The 2020 MGFA Scientific Session was held within the virtual American Association of Neuromuscular and Electrodiagnostic Medicine Annual Meeting on October 3, 2020. The program chairs were: Araya Puwanant, MD from Wake Forrest University, Winston-Salem, NC; Srikanth Muppidi, MD from Stanford Univ Hosp., Palo Alto, CA and Shruti M. Raja, MD from Duke University, Durham, NC. Most presentations addressed ongoing and planned clinical efforts to improve treatments and to ultimately find a cure for MG. I urge people to visit the federal clinical trials website (https://clinicaltrials.gov) and search for "myasthenia gravis" to find out about clinical trials related to MG. Additionally, I encourage people with MG to consider joining a clinical trial for which they may be eligible.

In order to improve understanding of the research presentations, I will present a brief overview of MG and relevant aspects of immunology. I also encourage people to review the background material about MG on the MGFA website.

Immunology Overview - MG is an auto-immune disease involving the site of chemical communication between nerve and muscle called the neuromuscular junction (NMJ). The immune system normally recognizes chemicals that are part of your body – "recognizes self." In MG, the immune system malfunctions and attacks specific proteins at the NMJ. The most common targets of the autoimmune attack are the acetylcholine receptor (AChR) and an associated protein called MuSK. About 75-80% of MG patients have detectable antibodies to AChR and about 10% have MuSK antibodies. About 5% of MG patients have antibodies to other molecular components of the NMJ such as agrin or a protein called LRP4. Lymphocytes (one type of "white blood cell") are a class of immune cells that are divided into two large groups: Thymus-derived lymphocytes (T-cells) and B-cell lymphocytes. T-cells are involved in cell-medicated immune responses in which cells attack immune targets. T-cells also modulate the activity of B-cells. B-cells are responsible for producing antibodies, chemicals that target specific parts of proteins called epitopes. MG is T-cell dependent antibody mediated disease in which T-cells modulate the activity of B-cells that produce antibodies that are directed primarily against NMJ proteins such as AChR, MuSK, agrin or LRP4. Pathologic antibodies binding in MG, particularly antibodies targeting AChR damage the NMJ by activating a chemical chain reaction involving a complement. Complement is an immune-medicated chemical cascade that destroys proteins and injures or destroys cells. A key element in the complement cascade is component 5 (C_5). Tolerance refers to a process in which an immune response to a specific agent is suppressed. For example, a person might overcome a specific allergy, with medical assistance, by becoming tolerant to the agent inducing the allergy. One mechanism of tolerance is for T-cells to become insensitive to a disease-inciting antigen.

There are three summaries corresponding to the nature of the presentations: 1) Keynote and platform presentations, 2) Data Blitz presentations and 3) Posters. Here I summarize group #1. Data Blitz presentations and posters summaries follow separately.

Keynote Presentation

MGNet: Rare Disease Network for Myasthenia Gravis – Henry J Kaminsky, George Washington Univ, Washington DC

People with MG know it is a rare disease. Providers, advocates and patients need to be organized to determine what interventions work, encourage researchers to develop new treatment strategies and make healthcare organizations aware of the needs of people with MG. MGNet is a new member of 23 NIH supported networks of designed to support clinical and other forms of research related to specific rare diseases. MGNet includes 9 university medical centers, major advocacy groups such as MGFA and pharmaceutical partners. MGNet's aims include research to better understand the triggers and treatment options for MG. Establishing a robust clinical network greatly facilitates preforming and completing clinical trials. MGNet also mentors young clinicians and basic researchers to provide a pathway for the emergence of future leaders in MG treatment and research. In addition, the network aims to improve awareness of physicians, scientists, and laying public regarding the unique needs of patients with MG. Besides the NIH funding, MGFA has pledged in support of the network research pilot study program. The MGNet's future plans include expanding the new clinical sites and the patient advocate partners which I think it is important. I proud of the successful efforts of many including MGFA to develop MGNet and successfully obtain NIH funding. I am certain that MGNet will improve the lives of people with MG by enhancing clinical treatment and research.

