Abstract #1

OUTCOME ON KERATITIS AND TEAR SECRETION OF 2 PATIENTS DIAGNOSED WITH MYASTHENIA GRAVIS WITH ASSOCIATED AUTOIMMUNE DISEASES, WHO WERE RANDOMIZED IN THE NORTHERN LIGHTS TRIAL

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INTRODUCTION: Myasthenia Gravis patients are more likely to develop other immune-related disorders. These autoimmune diseases may be associated with ophthalmic symptoms including blurry vision, tearing, pain, photophobia, foreign body sensation, and ophthalmic signs including moderate-to-severe keratitis.

OBJECTIVE: The aim of this study is to describe the outcome on keratitis and tear secretion of 2 patients diagnosed with MG with associated autoimmune diseases, who were randomized in the clinical trial.

METHODS: The trial is a randomized, double masked, controlled multicentre European trial that assessed MC2-03 eyedrops (ciclosporin 0.03% and 0.06%) for the treatment of moderate-to-severe DED in 255 patients having corneal fluorescein staining score 3 or 4 at baseline. The Schirmer score (per 5 min) was also assessed. 2 patients with medical history of Myasthenia Gravis, a rare disease, were randomized in the trial

RESULTS: Demographics and baseline disease characteristics were comparable with patients being both women, aged over 65 years with severe keratitis (CFS 4) and Schirmer score <10mm/5 min. The MG patient with severe keratitis (CFS 4) at baseline treated with MC2-03 0.03% achieved a 3-grade improvement in CFS at Month 6 whereas the patient treated with the vehicle had a CFS score unchanged at Month 6 (CFS 4). The mean Schirmer score improved from baseline to month 6 for MC2-03 0.03% eye drops (+4mm) compared to a worsening for the vehicle (-2mm).

SUMMARY/CONCLUSION: MC2-03 eyedrops has shown efficacy in Sjögren's patients and cases presented indicate that patients with MG could benefit from ciclosporin eyedrops to improve signs of DED (keratitis, tear secretion).

Disclosures:

Abstract #2

REAL-WORLD PATIENT-REPORTED IMPACT OF MYASTHENIA GRAVIS: INITIAL DATA FROM THE MYREALWORLD MG STUDY

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INTRODUCTION: Myasthenia gravis (MG) is a chronic immunoglobulin G-mediated autoimmune disease, causing debilitating muscle weakness.

OBJECTIVE: To explore the real-world patient-reported impact of MG.

METHODS: This is an ongoing two-year, international, prospective, observational study of ~2,000 adults with MG. Participants use a smartphone application to complete a personal profile about demographics, MG characteristics, and previous care; a monthly tracker about treatments, healthcare visits, adverse events, and productivity; and a monthly selection of validated patient-reported outcomes surveys about symptoms, functioning, quality of life, and the impact of the COVID-19 pandemic.

RESULTS: As of March 9 2021, 1,110 people were enrolled. At least 650 participants provided data for each of the following outcomes. 69% of respondents were female. Median age at MG symptom onset was 37 years (interquartile range [IQR] 24–52); median age at diagnosis was 39 (IQR 26–53). 57% of respondents were positive for MG antibodies, 25% were negative, and 18% did not know their status. The most common Myasthenia Gravis Foundation of America (MGFA) grades at most recent profile update were III (36% of respondents), II (28%), and IV (16%). Median Myasthenia Gravis Activities of Daily Living scale (MG-ADL) score at most recent survey completion was 5 (IQR 3–9). Median Myasthenia Gravis Quality of Life 15-item revised scale (MG-QOL15r) score was 11 (IQR 6–18).

SUMMARY/CONCLUSION: This first analysis of data from the MyRealWorld MG study provides a snapshot of the patient-reported impact of MG. A full interim analysis was performed in May 2021, with further analyses scheduled over the study duration.

Abstract #3

MYCOPHENOLIC ACID LEVELS IN MYASTHENIA GRAVIS

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•INTRODUCTION: Mycophenolate mofetil (MMF) is commonly used to treat myasthenia gravis (MG). Two trials failed to demonstrate a steroid-sparing effect of MMF; further analysis demonstrated its effectiveness but delayed onset of action. When used for post-organ transplantation rejection prophylaxis, MMF is dosed by serum mycophenolic acid (MPA) levels. Significant variability in MPA levels exists in transplant patients receiving fixed doses of MMF.

