Randomized, multicenter, double-blind, placebo-controlled, parallel group phase III study to investigate the efficacy, safety, and tolerability of 2 different doses of IgPro20 (subcutaneous immunoglobulin) for the treatment of chronic inflammatory demyelinating polyneuropathy (CIDP).

Published: 14-03-2012
Last updated: 26-04-2024

The primary objective of the study is to determine the efficacy of 2 different doses of IgPro20 (0.2 g/kg bw and/or 0.4 g/kg bw) in the maintenance treatment of CIDP in comparison to placeboSecondary objectives:* To investigate the efficacy of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immunodeficiency syndromes
Study type	Interventional

Summary

ID

NL-OMON39905

Source
ToetsingOnline

Brief title
PATH study

Condition

- Immunodeficiency syndromes
- Demyelinating disorders

Synonym
peripheral nerve damage, polyneuropathy

Research involving
Human

Sponsors and support

Primary sponsor: CSL Behring BmbH
Source(s) of monetary or material Support: CSL Behring (farmaceutische industrie)

Intervention

Keyword: CIDP, IgPro20, phase 3, Subcutaneous Immunoglobuline

Outcome measures

Primary outcome

The proportion of patients who experience CIDP relapse based on the INCAT disability score assessed at baseline (Week 10), and any time thereafter until completion visit. CIDP relapse is defined at a subject level as an increase of at least 1 adjusted INCAT disability score point confirmed by the evaluating physician between baseline and any time thereafter until completion visit, OR are withdrawn from the study for any reason after the start of SC treatment without CIDP relapse

Secondary outcome

Changes in means during the SC Treatment Period for:

- INCAT score

- Maximum grip strength score

- Medical Research Council (MRC) sum score

- Rasch-built Overall Disability Scale (R-ODS)

* Time to CIDP relapse or withdrawal due to any other reason

* Time to improvement after CIDP relapse in the SC Treatment Period,

defined as a decrease in INCAT score back to or below the baseline score

* Time to improvement after CIDP relapse during IgPro10 rescue

therapy, defined as a decrease in INCAT score back to or below the

baseline score

* Changes in means during IgPro10 re-stabilization or rescue therapy in:

- Mean grip strength

- MRC sum score

- R-ODS

- INCAT score

* Time to improvement on IgPro10 re-stabilization therapy (INCAT score

decrease, R-ODS improvement, Mean grip strength improvement)

Safety:

* Rate of AEs per SC infusion, number and % of subjects with AEs during

the SC Treatment Period

* Rate of AEs per IgPro10 infusion, number and % of subjects with AEs

during IgPro10 Restabilization Period or Rescue Therapy

Study description

Background summary

CIDP is an acquired neurological, demyelinating disease with an assumed autoimmune-mediated pathogenesis. Its presentation is heterogeneous, and the individual diagnostic procedures (clinical, serologic, and electrophysiological) all have limitations so diagnosis relies on findings from

multiple modalities. The probable autoimmune nature of the condition is most strongly suggested by response to immunotherapies such as intravenous immunoglobulins (IVIGs), plasmapheresis (PE), and corticosteroids (Köller et al., 2005).

Apart from IVIGs, there are currently no other drugs approved for the treatment of CIDP. To allow for another treatment option for CIDP, administration of IgPro20 by the subcutaneous route allows the subject to self-administer the product in the home setting. In this study the two different doses for CIDP SC home treatment will be tested.

Study objective

The primary objective of the study is to determine the efficacy of 2 different doses of IgPro20 (0.2 g/kg bw and/or 0.4 g/kg bw) in the maintenance treatment of CIDP in comparison to placebo

Secondary objectives:
* To investigate the efficacy of IgPro20 with additional clinical outcome measures in comparison to placebo.
* To investigate the safety and tolerability of IgPro20 in comparison to placebo.
* To investigate the safety and efficacy of IgPro10 re-stabilization therapy.
* To investigate the safety and efficacy of IgPro10 rescue therapy.

Study design

This is a prospective, multicenter, randomized, double-blind, placebo-controlled, parallel-group study to investigate 2 different doses of IgPro20 SC compared to volume-matched placebo SC for maintenance IgG treatment of subjects with CIDP.

Intervention

10-13 weeks if IVIG (IgPro10) treatment, followed by randomisation to a subcutaneous injection of 0,2 g /kg of 0,4 g/kg bodyweight of Hizentra or placebo once a week.

Study burden and risks

In general, IgG preparations have a well-known safety and efficacy profile. They have been used clinically for many years via IV, IM and SC routes and the adverse events (AEs) of such treatment are well described.

Experience with SCIGs is more limited in high dose indications (e.g., polyneuropathies), but a feature common to all reports of SCIG usage is improved systemic tolerability to IVIGs (as measured by documented low rates of those adverse reactions common to IVIG usage in clinical trials)

The principle benefits likely to arise from study participation are a reduction in systemic AEs and an increase in subject autonomy (through self treatment). Conversely the main risks are administration site reactions associated with subcutaneous treatment and the risk of disease relapse due to randomization or lack of efficacy of the IMP (for which subjects will be closely monitored and rescue therapy provided). The other procedures and practices included in this protocol are unlikely to produce risk or substantial discomfort to subjects.

