Auto-antibody sequencing in patients with autoimmune myasthenia gravis and pemphigus

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

Summary

ID

NL-OMON50392

Source
ToetsingOnline

Brief title
Auto-antibody sequencing in patients with autoimmune disease

Condition

- Autoimmune disorders

Synonym
MG, Myasthenia gravis, Pemphigus

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: kostenplaats JJGM Verschuuren.

Intervention

Keyword: Auto-antibody, Myasthenia gravis, Pemphigus, Sequencing

Outcome measures

Primary outcome

Primary Objective:

- To isolate PBMC from patients with AChR MG, MuSK MG, LEMS or pemphigus to

determine the pathogenic B cell receptor sequences.

Secondary outcome

Secondary Objective(s):

- To generate recombinant antibodies derived from pathogenic auto-antibodies

from AChR MG, MuSK MG, LEMS or pemphigus patients.

- To determine the phenotype of pathogenic antibody producing B cells.

- To correlate disease severity and other patient characteristics with

pathogenic antibody producing B cell numbers and B cell receptor sequences.

Study description

Background summary

Myasthenia gravis (MG) and Lambert-Eaton myasthenic syndrome are neuromuscular autoimmune diseases hallmarked by fluctuating and fatigable muscle weakness. These disorders are caused by auto-antibodies inhibiting the function of acetylcholine receptors (AChR), muscle-specific kinase (MuSK) or voltage-gated calcium channels (VGCC) respectively, which culminates in failure of neuromuscular transmission and muscle weakness. Pemphigus is a group of skin disorders in which antibodies are formed against desmosomes leading to blister formation of mucosa and skin.
Pre-clinical studies currently depend on the availability of patient serum and plasmapheresis material. Moreover, the auto-antibody response has only been studied through indirect experimental approaches. Myasthenia gravis and

pemphigus share (immunological)_ disease features.

Study objective

The main objective of this study is to characterize the pathogenic B cells and the auto-antibodies that are responsible for causing the myasthenic or pemphigus syndromes. The secondary objective is to generate recombinant antibodies based on the auto-antibody sequences identified. This would result in an unlimited source of auto-antibodies for pre-clinical studies.

Study design

This is a prospective, single blood donation study.

Study burden and risks

Patients will be invited to participate in this study two weeks before their regular outpatient clinical visit. When the patient consents to participate they will undergo regular MG/pemphigus assessment to determine MG/pemphigus severity. After the standard clinical assessment, 120mL of blood will be withdrawn. Two tubes are part of the standard procedure for auto-antibody titre and haematological and kidney and liver function testing. The remainder will be used to isolate PBMC. One hundred twenty ml of blood withdrawal can be considered safe as in a blood donation setting a 5 fold of blood volume is withdrawn without significant risks for the donator. All procedures mentioned for this protocol are part of the standard outpatient clinical visit except the volume of blood that is withdrawn. The risk for the patients to participate in this study is therefore considered low. The patient might benefit from this study in the future as the proposed study might yield more insight in the disease mechanism and facilitates pre-clinical therapeutic tests.

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

For myasthenia gravis:
1. Males and females aged between 18 years and older at the time of the blood donation.
2. Patient with ocular or generalized AChR MG, MuSK MG or LEMS; and
3. A positive serologic test for AChR antibodies > 0.5 nmol/l or MuSK antibodies >0.1 nmol/l or VGCC antibodies >20 fmol/l. , For Pemphigus:
1. Males and females aged between 18 years and older at the time of the blood donation.
2. Patient with pemphigus subtypes and
3. A positive serologic test for Dsg1 antibodies > 0.5 nmol/l or Dsg3 antibodies >0.1 nmol/l.

Exclusion criteria

For myasthenia gravis and pemphigus:
1. Any confirmed or suspected immunosuppressive or immunodeficient condition not related to the treatment of MG, including human immunodeficiency virus (HIV) infection, or a family history of congenital or hereditary immunodeficiency.
2. History or evidence of administration of immunoglobulins within 1 month prior to the blood withdrawal.
3. The investigator can exclude patients for this trial which are deemed not suitable for any reason.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-03-2017
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO

Date:	28-02-2017
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	22-05-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	23-07-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL60336.058.16