•OBJECTIVE: Determine whether standard dosing of MMF is effective in all MG patients and evaluate whether patients with higher MPA levels have better disease control.

•METHODS: Patients on MMF at stable dosing for 3 months prior to study entry were recruited. Serum MPA trough levels were drawn 10-14 hours after a dose of MMF. MGFA PIS, MG composite (MGC), and MG-QOL15R scales were performed at baseline and visits 3-6 and 9-12 months later. Chi square tests were performed to evaluate for correlations between MPA levels and clinical measures.

•RESULTS: Nine patients were enrolled and completed the study. Correlations between MPA levels and MGFA PIS were $r=0.093$, $r=0.388$, $r=0.00$, between MPA levels and MGC were $r = 0.256$, $r= -0.631$, $r=0.382$, and between MPA levels and MG-QOL15R were $r= -.345$, $r=0.775$, $r= -0.289$, at 0, 3-6, and 9-12 months, respectively. There was no statistical significance of these correlations at any time point.

•SUMMARY/CONCLUSION: In this small study, no correlation was found between MPA levels and measures of disease control. A larger study is required to better ascertain this association and potential implications for MMF dosing in patients with MG.

Abstract #4

POSTSYNAPTIC NEUROTRANSMITTER RECEPTORS REGULATE PRESYNAPTIC NEUROTRANSMITTER IDENTITY AT THE NEUROMUSCULAR JUNCTION

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INTRODUCTION:
Postsynaptic targets are known to influence presynaptic properties. In consideration of alternative therapies for myasthenia gravis, we investigated if postsynaptic receptors participate in retrograde signaling.

OBJECTIVE:
To test whether targeted expression of novel neurotransmitter receptors in myocytes induce expression of the cognate neurotransmitter in presynaptic motorneurons (MNs).

METHODS:
GABARabg receptor transcripts microinjected into a Xenopus laevis ventral blastomere for sparse GABAR expression in myocytes. Immunohistochemistry for GABAergic and cholinergic markers 3 days post fertilization (dpf). GABARa-only and GABARabE179Qg mRNA used as controls. Sharp electrode recordings of miniature endplate potentials (mEPPs) in control and GABARabg tadpoles 4dpf.

RESULTS:
Sparse ectopic expression of GABARabg in the postsynaptic myocytes of Xenopus NMJ during development induces expression of GABA neurotransmitter in presynaptic cholinergic MNs. Co-expression of the MN markers Hb1 and ChAT confirms that these cholinergic-GABAergic- neurons are MNs. The appearance of the GABA synthetic enzyme GAD67 and vesicular GABA transporter in these MNs suggests that MNs are capable of synthesizing and packaging GABA. Misexpression of GABAR-a only, resulting in a non-functional GABAR, does not induce these changes. Electrophysiological recordings from the myocytes reveal that the GABARabg NMJs exhibit GABAergic along with cholinergic mEPPs, indicating that GABA is functionally released.

SUMMARY/CONCLUSION:
Targeted expression of a novel receptor in myocytes induces expression of cognate neurotransmitter in motorneurons, forming a functionally active synapse. Such receptor-mediated retrograde signalling at the synapse may be an "acknowledgment" signal for maintaining transmitter identity under normal conditions and could provide an alternative therapy for receptor-associated disorders including myasthenia gravis.

Abstract #5

EFFECT OF COVID-19 ON MYASTHENIA GRAVIS

Timothy Quezada (Pittsburgh, PA)

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INTRODUCTION: Certain neurological conditions are known to worsen with infection by SARS-CoV-2. Little is known regarding the effects of COVID-19 on patients with myasthenia gravis (MG). In this report, we describe the outcomes of fifteen cases of patients with confirmed MG and COVID-19.

OBJECTIVE: It is unclear whether infection with COVID-19 leads to worse neurological outcomes in patients with MG regarding common symptoms such as limb weakness, oculobulbar weakness, and respiratory failure. The aim of this study is to determine if COVID-19 infection worsens short term MGFA grading in a cohort of myasthenia gravis patients, with the intent to help providers understand the effect COVID-19 may have on patients with MG.