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. Definite or probable CIDP according to the EFNS/PNS criteria 2010.
2. An IVIG treatment during the last 8 weeks prior to enrollment.
3. Age *18 years.
4. Male or female.
5. Written informed consent for study participation obtained before undergoing any study-specific procedures.

Exclusion criteria

1.Any polyneuropathy of other causes, including:
1a.Multifocal motor neuropathy (MMN).
1b.Monoclonal gammopathy of uncertain significance (MGUS) with anti-MAG Immunoglobulin M (IgM) antibodies.
1c.Hereditary demyelinating polyneuropathy.
1d.POEMS syndrome.
1e.Lumbosacral radiculoplexus neuropathy.
1f.Polyneuropathy associated with diabetes mellitus.
1g.Polyneuropathy associated with systemic lupus erythematosus (SLE).
1h.PNS lymphoma or amyloidosis with evidence for demyelinating polyneuropathy.
1i.Borrelia burgdorferi infection (Lyme disease), diphtheria, drug or toxin exposure.
2.Any other disease (mainly neurological or chronic orthopedic) that has caused neurological symptoms or may interfere with treatment or outcome assessments, e.g.:
2a.Post-polio syndrome.
2b.M. Parkinson.
2c.Myelopathy.
2d.Osteosclerotic myeloma.
2e.Prominent sphincter disturbance of bladder and bowel.
3.Severe diseases and conditions that are likely to interfere with evaluation of the study product or satisfactory conduct of the study, e.g.:
3a.Current malignancy or history of allogeneic bone marrow/stem cell transplant.
3b.Cardiac insufficiency (New York Heart Association [NYHA] III/IV), cardiomyopathy, significant cardiac arrhythmia requiring treatment, unstable or advanced ischemic heart disease, congestive heart failure or severe hypertension.
3c.Chronic kidney disease stage IV and V.
3d.Known hyperprolinemia.

3e.Known bleeding disorders.
3f.Severe skin disease at the planned injection sites.
3g.Alcohol, drug or medication abuse.
4.History of thrombotic episodes within the 2 years prior to enrolment, e.g.:
4a.Pulmonary embolism.
4b.Deep vein thrombosis.
4c.Myocardial infarction.
4d.Thromboembolic stroke.
4e.Known hypercoagulable state.
5.Known allergic or other severe reactions to blood products including intolerability to previous IVIG:
5a.History of hemolysis after IVIG infusion
5b.Aseptic meningitis.
5c.Recurrent severe headache.
5d.Hypersensitivity.
5e.Severe generalized skin reaction.
6.Treatment with the following medications before enrolment:
6a.Within 3 months before enrolment: plasma exchange (PE).
6b.Within 6 months before enrolment: cyclophosphamide, interferon, TNF-alpha inhibitors, or any other immunosuppressive medications.
6c.Within 12 months before enrolment: rituximab, alemtuzumab.
6d.Methotrexate, azathioprine or mycophenolate with a change in treatment within 3 months before enrolment.
6e.Patients on corticosteroids not on a maintenance dose and where the dosage is likely to be tapered during the duration of the trial.
7.Laboratory results:
7a.Serum Immunoglobulin A (IgA) level less than 5% of the lower limit of normal (LLN).
7b.A positive result at screening on any of the following viral markers: human immunodeficiency virus-1 (HIV-1), HIV-2, hepatitis C virus, or hepatitis B virus.
7c.Abnormal laboratory parameters: creatinine greater than 1.5 times the upper limit of normal (ULN), hemoglobin less than 10 g/dL.
8.General criteria:
8a.Inability to comply with study procedures and treatment regimen (e.g., SC self-administration of the subject, a family member, or other locally available person).
8b.Rescreening after failing to fulfill any additional inclusion criterion (i.e. CIDP relapse during the IVIG withdrawal period or no stabilization during restabilization period).
8c.Mental condition rendering the subject (or the subject*s legally acceptable representative[s]) unable to understand the nature, scope and possible consequences of the study.
8d.Pregnancy or nursing mother.
8e.Intention to become pregnant during the course of the study.
8f.Female subjects of childbearing potential either not using, or not willing to use, a medically reliable method of contraception for the entire duration of the study, or not sexually abstinent for the entire duration of the study, or not surgically sterile.
8g.Participation in another clinical study or use of another IMP within 3 months before enrolment.
8h.Employee at the study site, or spouse/partner or relative of any study staff (e.g.,

investigator, sub-investigators, or study nurse)

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-01-2013
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Hizentra
Generic name:	Human Immunoglobuline (SCIg)
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	14-03-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	11-05-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-06-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-09-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-10-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-11-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	10-09-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-11-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-03-2016
Application type:	Amendment
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
EudraCT	EUCTR2011-003448-28-NL
CCMO	NL38269.018.12