IVIG in myositis: TIME IS MUSCLE (TIM)

Gepubliceerd: 10-09-2021 Laatst bijgewerkt: 18-08-2022

Early IVIg treatment in addition to prednisone results in a meaningful clinical response in treatment naive myositis patients in the short term and increased HR-QoL in the long term

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON26160

Bron
NTR

Verkorte titel
TIM trial

Aandoening

Idiopathic inflammatory myopathy, with the exception of inclusion body myositis.

Ondersteuning

Primaire sponsor: Prinses Beatrix spierfonds, Sanquin Plasma Products
Overige ondersteuning: N/A

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Change in Total Improvement Score (week 12 compared to baseline)

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:
In patients with myositis early immunomodulation by intensive treatment (“hit-early/hit-hard” principle) may induce faster reduction of disease activity and prevent chronic disability by disease damage. Intravenous immunoglobulin (IVIg) in addition to standard treatment with prednisone may be beneficial for this purpose: add-on IVIg improves symptoms in steroid-resistant myositis, and monotherapy IVIg leads to a fast and clinically relevant response in nearly 50% of the patients with myositis who were treatment naive (pilot study in 20 patients).

Objective:
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 of the intervention on health-related quality of life, physical activity and a biomarker (muscle MRI) on the short and longer term.

Study design:
A double blind controlled randomized clinical trial.

Study population:
Adult patients (≥18 years) diagnosed with idiopathic inflammatory myopathy (except inclusion body myositis) will be invited.

Intervention (if applicable):
Administration of 2 gram/kg IVIg at baseline and 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.

Main study parameters/endpoints:
The Total Improvement Score (TIS) of the myositis response criteria at week 12 (compared to t=0).

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
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 treatment in neuromuscular disorders. A second study treatment 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 study clinic visits at baseline and after 12, 26 and 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), 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 for three episodes of two weeks within the first 12 weeks anf for one week after 26 weeks

Doel van het onderzoek

Early IVIg treatment in addition to prednisone results in a meaningful clinical response in treatment naive myositis patients in the short term and increased HR-QoL in the long term

Onderzoeksopzet

Week 0, week 4, week 8, week 12, week 26, week 52

Onderzoeksproduct en/of interventie

Three times 2g/kg IVIg or placebo, at 4-week-intervals, directly following a diagnosis of IIM

Contactpersonen

Publiek

Amsterdam UMC, locatie AMC
Renske Kamperman

020-5663856

Wetenschappelijk

Amsterdam UMC, locatie AMC
Renske Kamperman

020-5663856

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

• 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
• Minimal disability defined as at least 10% loss on Manual Muscle Testing (MMT) and abnormal scores on two other Core Set Measures (CSMs) of the international Myositis Assessment and Clinical Studies (IMACS) group (see 'Primary and secondary outcomes').
• Signed informed consent

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

A potentially eligible patient who meets any of the following criteria will be excluded from participation in this study:

• Disease duration > 12 months
• Immunosuppressive medication or immunomodulatory treatment within the last 3 months (e.g. azathioprine, methotrexate, mycophenolate mofetil, tacrolimus, cyclophosphamide, ciclosporine, IVIg, biologicals, Janus kinase inhibitors, plasmapheresis).
• Severe muscle weakness (i.e. bedridden, severe dysphagia, or respiratory muscle weakness) necessitating more intensive treatment than standard glucocorticoids.

Exceptions to abovementioned exclusion criteria:
Prior use of steroids will be carefully judged by the treating physician. Patients are eligible for inclusion if there is no clinical evident response to prior treatment with:
• High-dosed steroids, such as dexamethasone or intravenous methylprednisolone (e.g. 1000mg daily for three days) within 1 week prior to inclusion.
• Daily dosed prednisone 1mg/kg, or equivalent, used for up to 2 weeks prior to screening visit.
• Treatment with low dose prednisone up to three months before screening.

• Use of biologicals or other immunosuppressive or immunomodulatory treatment when meeting the following criteria:
- Stable dose for the past 6 months
- The biological has been approved for a non-muscular condition (e.g. hematological condition, eczema) and is not known for its use in idiopathic inflammatory myopathy
- No history of biological-induced inflammatory myopathy

• 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)
- Use of loop diuretics
- Use of nephrotoxic medication

• 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)

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	13-09-2021
Aantal proefpersonen:	48
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	10-09-2021
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9722
Ander register	METC AMC : METC2020_180

Resultaten