METHODS: Retrospective chart review of fourteen patients with MG and COVID-19. Information regarding gender, age, MG phenotype (ocular MG, generalized MG), antibody status, disease severity prior to infection (using Myasthenia Gravis Foundation of America classification criteria), disease medications prior to COVID-19 infection, and clinical outcomes after COVID-19 infection were collected. All patients within our institution with clinically and/or serologically confirmed MG and a SARS-CoV-2 infection were included.

RESULTS: After four months or more follow up of COVID-19 infected myasthenia gravis patients, the 2/3 who survived showed no change in MGFA grade. In patients succumbing to infection by SARS-CoV-2, all evidence points towards isolated, devastating inflammatory lung disease without obvious myasthenia gravis exacerbation contributing to mortality.

SUMMARY/CONCLUSION: Our series of patients with myasthenia gravis and COVID-19 infection did not reveal MGFA score worsening in those in whom it could be tested.

NOMOGRAM FOR SHORT-TERM OUTCOME ASSESSMENT IN ACHR SUBTYPE GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: An accurate prediction for the prognosis can help in guiding the therapeutic options and optimizing the trial design for generalized myasthenia gravis (gMG). We aimed to develop and validate a predictive nomogram to assess the short-term outcome in patients with anti-acetylcholine receptor (AChR) antibody-positive gMG.

METHODS: We studied 165 patients with MG who were immunotherapy naïve with the AChR subtype at 5 tertiary centers in China (96 patients for derivation, 24 for temporal validation, and 45 for external validation). A total of 120 gMG patients in Huashan Hospital were enrolled for derivation(n=96) and temporal (n=24) validation. Then, this nomogram was externally validated using 45 MG patients from other 4 hospitals. The short-term clinical outcome is defined as the achievement of minimal symptom expression (MSE) at 12 months after baseline recruitment. Multivariate logistic regression was used to screen independent factors and construct the nomogram.

RESULTS: The duration≤12 months (p=0.021), ocular score≤2 (p=0.006), QMG score>13 (p=0.008), and gross motor score≤9 (p=0.006) were statistically associated with MSE in AChR antibody-positive gMG patients. The ability of this nomogram in predicting MSE is excellent as the concordance indexes are 0.81 (95% CI, 0.72-0.90) , 0.944 (95% CI 0.83-1.00) and 0.773 (95% CI, 0.63-0.92) in the development, temporal validation, and external validation cohort, respectively.

SUMMARY/CONCLUSION: The nomogram achieved an optimal prediction of MSE in AChR subtype gMG patients using the baseline clinical characters.

Disclosures:

Rui Zhao - The authors declare that they have no conflict of interest.

Ying Wang - The authors declare that they have no conflict of interest.

Xiao Huan - The authors declare that they have no conflict of interest.

Huahua Zhong - The authors declare that they have no conflict of interest.

Jie Song - The authors declare that they have no conflict of interest.

Lei Zhou - The authors declare that they have no conflict of interest.

Jun Lu - The authors declare that they have no conflict of interest.

Jianying Xi - The authors declare that they have no conflict of interest.

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Ting Chang - The authors declare that they have no conflict of interest.

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Abstract #7

INDEPENDENT PREDICTORS FOR DIFFICULT-/PROLONGED-WEANING AFTER INVASIVE MECHANICAL VENTILATION IN MYASTHENIC CRISIS

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INTRODUCTION: The Weaning according to a New Definition (WIND) classification has not been tested in myasthenic crisis (MC) who required invasive mechanical ventilation (MV).

OBJECTIVE: To evaluate the association between the weaning process and clinical outcome, as well as to determine independent predictors for difficult-/prolonged-weaning in MC patients.

METHODS: MC patients requiring invasive MV were recruited from five intensive care units of Huashan Hospital Fudan University from Jan 2014 through Sep 2020.All patients were classified into different groups according to the WIND classification. Differences in clinical variables were compared. Independent predictors for difficult-/prolonged-weaning were analyzed by multivariate logistic regression analysis.

