Intravenous immunoglobulins as early treatment in newly diagnosed idiopathic inflammatory myopathies (IMMEDIATE): a pilot study.

Published: 21-12-2016
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Explore efficacy, safety, and feasibility (of an eventual future phase 3 trial) of intravenous immunoglobulins as treatment for patients with idiopathic inflammatory myopathies.

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

Summary

ID

NL-OMON46904

Source
ToetsingOnline

Brief title
IMMEDIATE

Condition

- Autoimmune disorders

Synonym
muscle inflammation, myositis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Biotechnologische industrie,CSL Behring,

Zwitserland

Intervention

Keyword: Early treatment, Idiopathic inflammatory myopathies, Intravenous immunoglobulins, Pilot

Outcome measures

Primary outcome

The number of patients with clinical significant improvement, defined as *40

points improvement on a continuous, weighted score of 6 core set measures (a

internationally validated and combined outcome measure of the International

Myositis Assessment and Clinical Studies group) after 9 weeks of treatment.

1. Physician Global Activity

2. Patient Global Activity

3. Manual Muscle Testing

4. Health Assessment Questionnaire

5. Muscle enzymes

6. Extra-Muscular Activity

Secondary outcome

Efficacy of IVIg (measured 9 weeks after treatment)

1. Time to at least moderate improvement on the CIS

2. Minimal improvement (20-40 points) on each of the 6 IMACS CSMs

a. Physician Global Activity

b. Patient Global Activity

c. Manual Muscle Testing

d. Health Assessment Questionnaire

e. Muscle enzymes

f. Extra-Muscular Activity

3. Moderate improvement or more (*40 points) on each of the 6 IMACS CSMs

a. Physician Global Activity

b. Patient Global Activity

c. Manual Muscle Testing

d. Health Assessment Questionnaire

e. Muscle enzymes

f. Extra-Muscular Activity

4. The number of deterioration patients needing rescue therapy

5. Significant improvement in Academic Medical Center Linear Disability Scale

(ALDS)

6. Significant improvement in Modified Rankin Scale (MRS)

7. Significant improvement of dysphagia (if present) on the Amyotrofic Lateral

Sclerosis Severity Scale Swallowing (ALSSS-SW)

8. Significant improvement in dynamometric muscle strength

9. Significant improvement on the Rasch modified MRC Sum Score (Rasch-MRC)

10. Significant improvement on the EuroQol Group Health Questionnaire (EQ-5D-5L)

11. The number of participants with significant decrease of T2 weighted

(T2)/short tau inversion recovery (STIR) hyperintensity of muscles and fascia

on MRI

12. The number of patients with significant change of size and echo intensity

of muscles and fascia on ultrasound (US)

13. The number of patients with change of highly expanded B-cell clones

14. RNA and RBM20 expression before and after IVIg treatment

15. galectin-9 and CXCL10 levels before and after IVIg treatment

16. relation between treatment respons and serum IgG

Safety of IVIg (measured during the total duration of the study)

The number of serious adverse events (SAEs)

Feasibility of a future trial (assessed at end report)

1. Process

a. recruitment rate

b. retention rate

2. Resources

a. Estimation of total time investment

b. Estimation of total financial investment

3. Management:

a. Potential human/personnel concerns

b. Potential data concerns

c. Potential logistics concerns

Study description

Background summary

Idiopathic inflammatory myopathies , IBM excluded, are a group of treatable auto-immune disorders. Due to insufficient efficacy or side-effects of corticosteroids, additional immunosuppressive treatment is often needed. Clinical outcome is often disappointing, with many patients having a polyphasic

or chronic clinical course. Relative under treatment in the first period resulting in irreversible damage, is thought to contribute to this. While not yet formally investigated, there are suggestions that early treatment with intravenous immunoglobulins might induce a fast response. We hypothesize that the use of early IVIg leads to fast improvement in newly diagnosed patients, which may ultimately lead to improved short and long term outcome.

Study objective

Explore efficacy, safety, and feasibility (of an eventual future phase 3 trial) of intravenous immunoglobulins as treatment for patients with idiopathic inflammatory myopathies.

Study design

Investigator initiated, multicenter pilot study with an uncontrolled pre/posttest design.

Intervention

Standaard regimen
- Week 0: IVIg 2g/kg
- Week 3: IVIg 1g/kg
- Week 6: IVIg 1g/kg
- Week 9: IVIg 1g/kg + start standaarbehandeling

Optiona regimen: in case of insufficient respons on evaluation at week 4
- Week 0: IVIg 2g/kg
- Week 3: IVIg 1g/kg
- Week 4: IVIg 1g/kg
- Week 8: IVIg 2g/kg
- Week 9: start standard treatment

Study burden and risks

Structured risk analysis shows a negligable risk for patients. Side effects: treatment with intravenous immunoglobulins may lead to mild infusion reactions and rarely to serious adverse events such as thrombo-embolic events or hemolysis. Indeed, extensive experience from comparable patient populations have shown that IVIg is generally well tolerated. Possible, temporary undertreatment in the first 9 week in case of IVIg unresponsivity. However, we consider this as temporary and adequately managable with escape medication (consisting of standard corticosteroid therapy) and the option to intensify the maintenance infusion from 1g/kg to 2g/kg. Extra follow-up ancillary investigations (one MRI, one ultrasound and two times an extra laboratory sample (70.5 ml per sampling moment, which will be in principle, combined with

a regular laboratory investigation) and clinical visits for infusion of intravenous immunoglobulin are considered a minor inconvenience to study participants.

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

* Adult patients (age * 18 years);* Subacute-onset of disease (disease duration of * 9 months) of muscle symptoms;* Biopsy proven IIMs (see for diagnostic criteria Hoogendijk et al. 2004, note: ASS is considered a separate entity, but new criteria in which it has been included, has yet to be published).
o Dermatomyositis
o Non-specific myositis/antisynthetase syndrome
o Immune-mediated necrotizing myopathy;* Minimal disability of:

o MMT score reduction of 10% or lower and,
o 2 other of the core set measures score abnormalities defined as:
- Physician Global Activity 2 cm or more
- Patient Global Activity 2 cm or more
- Health Assessment Questionnaire 0.25 or more
- Muscle enzymes more than 1.5 times upper limit of normal
- Extra-Muscular Activity 2 cm or more

Exclusion criteria

* IVIg treatment related:
o Subjects who have received clinical relevant immunosuppressive medication (e.g. plasmapheresis, biologicals, immune therapy etc.) within the last 6 months with the exception of prednisone dosed as follows:
* daily dose of 20mg or lower
* used for 2 weeks or less
* no evident clinical response;o history of thrombotic episodes within the 2 years prior to enrolment
o known allergic reactions or other severe reactions to any blood-derived product
o known IgA deficiency and anti-IgA serum antibodies
o pregnancy (wish).;* Conditions that are likely to interfere with:
o compliance (legal incompetent and/or incapacitated patients are excluded) or,
o evaluation of efficacy (e.g. due to severe pre-existing disability as result of any other disease than IIM or language barrier).;* Lack of informed consent (IC)

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-04-2017

Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Privigen
Generic name:	Normal human immunogloblins
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	21-12-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-03-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	19-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-12-2018
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	EUCTR2016-004766-26-NL
CCMO	NL58747.018.16

Study results

Date completed:	13-04-2019
Actual enrolment:	20