# Predicting by means of in vitro tests the treatment response in patients with MG

Published: 19-12-2022
Last updated: 30-01-2025

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Autoimmune disorders |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON51603

**Source**
ToetsingOnline

**Brief title**
Towards personalized medicine in MG

### Condition

- Autoimmune disorders
- Muscle disorders
- Cardiac therapeutic procedures

**Synonym**
Autoimmune disorder, neuromuscular disease

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Medisch Universitair Ziekenhuis Maastricht
**Source(s) of monetary or material Support:** NIH grant - Rare Disease Network for Myasthenia Gravis

## Intervention

**Keyword:** Op zoek naar persoonlijke medicatie in MG

## Outcome measures

### Primary outcome

- Measure AChR autoantibodies in blood by RIA at different time points before, during and after treatment with immunomodulatory drugs.

- Measure the total IgG titres in blood by ELISA. This can correlate to the aforementioned anti-AChR titres since predominantly AChR-MG is mediated via IgG.

- Identify the immune cell populations through FACs and microscopy analysis.

- Assess disease severity and treatment efficacy based on clinical response at different time points using QMG score.

- Identify TLH and increased germinal centres using 3-Tesla imaging.

### Secondary outcome

To compare resistance and effectiveness of treatment in vitro after 1 year of follow-up.

# Study description

### Background summary

Myasthenia gravis (MG) with the presence of antibodies against the acetylcholine receptor (AChR) is a well-characterized neurological autoimmune disease. Overall, treatment strategy is established, however, treatment responses vary widely between patients. While some improve rapidly, many require long-lasting treatment with several immunosuppressive drugs to achieve (partial) remission, and many MG patients will remain treatment refractory. Muscle weakness, treatment side effects and treatment efficacy variability all contribute to a reduced quality of life, especially in severe and treatment-refractory MG patients.
Currently, there is no method available to predict the effect of

immunosuppressive drugs in individual patients.
Therefore, isolation of lymphocytes and plasma cells, including long-lived plasma cells (LLPCs), that are present in the thymus, blood and bone marrow could be helpful to study the efficacy of different therapies targeting these specific cell types. This could provide an overview of lymphocyte population and potential resistance by assessing in vitro response to various immunosuppressive drugs.

## Study objective

The first aim of this study is to use an in vitro approach using patient*s derived material to accurately and rapidly predict the optimal therapeutic approach that will predict a good clinical response in individual patients. The second aim of this study is to establish a new imaging modality that can accurately identify TLH from normal thymic tissue to prevent unnecessary surgery.

## Study design

This is an observational study with no pharmacological intervention performed in the Maastricht University Medical Centre+ (MUMC+). Combining imaging, pathology and molecular biology, patient material will be analyzed and the in vitro results correlated to clinical outcome of the patient.
Fresh thymus, BM and blood will be collected from patients undergoing thymectomy, processed and subsequently cultured for the purpose of testing immunosuppressive and novel therapeutics in vitro. 20 AChR-MG patients will undergo 3-T imaging to observe presence or absence of TLH. The in vitro and imaging results of these patients will be correlated with the clinical information available on disease severity and treatment response before and after thymectomy, during follow-up visits at the MUMC+ and/or other medical centers. The 3-T imaging is only additional and will not interfere with any surgery/treatment decisions.

## Study burden and risks

Blood withdrawl: 80 mL blood is taken during outpatient clinic and then at 3 further follow-up time points. It involves minimal risk and discomfort.
Thymectomy: robotic assisted thorascopic thymectomy is part of standard treatment in AChR-MG patients and it is considered low-risk. In non-MG thymoma patients, resection is usually performed as a regular treatment as well. Rest material retrieved post-thymectomy does not change the burden on patients.
Bone marrow biopsy: 10-20 mL of BM aspirate will be obtained under general anesthesia from the posterior superior iliac crest. Additionally a bone marrow biopsy cylinder will be removed from the solid bone marrow in the same bone. BM aspirate and biopsies are considered low risk. Patients will not experience discomfort during the procedure as they will be under anaesthesia, however,

some pain can be experienced post-biopsy. Main risks include: fever, infection and/or prolonged bleeding at biopsy site.
Patients will be asked if they agree that their material will be stored in the biobank for the purposes described in this study and/or other related studies. Patients will be informed that their stored samples will be disposed of, upon the patient*s request, and according to laws and regulations.
The results could provide the basis to predict an efficient therapeutic strategy for every individual patient, resulting in personalized immunosuppressive treatment strategies.
The patients will not directly benefit from participating in this study but the research could help to understand the disease mechanisms and whether the therapeutic response observed in vitro mimics the clinical improvement of the patient. In the future this approach can be used as a predictive assay for therapeutic efficacy of different compounds.

# 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

- Thymectomy at the MUMC+
- Capacity to give inform consent
- Willingness to undergo QMG score before thymectomy and at follow up visits
- Willingness to donate blood pre-thymectomy and thymus tissue for research (required)
- Willingness to donate bone barrow (optional)
- Willingness to donate blood pre and post-thymectomy (required)
(3-T Imaging additional inclusion criteria)
- Willingness to undergo 3-T MRI pre-thymectomy
- AChR-MG without suspicion of thymoma
- Ability to perform breath holds

### Exclusion criteria

Exclusion criteria
- Purely ocular AChR-MG
- <16-years old
3-T Imaging exclusion criteria
- Irregular heart rate
- Inability to perform breath holds
- Presence of ferro magnetic materials

## Study design

### Design

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| Study type: | Observational invasive |
| Intervention model: | Other |
| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Basic science |

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 09-12-2024 |
| Enrollment: | 75 |
| Type: | Actual |

## Ethics review

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| Approved WMO Date: | 19-12-2022 |
| Application type: | First submission |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |

## 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 |
|---|---|
| CCMO | NL81592.068.22 |