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Intravenous immunoglobulin overtreatment in chronic inflammatory demyelinating polyneuropathy

Submission date
06/12/2013

Recruitment status
No longer recruiting

Registration date
25/03/2014

Overall study status
Completed

Last Edited
01/11/2022

Condition category
Nervous System Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Chronic inflammatory demyelinating polyneuropathy (CIDP) is a neuropathy that can lead to considerable disability (walking difficulties and loss of arm dexterity.) Intravenous immunoglobulin (IVIg) is an effective treatment for CIDP. There is however no evidence on how long the treatment should last. This is particularly challenging given the variable and unpredictable course of the disease. In some patients currently treated with IVIg, the disease is actually not active and further treatment is not necessary. Several recent studies have confirmed that there is overtreatment with IVIg. Unfortunately, the only way currently to assess whether treatment is needed is to try and stop treatment. Because of the fear of deterioration in IVIg-dependent patients, attempts to reduce IVIg treatments are not performed frequently. In this study we aim to quantify and reduce overtreatment with IVIg in patients with CIDP. We will introduce a standardised IVIg restabilisation protocol to limit the increase in disability in participants who turn out to be IVIg-dependent. We will explore possible predictors of IVIg dependency to guide long-term IVIg treatment in the future.

Who can participate?
Adult patients with CIDP currently receiving maintenance IVIg infusions are eligible for this study.

What does the study involve?
Participants will be randomly allocated to oe of two groups: IVIg withdrawal group or continuation of IVIg treatment group. Participants in IVIg withdrawal group will start with a tapering phase consisting of 3 infusions which will be followed by 100% placebo infusions. Participants in continuation of IVIg treatment group will receive the same IVIg treatment as before the study. All treatments will be provided by home-care nurses. Subjects will be followed for at least 24 weeks after inclusion.

What are the possible benefits and risks of participating?
Successful IVIg withdrawal will reduce adverse events, the discomfort caused by regular infusions and related health care costs. The main risk is deterioration during the study.

Participants will be closely monitored, IVIg treatment will be resumed if the participants condition gets worse and the increase in disability will be limited to a very short time period.

Where is the study run from?
Participants will be recruited from Dutch neuromuscular centers.

When is the study starting and how long is it expected to run for?
The study will start in April 2014 and is expected to run until October 2016, including a 24-week follow-up period.

Who is funding the study?
Dutch Governmental grant and by Sanquin Blood Supply.

Who is the main contact?
Dr Filip Eftimov
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2013-005363-52

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
IOC

Study information

Scientific Title

Intravenous immunoglobulin overtreatment in chronic inflammatory demyelinating polyneuropathy: a randomized controlled non-inferiority trial

Acronym
IOC (IVIg Overtreatment in CIDP)

Study objectives
The hypothesis is that there is overtreatment in patients receiving long-term maintenance intravenous immunoglobulin (IVIg) treatment. The primary objective of the study is to determine whether subjects with chronic inflammatory demyelinating polyneuropathy (CIDP) are overtreated with maintenance IVIg treatment and to reduce overtreatment-associated subjects burden and healthcare costs.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Medical Ethical Committee of the Academic Medical Center, 18/03/2014, Ref: 2014-018#B2014239a

Study design
Multicentre randomized double-blind standard treatment-controlled non-inferiority trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Chronic inflammatory demyelinating polyneuropathy (CIDP)

Interventions
Subjects will be randomised to one of the following two treatments:
1. IVIg withdrawal (tapering consists of three infusions (75%, 50% and 25% respectively of the subjects pre-study 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 receive the same IVIg infusions (dose and interval) as prior to the study.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
The change between baseline and endpoint Rasch-Overall Disability Score (R-ODS). An endpoint will be reached in case of one of the following: final visit at 24 weeks or deterioration on the R-ODS by more than 0.652 logits during follow-up.

Secondary outcome measures
1. The proportion of subjects remaining stable on their individual R-ODS score and completing the follow-up period. An individual subject will be considered stable if the difference between his or her baseline and endpoint R-ODS scores is less than 0.652 logits.
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 (INCATSS, range 0-20).
5. Subjects perception of clinical deterioration on a 5-point Likert scale.
6. Disease-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, an 11-point scale).
9. Fatigue using a 7-item linear modified Rasch-built fatigue scale.
10. Costs of healthcare 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

All secondary outcomes will be measured when an endpoint is reached. An endpoint will be reached in case of one of the following:
1. Final visit at 24 weeks
2. Deterioration on the R-ODS by more than 0.652 logits during follow-up

Overall study start date
01/04/2014

Completion date
31/07/2019

Eligibility

Key inclusion criteria
1. Probable or definite CIDP according to the European Federation of Neurological Societies /Peripheral Nerve Society (EFNS/PNS) criteria 2010
2. Stable disease for 6 months (i.e., no progression of disease in the last 6 months)
3. IVIg treatment for at least 6 months
4. IVIg infusion interval of 2 to 6 weeks
5. Age > 18 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
60

Total final enrolment
60

Key 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

Date of first enrolment
01/04/2014

Date of final enrolment
01/10/2016

Locations

Countries of recruitment
Netherlands

Study participating centre
Academic Medical Centre
Amsterdam
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1105 AZ

Sponsor information

Organisation
Academic Medical Center Amsterdam (Netherlands)

Sponsor details
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Sponsor type
Hospital/treatment centre

Website
http://www.amc.nl/web/Research/ResearchAMC/AMC-a-glance.htm

Funder(s)

Funder type
Government

Funder Name
ZonMw/Rational Pharmacotherapy programme (Netherlands) (Dutch Governmental grant)

Funder Name
Sanquin Blood Supply (Netherlands) (logistical support)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
01/01/2021

Individual participant data (IPD) sharing plan
The datasets with clinical data that do not include confidential patient information generated during and/or analysed during the current study will be available upon reasonable request from F. Eftimov (f.eftimov@amsterdamumc.nl) after publishing the results.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		03/06/2022	01/11/2022	Yes	No