Modifiers in PMP22 related neuropathies

Published: 21-10-2008
Last updated: 11-05-2024

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

Summary

ID

NL-OMON32269

Source
ToetsingOnline

Brief title
Modifiers in PMP22 related neuropathies

Condition

- Neurological disorders congenital
- Peripheral neuropathies

Synonym
Charcot-Marie-Tooth disease, Hereditary Motor and Sensory Neuropathy

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: aanvraag ingediend bij Prinses Beatrix Fonds

Intervention

Keyword: CMT1A, HNPP, modifier genes, phenotype-genotype correlation

Outcome measures

Primary outcome

The presence or absence of copy number variants (CNV) and sequence variants of CMT genes and genes involved in the immune system between the most severely and mildest affected patients.

Secondary outcome

not applicable

Study description

Background summary

Amongst hereditary neuropathies, Charcot-Marie-Tooth disease (CMT) or hereditary motor and sensory neuropathy (HMSN), is the most prevalent. Over 30 loci and genes are identified. The most frequent demyelinating form (CMT1A) is most often caused by a duplication of the PMP22 gene, whereas a deletion of one copy of the PMP22 gene causes hereditary neuropathy with liability to pressure palsies (HNPP). The variability of the CMT1A phenotype, even within families, suggests the presence of modifiers but none have been identified thus far.

Study objective

The objective is to determine the disease severity in genetically proven CMT1A/HNPP patients and to correlate this with sequence variants in CMT and immunity related genes.
Identification of genotype-phenotype correlations in CMT1A will allow prognostic counselling of the patients. Insight in modifiers of the disease process may yield new therapeutic targets. Finally, this study will yield a biobank of well-characterized neuropathy patients which is essential for future studies on CMT.

Study design

Cross sectional study.

750 patients with known CMT1A duplication and 330 HNPP deletion patients will be approached to complete a questionnaire Subsequently, the 100 most severely and 100 mildest affected CMT1A patients and 50 HNPP patients at both ends of the spectrum will be selected and invited to the hospital for detailed neurological tests and DNA-analysis.

Study burden and risks

For most patients participation will only consist of completing a questionnaire by telephone.
300 patients (200 CMT1A and 100 HNPP patients) who belong to the most severely and the mildest affected patients, will be invited for a single hospital visit with a duration of 2.5 hours. A family history will be taken. The following tests will be applied: physical neurological examination, testing muscle strength, testing sensibility, 4 tests of hand function, a 10 meter timed walk, electrophysiological test of the ulnar nerve, a single blood draw and 3 questionnaires concerning daily activities and quality of life.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

duplication or deletion of PMP22-gene,
age 12-60 year

Exclusion criteria

- Use of medication or suffering from other disease than CMT/HNPP that can cause neuropathy
- comorbidity interfering with mobility
- non-Caucasian patients

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):	24-08-2009
Enrollment:	1080
Type:	Actual

Ethics review

Approved WMO
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	NL23232.018.08