Multicenter Study of LRP4 and Agrin Antibodies in Myasthenia Gravis (MG)
Michael Rivner (Augusta, GA), plus 16 sites across the US

About 90% of people with immune-mediated generalized MG have antibodies to AChR or MuSK. This program focuses on remaining 10% of patients (antibody- or sero-negative MG, aka double negative MG (DNMG)). Prior studies found that some DNMG had antibodies to important proteins in the muscle endplate, LRP4 and agrin. These antibodies are likely disease-causing because they can produce MG when injected into rodents. Among 182 DNMG patients, 12.6% (23) had LRP4 antibodies and 13.7% (25) had agrin antibodies. Twenty-two of the subjects (12.1% of the total) had both LRP4 and agrin antibodies. Overall, about 14% of DNMG patients had antibodies to LRP4, agrin or both. When initially evaluated, 70% of patients had moderate or more severe MG. Ocular manifestations and bulbar manifestations were common. Most patients’ symptoms were controlled with standard therapies. With treatment, 92.3% of patients had only ocular manifestations or mild severity generalized MG.

Sensitivity of Neurophysiologic Tests Regarding the Neuromuscular Junction in Patients with Congenital Myasthenic Syndromes (CMG)
Vitor Marques Caldas (Brasília, Brazil), plus several collaborators in Brazil

Congenital means present at birth. CMG encompasses a variety of rare genetic disorders that compromise function of the neuromuscular junction. CMG is caused by mutations of important proteins that are involved with ACh release; ACh processing in the very small space between the nerve terminal and endplate region of the muscle fiber and conversion of chemical trigger (ACh) into an electrical response at the endplate by the ACh receptor and supporting structural proteins. In part due to the large number of different proteins that can be distorted to produce a CMG, the clinical manifestations of CMG are much more variable than the presentations of acquired MG. In addition, because the mutated proteins might be involved in functions at other places in the body, CMG can have manifestations in organs other than muscle. There is no blood test for CMG. Specifically when both repetitive stimulation EMG studies and single fiber EMG (one measure of SFEMG is something called jitter) are used clinicians can identify CMG with high sensitivity and distinguish CMG from other conditions with high specificity. Therefore this study is extremely important because it demonstrated that specific types of EMG testing can distinguish CMGs from other congenital disorders that produce weakness. Imagine that you are a parent of child who suffers from weakness. The clinicians treating your child need to know precisely what your child has in order to develop an effective treatment strategy. This study showed that specific EMG tests can determine if your child has CMG.
Phenotypic Variation between Early Onset and Late Onset Myasthenia Gravis
Pragma Roy (South Burlington, VT), Michael Hehir (South Burlington, VT)

This was a large study involving 551 people with MG. The study group was divided into 2 groups. Early onset MG began at or before 59 years of age (182 subjects), while late onset MG manifests at age 60 or later (369 subjects). EOMG patients were more likely to be women. LOMG patients were more likely to have AChR-MG. EOMG tended to be more severe at onset. Subjects with LOMG were more likely to achieve a state in which they had minimal manifestations, prolonged remission (symptom-free) or a state of remission from symptoms while receiving treatment.

Myasthenia Gravis Patient and Physician Opinions about Immunosuppressant Dose Reduction
Michael Hehir (South Burlington, VT), Emma Ciafaloni (Rochester, NY), Anna Punga (Uppsala, Sweden)

International MG Consensus Guidelines define successful MG treatments as those that result in minimal disease manifestations or remission with no more than minimal adverse events (AE). This is a part of a large study on the ability to reduce immune-suppressant therapy dosages without triggering a relapse. This study considers both the clinician and patient’s opinion as to what the best balance between symptoms of MG and side effects of treatment is. The objective is to devise strategies for tapering MG treatments that meet a patient’s desired balance between MG manifestations and treatment side effects. The study is in progress.

Minimal Manifestations Status and Prednisone Withdrawal in the MGTX Trial
Ikjae Lee (Birmingham, AL), plus a large number of collaborators from the MGTX trial

The MG thymectomy trial (MGTX) was a large international study that demonstrated that subjects who had a thymectomy had a better clinical course than subjects just treated with medication. This study examined the how rapidly subjects achieved a state of minimal MG symptoms (MMS) and how likely a subject was to be able to be completely tapered off of prednisone. Subjects who had a thymectomy were more likely to achieve MMS status and achieved MMS faster than subjects only on medication. Additional thymectomy subjects were more likely to be able to be completely tapered off of prednisone. Subjects felt better if they could completely taper off of prednisone. Subject perception of stress increased with higher doses of prednisone.

A Randomized, Placebo-Controlled, Parallel Group Study to Evaluate the Effect of Amifampridine Phosphate in Patients with MuSK Antibody Positive Myasthenia Gravis
Stanley Iyadurai (Coral Gables, FL), Christian Buettner (Greensboro, NC)

Amifampridine (4-aminopyridine, (4-AP)) is a chemical that increases release of ACh. It has been used in some neuromuscular disorders. It is not very useful for most people with AChR-MG. People with MuSK-MG respond differently to treatments than AChR-MG patients and this study considers whether 4-AP may benefit people with MuSK-MG. This study is open with 29 patients enrolled at the time of submission. 15 sites around the US involved in study.