T-cell clonal expansion in chronic demyelinating inflammatory polyradiculoneuropathy (CIDP)

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

Summary

ID

NL-OMON37266

Source
ToetsingOnline

Brief title
TEC

Condition

- Autoimmune disorders
- Peripheral neuropathies

Synonym
chronic demyelinating inflammatory polyradiculoneuropathy (CIDP), no lay term

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,onderzoekssubsidie

(unrestricted grant aan uitvoerend onderzoeker) door de Peripheral Nerve Society

Intervention

Keyword: CIDP, clonal expansion, T-cells

Outcome measures

Primary outcome

1) Frequency and overlap of expanded T-cell clones in sural nerve biopsies and

peripheral blood in patients with active disease (Group 1).

2) Change in frequency of expanded clones in blood

a) comparing active disease with stable disease (Group 1)

b) comparing stable disease during IVIg maintenance treatment and active

disease after stopping treatment (Group 2).

Secondary outcome

1. MRC sum score

2. INCAT sensory sum score

3. INCAT disability scale

4. Sural nerve biopsy questionnaire (applicable only for Group 1)

Study description

Background summary

Corticosteroids, intravenous immunoglobulin (IVIg) and plasma exchange are the only proven effective therapies in CIDP. Still, around 20% of patients do not or insufficiently respond to treatment. Most patients need long-term treatment such as daily prednisolone and/or interval infusions with IVIg which have their specific drawbacks. Corticosteroids frequently results in serious adverse events such as diabetes, hypertension and osteoporosis. IVIg is relatively difficult to administer as it has to be given intravenously at regular intervals and is very expensive. Long-term maintenance treatment is further

complicated by the difficulty in identifying patients that require lower doses or no treatment at all as most patients have no or only minor symptoms during maintenance treatment. This has been illustrated by a recent trial in which maintenance doses could be significantly reduced in almost half of patients with placebo add-on treatment. Alternatively, clinical deterioration is often a late manifestation of active disease due to under treatment and can lead to permanent axonal damage.

The key mechanisms in the pathogenesis have not been identified although several studies have highlighted the role of T-cells in CIDP. Better understanding of the pathogenesis is needed to identify new treatment strategies and to develop biomarkers that correlate with disease activity that could help guide maintenance treatment. Recently, our Genome Analysis Department developed a new method for TCR repertoire typing based on high throughput sequencing (HTS) using T-cel RNA. Using this method we will explore whether expanded T-cell clones can be observed in both nerve biopsies as in peripheral blood of newly diagnosed CIDP patients.

Study objective

1) The primary objective of this pilot study is to compare the clonal composition of the TCR repertoire in anterior fascicular sural nerve biopsies with the TCR repertoire in peripheral blood of CIDP patients with active disease in order to identify disease-associated T-cell clones.
2) The second objective is to compare the frequency of expanded T-cell clones in peripheral blood during different disease activity states.

Study design

Observational pilot study.

Study burden and risks

The main risk of anterior sural fascicle biopsies is the occurrence of a persistent sensory deficit in about 1/3 of patients corresponding with the territory innervated by the nerve (sensation loss in lateral foot). Other immediate complications of sural nerve biopsies (whole and anterior fascicle sural nerve biopsies) are postoperative pain, parasthesia and dysesthesia (unpleasant feeling of touch) in about 1/3 of patients and wound infection (8%). Long-term follow-up studies have suggested a decrease in symptoms up to 5 years after biopsy. In almost all patients sural biopsy complications were judged to be mild and did not lead to functional impairment.

Nerve biopsy will be only performed in patients with clinical and electrophysiological signs suggesting already severely impaired sural nerve function. This is important not only to avoid sampling error (absence of

T-cells in sural nerve) but also because it would strongly reduce the chance that permanent sensory deficit is caused by the anterior fascicle biopsy. Most patients responding to treatment improve in muscle strength whereas distal sensory residual symptoms normally persist.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Group 1
- Adult patients (> 18 years)
- Fulfilment of the EFNS/PNS criteria for probable or definite CIDP
- Clinical sensory deficit corresponding with sural nerve in one or both legs AND absent sensory nerve action potential (SNAP) on nerve conduction studies.
Group 2

- Adult patients (> 18 years)
- Fulfilment of the EFNS/PNS criteria for probable or definite CIDP
- Patients with intravenous immunoglobulin (IVIg) maintenance treatment who are eligible for IVIg withdrawal to confirm IVIg dependency
- No fluctuation of clinical condition or dose of IVIg in the last 3 months

Exclusion criteria

- Other diseases known to cause neuropathy
- Use of drugs which are known to cause neuropathy
- Use of immunomodulatory drugs in the last 3 months
- Refusal to give informed consent or withdrawal of previously given permission
- Legally incompetent adult

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-03-2013
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	22-01-2013
Application type:	First submission
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
CCMO	NL42328.018.12