Intravenous immunoglobulin and intravenous methylprednisolone as optimal induction treatment in CIDP

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Primary objective of this randomized controlled trial is to assess whether combining IVIg and methylprednisolone leads to more frequent long-term remission in CIDP compared to treatment with IVIg alone.

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON21678

Bron
Nationaal Trial Register

Verkorte titel
OPTIC

Aandoening

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

Ondersteuning

Primaire sponsor: Amsterdam UMC, location AMC
Overige ondersteuning: ZonMW, Prinses Beatrix Spierfonds, Sanquin (logistical support)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Remission at 1 year

Toelichting onderzoek

Achtergrond van het onderzoek

Background and study aims
Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare neurological disorder which causes chronic inflammation (swelling) of nerves causing weakness and sensory problems in legs and arms. Induction treatment (the first phase of treatment) CIDP currently consists of either intravenous immunoglobulin (IVIg) (treatment made from donated blood that contains health anitbodies) infusions or high dose corticosteroids (anti-inflammatory medication), including daily oral prednisolone, pulsed dexamethasone or pulsed intravenous methylprednisolone (IVMP) (types of steroids). 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 (meaning the symptoms are gone). Corticosteroids may lead to long term remissions. Both fast clinical response and long term remissions can be considered equally important. The aim of this study is to determine whether the addition of methylprednisolone to IVIg as induction treatment leads to a better outcome.

Who can participate?
Adults aged 18 and older who have probably or definite CIDP.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive intravenous immunoglobulin (IVIg) + intravenous methylprednisolone. Those in the second group receive intravenous immunoglobulin (IVIg) + placebo (saline infusion). Participants receive seven infusions every three weeks over the course of 18 weeks. During the 18 week intervention period participants are prescribed osteoporosis prophylactics (vitamin D daily and alendronic acid weekly). In the Netherlands the first treatment is given in the hospital and the remaining six infusions are given at home. Outpatient clinic visits are planned every six weeks during the intervention period and a consultation by phone is planned three weeks after start of intervention period. Three follow-up visits are planned in week 24, 52 and 104. Unscheduled visits can be planned at any time during study.

What are the possible benefits and risks of participating?
Participants can benefit from the combination therapy: a fast improvement of symptoms(attributed to the IVIg) and long term remission (attributed to the methylprednisolone), without the need for further treatments. Risks include medication induced side effects. These side effects include (and not limited to) gastro-intestinal complaints, headaches, muscle aches, oedema, mood/behavior disorders (methylprednisolone); musculoskeletal complaints (muscle, joint and/or bone aches) and

gastro-intestinal complaints (alendronic acid); skin rash, hypertension, headaches and gasto-intestinal complaints (IVIg, standard care).

Doel van het onderzoek

Primary objective of this randomized controlled trial is to assess whether combining IVIg and methylprednisolone leads to more frequent long-term remission in CIDP compared to treatment with IVIg alone.

Onderzoeksopzet

Remission status is assessed at 1 year. Remission is defined as sustained improvement. Improvement is assessed at 18 weeks post-randomization. Patients visit outpatient clinic every six weeks the first half year, with a consultation by phone three weeks after first treatment. Total follow-up is two year, with a long term safety assessment taking place two years after randomization.

Onderzoeksproduct en/of interventie

Intravenous methylprednisolone

Contactpersonen

Publiek

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Sander Bus

020 566 6889

Wetenschappelijk

Amsterdam UMC, location AMC
Sander Bus

020 566 6889

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Probable or definite CIDP according to the EFNS/PNS criteria 2010 (all CIDP phenotypes)
2. Age ≥ 18 years
3.1. Treatment naïve patients; or
3.2. Previously treated patients who have a relapse after a remission of at least 1 year; or
3.3. Patients treated with subjective or objective improvement after a single loading dose of IVIg in the last 3 months, and subsequent deterioration as judged by his or her treating physician.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

A potential patient who meets any of the following criteria will be excluded from participation in this study:
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 or low dose prednisolone (20 mg or less) during a short period (maximum duration of two weeks).
4) Known serious adverse events with previous IVIg or corticosteroid treatment. Hypersensitivity to methylprednisolone or any component of the formulation. Hypersensitivity to the human immunoglobulins or to any of the excipients. Selective IgA deficiency patients who developed antibodies to IgA.
5) Systemic fungal infections, unless specific anti-infective therapy is employed.
6) Known hyperprolinaemia type I or II or known fructose intolerance.
7) 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 (glomerular filtration rate < 30 ml/min)
8) History of osteoporosis or osteoporotic fractures
9) Known active malignancy, currently treated with chemotherapy or immunomodulatory drugs, or with a life expectancy of less than 1 year.
10) Bodyweight more than 120 kg
11) 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. A woman is considered of childbearing potential from menarche and until becoming post-menopausal, unless permanently sterile. Permanent sterilisation methods include hysterectomy, bilateral salpingectomy and bilateral oophorectomy. A postmenopausal state is defined as no menses

for 12 months without an alternative medical cause. Acceptable methods of contraception are: combined (oestrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (whether oral, intravaginal or transdermal), progestogen-only hormonal contraception associated with inhibition of ovulation (whether oral, injectable or implantable), progestogen-only oral hormonal contraception, where inhibition of ovulation is not the primary mode of action, male or female condom with or without spermicide, cap or diaphragm, intrauterine device (IUD), intrauterine hormone-releasing system (IUS), bilateral tubal occlusion, vasectomised partner (provided that partner is the sole sexual partner of the trial participant and that the vasectomised partner has received medical assessment of the surgical success).
12) Known cataract or cataract obvious on fundoscopy
13) Current psychosis or past history of psychosis
14) Poor dental status
15) Known pulmonary embolism or other deep venous thrombosis in patient’s medical history, without current anticoagulant therapy
16) Adults lacking capacity to give informed consent.
17) Lack of written informed consent

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	19-02-2019
Aantal proefpersonen:	96
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Toelichting

The data sharing plans for the current study are unknown and will be made available at a later date. When this information becomes available we will disclose it.

Ethische beoordeling

Positief advies

Datum:	24-07-2019
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	NL7895
Ander register	The Medical Ethical Committee of the Academic Medical Center, (approval granted 15/01/2018) : 2017_316

Resultaten

Samenvatting resultaten
Planned publication in a high-impact peer reviewed journal, with the intent to publish the results in one year following overall trial end date