RESULTS: Among the 124 consecutive MC patients enrolled, we finally included 66 MC patients into no-weaning group and weaning group. The weaning group was then sub-divided into short-weaning group (n=13, 19.7%), difficult-weaning group (n=26, 39.4%), and prolonged-weaning group (n=22, 33.3%). Short-weaning group had a lower prevalence of pneumonia (23.1% vs. 75.0%, p <0.001) and systemic inflammatory response syndrome (SIRS) (38.5% vs. 85.4%, p<0.001), and a higher value in the lowest hemoglobin level (123.0±12.9g/L vs. 108.3±18.1 g/L, p=0.008) and the lowest serum albumin level (33.2±3.4 g/L vs. 29.9±4.2g/L, p=0.014) than the difficult-/prolonged-weaning group. Multivariate logistic regression analysis identified pneumonia and the presence of SIRS within one week of MC as independent predictors for difficult-/prolonged-weaning.

SUMMARY/CONCLUSION: The weaning process classified by WIND classification is associated with clinical outcome in MC patients requiring ventilation. Pneumonia concurrence and the presence of SIRS within one week of MC were identified as independent predictors for difficult-/prolonged-weaning after invasive MV.

Abstract #8

THE DUKE MYASTHENIA GRAVIS CLINIC REGISTRY: SINGLE FIBER EMG FINDINGS

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Abstract – 248 words

Introduction. The Duke MG Clinic Registry contains physician-derived information on patients seen in the Duke MG Clinic since 1980.

Objective: To report single-fiber EMG (SFEMG) findings in Registry patients.

Methods: We reviewed Registry data from patients initially seen in the Duke MG Clinic between 1980 and 2017. Jitter was measured with SFEMG electrodes during voluntary activation using conventional techniques. The extensor digitorum (ED) or frontalis were usually tested first, depending on the distribution of symptoms.

Results: Data from 1,837 SFEMG studies on 1,081 patients with MG were included in the following analyses:

In the initial study jitter was increased in at least one muscle in 990 patients (92%), including 84% of 228 with purely ocular muscle weakness and 94% of 853 with generalized MG. A limb (ED) and a facial muscle were both tested in 393 patients: both were abnormal in 60% of studies; the facial muscle alone was abnormal in 26% and the ED alone in 5%. Frontalis and orbicularis oculi (OO) were both tested in 73 patients: both were abnormal in 20%, OO alone in 42% and frontalis alone in 11%. Follow-up SFEMG studies were performed in 90 patients whose initial studies were negative, and were abnormal in 23 (26%).

THE DUKE MYASTHENIA GRAVIS CLINIC REGISTRY: FACTORS PREDICTING GENERALIZATION OF OCULAR MG

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Janice Massey (Durham, NC)

INTRODUCTION: The Duke MG Clinic Registry contains physician-derived information on 1,567 patients with MG seen at Duke since 1980.

OBJECTIVE: To determine factors associated with generalization in Registry patients with purely ocular weakness at their initial visit.

METHODS: We reviewed Registry data from patients initially seen between 1980 and 2017. Ocular MG was defined as weakness limited to the ocular and/or periocular muscles for at least 2 years after onset.

RESULTS: Of 950 (61%) patients who reported purely ocular symptoms at disease onset, 201 (21%) had weakness limited to the ocular and/or periocular muscles at their first visit–75 females and 126 males. Among the 59 of these (29%) who subsequently generalized within 2 years after disease onset, initial AChR-ab levels were higher, especially in females, and disease duration shorter at the first visit than in those who remained ocular. In multivariable logistic regression only AChR-ab levels remained a significant predictor of generalization (p=0.006) after adjustment for sex and disease duration. Although sensitivity was acceptable (82%), specificity was low (45%). There were no differences in onset age or jitter (limb or face muscle). Females tended to generalize earlier than males. 21 (10.5%) patients generalized more than 2 years after onset.

SUMMARY/CONCLUSION: MG patients with purely ocular weakness at their first Duke MG Clinic visit that became generalized within 2 years of disease onset were more likely to be female, have higher AChR antibody levels and have had MG symptoms for less time than those who remained ocular after 2 years.

Abstract #10

DIAGNOSTIC DELAY IN MYASTHENIA GRAVIS

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INTRODUCTION: Little is known about diagnostic latency in Myasthenia gravis (MG).

OBJECTIVE: To determine factors associated with diagnostic delay in MG.

