Intravenous immunoglobulin and prednisone vs. prednisone in newly diagnosed myositis: a double blind randomized clinical trial.

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This study has been transitioned to CTIS with ID 2024-516057-42-00 check the CTIS register for the current data. The primary aim is to examine whether early addition of IVIg to standard treatment with prednisone in patients with newly diagnosed...

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

Summary

ID

NL-OMON49246

Source
ToetsingOnline

Brief title
IVIG in myositis: TIME IS MUSCLE

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,Sanquin Plasma Products B.V, Amsterdam, Nederland

Intervention

Keyword: early treatment, idiopathic inflammatory myopathies, intravenous immunoglobulins, myositis

Outcome measures

Primary outcome

The Total Improvement Score (TIS) of the myositis response criteria after week

12 compared to baseline t=0, before treatment.

Total Improvement Score is based on 6 validated core set measures which each

determine disease activity as defined by the International Myositis Assessment

and Clinical Studies (IMACS) group.

Secondary outcome

1. Time to response (response defined as Total Improvement Score >40 points)

2. Total improvement score (IMACS)

3. Each of the cores set measures out of which IMACS TIS is composed.

4. Patient-Reported Outcomes. Three PROMs of the Patient Reported Outcomes

Measurement Information System (PROMIS) will be used. These

PROMs relate to different aspects of quality of life in patients with

myositis: fatigue, pain interference and physical function.

5. Health related quality of life assessed with EuroQol Group Health

Questionnaire (EQ5D).

6. Physical activity measured by accelerometry.

7. Fatigue via CIS Fatigue questionaire

8. Mean daily prednisone dosage

9. Muscle hyperintensities and fatty infiltration on total body MRI (T1 and

T2/STIR)

10. IgG blood levels

11. Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) in the

subgroup of patients with dermatomyositis

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 undertreatment 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 in addition to standard therapy with prednisone might induce a fast and clinically relevant response. We hypothesize that the use of early IVIg in addition to standard therapy with prednisone leads to fast and clinically relevant improvement in newly diagnosed patients, which may ultimately lead to improved short and long term outcome.

Study objective

This study has been transitioned to CTIS with ID 2024-516057-42-00 check the CTIS register for the current data.

The primary aim is to examine whether early addition of IVIg to standard treatment with prednisone in patients with newly diagnosed myositis leads to superior clinical outcome after 12 weeks.
Our secondary aims are to examine the effect the intervention on health-related quality of life, physical functioning and a biomarker (muscle MRI) on the short and longer term.

Study design

A double blind controlled randomized clinical trial.

Intervention

Administration of 2 gram/kg IVIg at baseline after 4 and 8 weeks (intervention arm), or placebo (Saline 0.9%) infusions at baseline and after 4 and 8 weeks (control arm). All patients will be treated with 1 mg/kg prednisone (max. 80 mg daily) which is standard care.

Study burden and risks

Following a screening visit at the outpatient clinic, patients will be admitted to the neurology ward of the Amsterdam UMC for the first day of the study treatment. The remaining study medication will be administered at home, according to routine clinical practice for IVIg. A second and third study intervention will be administered at home after 4 and 8 weeks. At baseline and after 4, 8, 12, 26 and 52 weeks outcome assessments will be performed at the outpatient clinic. The outpatient clinic visits at baseline and after 12, 26 en 52 weeks will be combined with regular outpatient clinic visits. The additional burden related to outcome assessments will consist of MRI muscle imaging after 12 weeks, basic physical examination (manual muscle strength testing) and blood sampling after 4 and 8 weeks and filling in questionnaires at baseline and after 4, 8, 12, 26 and 52 weeks. In addition, participants are asked to wear a watch from baseline for 12 weeks and return it at the outpatient clinic visit. After 26 weeks the participants will be given the watch at the outpatient clinic. They will be asked to wear it for one week and return it soon afterwards.

Treatment with intravenous immunoglobulins may lead to mild infusion reactions and rarely to serious adverse events such as thrombo-embolic events or hemolysis. Vena punctures may cause discomfort or lead to a hematoma. Additional study procedures will cause minor inconveniences for the study subjects.

Extensive experience from comparable patient populations have shown that IVIg is generally well tolerated. Moreover, the study has potential benefits for its subjects. Foremost, in case of superiority of the TIME IS MUSCLE protocol, patients will experience the advantage of IVIg in addition to prednisone, namely a more rapid treatment response/ early suppression of the inflammatory process preventing early disease damage, leading to improved short and long term outcome.

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 (18-80 years) with idiopathic inflammatory myopathy (IIM), according to diagnostic criteria:
- Dermatomyositis
- Non-specific/overlap myositis including antisynthetase syndrome; formerly known as polymyositis
- Immune mediated necrotizing myopathy
• Disease duration; 12 months
• Signed informed consent

Exclusion criteria

• Disease duration > 12 months
• Immunosuppressive medication within the last 12 months (azathioprine, methotrexate plasmapheresis, IVIg, biologicals). We will allow prednisone dosed as follows:
- Daily dose 20 mg or lower, used for two weeks or less
- Daily dose higher than 20 mg, used for 1 week or less

- No evident clinical response
• Related to IVIG:
- History of thrombotic episodes within 10 years prior to enrolment
- Known allergic reactions or other severe reactions to any blood-derived product
- Known IgA deficiency and IgA serum antibodies
- Pregnancy (wish)
• Conditions that are likely to interfere with:
- Compliance (legal incompetent and/or incapacitated patients are excluded), or,
- Evaluation of efficacy (e.g. due to severe pre-existing disability as a result of any other disease than myositis or due to language barrier)

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:	Recruiting
Start date (anticipated):	13-09-2021
Enrollment:	48
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	27-01-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-05-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-04-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	30-05-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389

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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
EU-CTR	CTIS2024-516057-42-00
EudraCT	EUCTR2020-001710-37-NL
CCMO	NL74270.018.20