Platform Presentations (talks)

A) **Validation of a Live Clustered Cell Based Acetylcholine Receptor Assay in a Cohort of Double Seronegative Definite Myasthenia Gravis Patients** – Jeff Guptill Duke, Durham, NC

B) **Live Cell-Based Assay for Antibodiest Clustered Acetylcholine Receptor in Myasthenia Gravis, Cross Validation, Inter-Assay Stability and Utility in a Pediatric Cohort Suspected for MG** – H Frykman Univ British Columbia, Vancouver, Canada

These were 2 studies of a new technique to detect antibodies in people with MG. About 10-15% of people with MG do not have detectable antibodies using currently available blood testing. !!This study evaluated another way of detecting antibodies. They studied people with a clinical diagnosis of MG who did not have detectable antibodies using current techniques. The new technique was able to detect antibodies in 12% of adults who were seronegative with the current assay. The new cell based assay was studied in children with MG and found to detect antibodies in all of the children who had antibodies with the current technology. The next step is to see if the cell based assay is able to detect antibodies in seronegative children. Finding a more sensitive assay for antibodies is an important step for people with MG because it will enable more people to utilize treatments designed for antibody positive people.

Affinity Maturation is Required for Pathogenic Monovalent IgG4 Autoantibody Development in Autoimmune Myasthenia Gravis - M Fichtner Yale, New Haven, CT
This was a technical study of the antibodies in people with MuSK MG. The results of this study increased understanding of the development of antibodies to MuSK.

Feasibility and Acceptability of Remote Monitoring of Patients with Myasthenia Gravis Using Digital Technology – A Guidon, Mass General Hosp, Boston, MA
During the current pandemic and possibly in years to come clinicians will need to perform virtual clinical assessments. This presentation described very clever use of readily available technology such as smart phones combined with intelligent use of existing measures of MG severity to create meaningful virtual clinical assessments that are reproducible so that clinicians can follow a person's progress. This study shows how clinical follow-ups can be done safely during a pandemic and for people in remote areas.

Covid-19 Associated Risks and Effects in Myasthenia Gravis (Care-Mg): An International Physician-Reported Registry - S Muppidi, Stanford Univ, Palo Alto CA and a host of others in the US, UK and Germany.
This study is designed to determine if people with MG who develop COVID are at greater risk of complications or death. The study reported on the initial 36 people studied. Ten died due to COVID-19 (28%). While this mortality fraction is higher than the general population mortality rate, the numbers are too small at present to draw any firm conclusions.

Overview for the next two studies
A phase 2 trial is designed to determine if a treatment works to benefit people with a specific condition. Phase 2 trials can also determine the proper dosing. A phase 3 study is done after the efficacy of an intervention has been established. A phase 3 study may compare the effectiveness of a new intervention to an established treatment.

A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, Efficacy, Pk, and Pd of Nipocalimab (M281) in Adults with Generalized Myasthenia Gravis - J Guptill Duke Univ, Durham, NC plus a large cohort of US and international collaborators.
Nipocalimab is a laboratory produced antibody that targets naturally occurring antibodies including the antibodies that cause disease in MG. This treatment is basically designed to supplement or replace other treatments that suppress antibody-mediated immune responses. The potential advantage of this treatment compared to a treatment such as prolonged use of prednisone (or equivalent agents) is less severe side effects. Prednisone is effective in MG, but causes problems because it breaks down body proteins and releases glucose. Hence, side effects of prednisone use include wasting of protein stores, which are muscle, bone, and skin. Prednisone also causes some types of fat to proliferate resulting in excess facial, abdominal and back fat. Additionally, people with MG respond differently to various treatments, which makes it imperative to develop multiple treatment options in order to treat as many people with MG as possible. This study has not advanced to the point of providing a definitive answer about the best dosing for Nipocalimab and how effective Nipocalimab is for MG.

Treatment of Patients with Myasthenia Gravis with Efgartigimod: Results of the Phase 3 Adapt Study - J Howard Univ NC, Chapel Hill, NC plus a cohort of US and international collaborators.
Efgartigimod, is a fragment of a human immunoglobulin (IgG1) that interferes with the normal processing of human antibodies leading to a decrease in disease-causing antibodies. This was a Phase 3, randomized, double-blind, placebo controlled, global multicenter 26-week study that evaluated the safety and efficacy of efgartigimod in patients with generalized MG. The study had 167 patients who were randomized to receive Efgartigimod or placebo, 129 subjects had AChR-Abs and 38 did not have detectable levels of AChR-Abs. Among subjects with AChR antibodies, 40% of people receiving Efgartigimod achieved state of minimal symptom expression compared to only 11% of placebo patients. The number of subjects who did not have AChR antibodies was small, but Efgartigimod also appeared to be effective for people who did not have

AChR antibodies. The study investigators concluded that Efgartigimod demonstrated significant efficacy in treating patients with MG with no significant safety issues. I feel that more subjects will need to be evaluated to establish that Efgartigimod is effective for AChR antibody negative patients.