METHODS: Patients with age ≥18 who were diagnosed with MG, living in the United States, and participating in the MGFA MG patient registry between 7/1/2013 and 1/15/2021 were included. Diagnostic delay was calculated by subtracting year of symptom onset from year of diagnosis. Basic demographics and disease-related history were compared between participants with >1 year vs ≤1 year of diagnostic delay. Multivariable negative binomial regression was performed to assess the association between diagnostic delay (in number of years) and pertinent demographic and disease-related variables.
RESULTS: A total of 3166 patients were included. Mean age of symptom onset was 44, 61% were female, and 85% White (5% Black, 10% other). Those with diagnostic delay >1 year were younger at symptom onset, more frequently female, less likely to report any positive serology, more likely to have seen a neurologist without specialty in MG, less frequently had ocular symptoms at onset, had higher numbers of autoimmune and neurologic comorbid conditions ($p<0.0001$ for all). In multivariable analysis, younger age at symptom onset ($p<0.0001$), being White ($p<0.0001$), absence of ocular symptom at onset ($p=0.0006$), absence of thymoma ($p<0.0001$), and presence of autoimmune and neurologic co-morbidities ($p<0.0001$ respectively) remained associated with longer diagnostic delay.

CONCLUSION:
We have identified factors associated with diagnostic delay in this study. Further study is needed to confirm these findings and establish any causal relationships.

Abstract #11

DEVELOPMENT OF A CELL-BASED ASSAY FOR MEASURING ACETYLCHOLINE RECEPTOR AUTOANTIBODY-MEDIATED COMPLEMENT ACTIVITY IN PATIENTS WITH MYASTHENIA GRAVIS

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INTRODUCTION: Autoantibodies targeting the acetylcholine receptor (AChR) in the serum of myasthenia gravis (MG) patients are broadly polyclonal and heterogeneous in their pathogenic capacity. AChR autoantibodies mediate pathology through three mechanisms: (i) complement-directed tissue damage, (ii) blocking the binding of acetylcholine and (iii) modulation (internalization) of the AChR.
OBJECTIVE: Develop a cell-based assay that measures AChR autoantibody-mediated complement deposition using flow cytometry.
METHODS: An HEK293T cell line, in which the complement regulator genes (CD46, CD55 and CD59) were knocked out using CRISPR/Cas9 genome editing, was generated and tested.
RESULTS: The assay measures AChR autoantibody-mediated complement deposition using human monoclonal antibodies or human serum.
SUMMARY/CONCLUSION: This assay will be valuable to studies that are focused on understanding the mechanisms driving MG pathology and may identify patients anticipated to respond to complement inhibitor therapeutics.

Disclosures:

Abstract #12

MYASTHENIA GRAVIS FROM THE PATIENT'S PERSPECTIVE: REDUCING FATIGUE IS A PRIORITY

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INTRODUCTION: Patients' perspectives of the most bothersome symptoms of generalized myasthenia gravis (gMG) have not been systematically characterized.

OBJECTIVE: To identify these symptoms, their impact on daily life, and patients' treatment goals.

METHODS: Semi-structured telephone interviews (~75 min) were conducted with 28 adult patients with gMG in the US currently receiving ≥1 gMG treatment. Transcripts were analyzed to identify important concepts and themes, without imposing an a priori theory.

RESULTS: Patients were aged 18–78 years; 18/28 (64%) were female and 26/28 (93%) were white. Myasthenia Gravis-Activities of Daily Living total score at baseline (mean ± SD) was 5.4 ± 3.55. Fatigue, blurry/double vision, difficulty swallowing, and breathing problems were reported as the most bothersome gMG symptoms. Patients distinguished between muscle weakness (reported by 86%) and physical fatigue (89%), and identified mental fatigue (46%) as a distinct symptom. Twenty-seven (96%) patients reported fluctuating symptoms, particularly fatigue and weakness. Twenty-six (93%) patients reported onset/worsening of fatigue with usual activities or as the day progressed (fatigability). Twenty-five (89%) patients reported the need to plan, modify, or cancel activities because of symptoms; most (23/25, 92%) did so because of fatigue, fatigability, or muscle weakness. Improvement in fatigue or weakness was the most common treatment goal cited by patients (39%).

