one or more points on the INCAT disability scale at 18 weeks compared to baseline. Sustained is defined as no deterioration between 18 weeks and 52 weeks, i.e. difference on the I-RODS of less than the individual MCID difference and one or more points on the INCAT disability scale. Patients will be considered as a treatment failure if they 1) receive additional CIDP treatment during the 18-week intervention period, 2) do not improve at 18 weeks, 3) restart CIDP treatment for any reason between 18 and 52 weeks, or 4) do not show a sustained improvement at 52 weeks as defined above.

Secondary outcome

Secondary parameters will be assessed at 18 and 52 weeks, or earlier if a preliminary endpoint is reached. Secondary parameters include:

1) The number of patients with improvement on disability equal or more than the MCID;

2) Time to improvement (>= MCID) on disability;

3) Mean change in disability;

4) Mean change in grip strength;

5) Mean change in muscle strength;

6) Mean change in sensory impairment;

7) Mean change in fatigue;

8) Mean change in pain;

9) Mean change in health related quality of life (HRQL);

10) Number of (serious) adverse events (including corticosteroid associated

adverse events);

11) Care use and overall healthcare-related costs.

Study description

Background summary

Induction treatment of CIDP currently consists of either intravenous immunoglobulin (IVIg) infusions or high dose corticosteroids, including daily oral prednisolone, pulsed dexamethasone or pulsed intravenous methylprednisolone (IVMP). Both IVIg and IVMP are recommended as first line treatment, but choice of induction treatment is usually based on patients* and physicians* preferences as both treatment options have their own specific advantages. Patients treated with IVIg usually respond fast, but this treatment rarely leads to long term remissions. Alternatively, corticosteroids probably lead to longterm remissions. Both fast clinical response and long term remissions can be considered equally important.

Study objective

Primary objective of this randomized controlled trial is to assess whether combining IVIg and IVMP leads to more frequent long-term remission in CIDP compared to treatment with IVIg alone. Main secondary objectives are to assess whether IVIg and IVMP leads more often to functional improvement and a faster

rate of functional improvement compared to IVIg alone.

Study design

A multicenter, randomized, double-blind, placebo-controlled trial.

Intervention

Intravenous methylprednisolone (1 gram) or placebo (sodium chloride 0.9%, 100 ml). All patients receive (weekly) alendronic acid and (daily) calcium/vitamin D during the 18-week intervention period according to national guidelines for prevention of glucocorticoid-induced osteoporosis.

Study burden and risks

This study is considered of moderate risk. Side effects associated with methylprednisolone are well documented and include hypertension, diabetes, osteoporosis, Cushinoid appearance, gastrointestinal complaints and mood changes. Total follow-up of the study is 104 weeks, including the final safety-follow-up. Follow-up hospital visits will be scheduled at 6, 12, 18, 24, 52 and 104 weeks. Patients are contacted by phone at 3, 30 and 42 weeks after start treatment to fill in a limited number of questionairres). Unscheduled visits (including visits during relapses) can be scheduled at any time.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam Zuid-Oost 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam Zuid-Oost 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion of patients is based on the presence of active disease and fulfillment of the probable or definite. EFNS/PNS criteria for CIDP. All new and untreated adult patients are eligible for the study. In addition we will include CIDP patients, treated previously, who have a disease relapse after a remission of at least 1 year, and patients who have responded to their first course of IVIg in the last three months but deteriorated afterwards. Deterioration after treatment is defined as any deterioration warranting treatment as judged by the treating physician.

Exclusion criteria

1) Presence of IgM paraproteinemia and/or anti-MAG antibodies or CIDP specific antibodies associated with poor treatment response to IVIg
2) Use of drugs associated with a demyelinating neuropathy
3) Use of any immunosuppressive or immunomodulatory drugs in previous 6 months (except for a single loading dose of IVIg within 3 months), with the exception of low dose prednisone (20 mg or less for the duration of two weeks).
4) Known serious adverse events with previous IVIg or corticosteroid treatment
5) One of more of the risk factors associated with increased risk of adverse events of IVIg or IVMP or conditions that could lead to unblinding of treatment (i.e. diabetes; IgA deficiency; gastric ulcers; psychosis; severe hypertension (180/110 mmHg or more on repeated measurements); hypocalcaemia (lower than 2.20 mmol/L, corrected for albumin); moderate or severe heart failure; severe cardiovascular disease (i.e. more than one myocardial infarction and or ischemic stroke); renal failure (glomerulal filtratrion rate less than 30 ml/min)
6) History of osteoporosis or osteoporotic fractures
7) Known malignancy with survival expectancy of less than 1 year
8) Bodyweight more than 120 kg
9) Pregnancy or nursing mother; intention to become pregnant during the course of the study; female patients of childbearing potential either

not using or not willing to use a medically reliable method of contraception for the entire duration of the study
10) Cataract
11) Psychosis
12) Poor dental status
13) Known pulmonary embolism or other deep venous thrombosis in patient*s medical history, without current anticoagulant therapy
14) Legally incompetent adults
15) Lack of written informed consent

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Suspended
Start date (anticipated):	19-02-2018
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NaCl
Generic name:	NaCl
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Sodium chloride 0.9% (NaCl)

Generic name:	Sodium chloride 0.9% (NaCl)
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Solu-Medrol
Generic name:	Methylprednisolone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	15-01-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-05-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-07-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-09-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-06-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-08-2019

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-05-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-06-2020
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	EUCTR2017-002511-34-NL
ISRCTN	ISRCTN15893334
CCMO	NL62561.018.17