Rotterdam Observational Study in CIDP of Pharmacokinetics of Intravenous γ-globulin

Published: 20-01-2014
Last updated: 23-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Peripheral neuropathies
Study type	Observational invasive

Summary

ID

NL-OMON37960

Source
ToetsingOnline

Brief title
ROCKY-1

Condition

- Peripheral neuropathies

Synonym
Chronic inflammatory dyemyelinating polyneuropathy (no lay-term).

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Prinses Beatrix Spierfonds.

Intervention

Keyword: Chronic Inflammatory demyelinating Polyradiculoneuropathy (CIDP), Intravenous immunoglobulin (IVIg), Non-linear mixed effects modeling (NONMEM), Pharmacokinetics (PK)

Outcome measures

Primary outcome

Serum IgG levels determined over the duration of two subsequent IVIg courses at standardized time points, before and after infusion.

Secondary outcome

Immunological parameters tested in order of high to low priority are: serum levels of IgG subclasses, albumin, liver and kidney function parameters, expression of Fc-receptors, genetic polymorphisms involved in IgG metabolism (including polymorphisms in the IgG Fc-receptors), peripheral blood leukocytes, cytokines, IgG glycoforms and IgG allotypes.

To confirm the clinical stability of the patients the following clinical outcome measures will be monitored: hand grip strength (Vigorimeter), R-ODS and R-FSS questionnaires.

Study description

Background summary

Intravenous immunoglobulin (IVIg) is an effective treatment for patients with chronic inflammatory demyelinating polyneuropathy (CIDP). The therapeutic effect, however, is usually transient and most patients require regular dosages of IVIg at standard intervals during maintenance treatment for years or even decades. The IVIg dosage and frequency is adapted to the clinical response of the patient by *trial and error*. There are at present no biomarkers to monitor the disease activity and treatment response. Individual patients who are considered to be clinically stable are usually treated with a fixed IVIg regimen, some however still slowly deteriorate (undertreatment). While other

patients still being treated with this costly therapy are in remission and do not need regular IVIg administrations any longer (overtreatment). The required dosage and interval of IVIg may differ between individual patients. Although IVIg is in use for decades, very little is known about the pharmacokinetics (PK) and pharmacodynamics (PD) (pharmacological profile) of IVIg treatment in CIDP. In addition, the factors that influence the pharmacokinetics of IVIg and determine the required dosages of IVIg in individual patients are unknown. A previous study in our center suggests that the pharmacokinetics of IVIg influence recovery of patients in a similar disease. Therefore serum IgG levels may be used as a biomarker to predict and monitor the clinical efficacy of IVIg.

Study objective

The main objective of the study is to determine the PK and PD of IVIg during maintenance treatment in patients with CIDP. These data will be used to conduct a NONMEM analysis in relation to the dosage, frequency and batch of IVIg used. The secondary objective is to investigate which factors influence the pharmacological profile of IVIg, including demographic, clinical and genetic factors.

Study design

Observational cohort study.

Study burden and risks

Subjects will be asked to undergo a series of tests as well as a number of blood drawings during a period of two subsequent IVIg courses (depending on their schedule 4 - 8 weeks).

Blood samples will be drawn at standard time points during two subsequent IVIg courses, including (1) 5 minutes before start of IVIg, treatment, (2) 15 minutes after finishing IVIg treatment, (3) 2 hours after IVIg, (4) 24 hours after, (5) 2 days, (6) 7 days, (7) 14 days and in case of a treatment interval of more than 3 weeks; (8) 21 days after IVIg. Proposed time points are not entirely fixed and the definitive schedule will be in consultation with the patient, to accommodate the sampling times as much as possible to the wishes of the patient. Furthermore, some patients have a treatment interval of 2 weeks or less. Time points will then be adjusted accordingly. EDTA blood sample for extraction of DNA will be obtained before the first IVIg course after inclusion in the study. The serum samples obtained 5 minutes before IVIg, and 15 minutes and 2 hours after IVIg and the single EDTA blood sample will be obtained via the peripheral catheter system. The other serum samples will be drawn by venipuncture. The sampling at day 21 is performed only in the vast minority of patients with an interval of IVIg maintenance treatment of 4 weeks or more.

Therefore, in the majority of patients the number of extra punctures, in addition to the routine puncture to administer IVIg, will be 4 per treatment course (8 for two courses). Hand grip strength (Vigorimeter) will be measured before (at) every infusion by the nurse administrating the IVIg and during certain time points (6-8) by qualified personnel of the Neurology department of the Erasmus MC or nurses from the homecare treatment. During two occasions patients are required to complete questionnaires (R-ODS and R-FSS). None of these clinical outcome measures is painful or has a psychological burden for the patient. The patients participating in the study will not directly profit, but in the future we aim to optimize and monitor the treatment regimen of this maintenance treatment for individual patients with CIDP.

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

1. Diagnosis of CIDP made by a consultant neurologist, fulfilling the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) clinical diagnostic criteria.
2. EMG findings compatible with the diagnosis CIDP showing peripheral nerve demyelination at least once during their illness. These findings should preferentially fulfill the electrodiagnostic criteria proposed by the European Inflammatory Neuropathy Cause and Treatment (INCAT) or EFNS/PNS.
3. Age >=18 years.
4. Patients require either to be on maintenance treatment with IVIg.
5. Signed informed consent by the patient.

Exclusion criteria

1. Known IgA deficiency or known allergic reaction to IVIg.
2. Known hereditary neuropathy or severe concomitant diseases such as HIV infection, Lyme disease, chronic active hepatitis, congestive heart failure, systemic lupus erythematosus, drug or toxin induced neuropathy, vasculitis, and malignancies.
3. Multifocal motor neuropathy (MMN), fulfilling the European Federation of Neurological Societies /Peripheral Nerve Society criteria.
4. IgM paraprotein with anti-myelin-associated glycoprotein (MAG) antibodies.
5. Atypical CIDP with pure sensory or persistent unifocal impairment or significant central nervous system involvement.
6. Severe known abnormalities in liver, kidney function or serum glucose level.
7. Concomitant treatment with prednisone.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-04-2014

Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Kiovig
Generic name:	Human normal immunoglobulin (IVIg)
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	20-01-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-01-2014
Application type:	First submission
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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	EUCTR2013-004988-32-NL
CCMO	NL46993.078.13