SUMMARY/CONCLUSION: Patients with gMG frequently and spontaneously described/highlighted fatigue and weakness necessitating adaptations and restrictions to their daily activities. The negative impact of fatigue and weakness on patients' lives was underscored by the fact that patients considered amelioration of these symptoms as their primary treatment goal.

Abstract #13

REDUCED FATIGUE AS A TREATMENT GOAL IN GENERALIZED MYASTHENIA GRAVIS: PATIENT AND PHYSICIAN PERSPECTIVES IN THE US

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INTRODUCTION: Patient and physician perspectives of generalized myasthenia gravis (gMG) symptoms have not been systematically characterized.

OBJECTIVE: To identify similarities and differences between patient and physician perceptions of bothersome symptoms and treatment goals for patients with gMG.

METHODS: Qualitative interviews were conducted with 28 US patients with confirmed gMG (~75 minutes) and five US physicians currently treating patients with gMG (60 minutes). Transcripts were analyzed to identify important concepts and themes, without imposing an a priori theory.

RESULTS: Patients reported blurry/double vision (43%), fatigue (36%), breathing problems (36%), and difficulty swallowing (29%) as the most bothersome gMG symptoms. Because of the heterogeneity of the patient experience, all physicians were reluctant to identify symptoms that were consistently most bothersome for patients. All physicians said they would welcome better ways to measure/manage fatigue; two reported not assessing fatigue due to measurement challenges; one reported assessing only presence/absence. Three physicians said fatigue is frequently problematic/bothersome for patients. Physicians consistently described a two-pronged treatment approach, focusing first on the most acutely serious symptoms (e.g., breathing, swallowing) and second on patients' priorities, which often centered on impacts (e.g., on social, family, and work life) associated with specific symptoms (e.g., weakness, ocular dysfunction, fatigue). Reducing fatigue/weakness was the most common treatment goal cited by patients (39%).

SUMMARY/CONCLUSION: Although patients identified fatigue as a key bothersome symptom, physicians' responses suggest that current clinical practice may not take this into consideration. However, physicians agreed that they would incorporate fatigue as a treatment goal if a patient identified it as a priority.

Abstract #14

ANALYSIS OF THE DUKE MYASTHENIA GRAVIS (MG) CLINIC REGISTRY: THYMECTOMY

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Janice Massey (Durham, NC)

Introduction:
The Duke MG Clinic Registry is a clinician-derived database that contains comprehensive information about patients seen in the Duke MG Clinic.
Objective:
To describe demographic and clinical characteristics of Registry patients who underwent thymectomy.
Methods:
Data from 339 Registry patients who underwent thymectomy at Duke University Medical Center from 1975-2017 were reviewed.
Results:
Among the 339 patients reviewed, 179 (53%) were female, 258 (76%) had acetylcholine receptor antibodies (AChR-ab-pos), and 70 (21%) did not (AChR-ab-neg). Muscle Specific Kinase (MuSK) antibodies were present in 14 AChR-ab-neg and 1 AChR-ab-pos patients. Antibody data were not available in 10.
Mean age at onset was 33±17 years in females and 42±19 years in males, and was similar in AChR-ab-pos (38±20 years) and neg (33±16 years) patients. 14% of patients had purely ocular disease (OMG). Mean disease duration at thymectomy was 3.0 years in AChR-ab-pos and 3.2 years in AChR-ab-neg patients. Thymoma was present in 45 (15%) patients, all of whom were AChR-ab-pos. Thymic hyperplasia was present in 39% of all patients, including 50% OMG and 29% with MuSK antibodies.
At 2 years post-thymectomy, 75% AChR-ab-pos and 72% AChR-ab-neg patients, including 75% with MuSK antibodies, achieved Minimal Manifestations or better. 3% AChR-ab-pos and no AChR-ab-neg patients, including those with MuSK antibodies, had achieved CSR.
Conclusion:
Among 339 Duke MG Clinic Registry patients who underwent thymectomy, thymic hyperplasia was the most common histologic finding regardless of antibody status or disease distribution. Outcomes were favorable in all subgroups, including AChR-ab-neg patients and those with MuSK antibodies.

Disclosures:

Abstract #15

CLINICAL SENSITIVITY AND SPECIFICITY OF MUSK ANTIBODY ASSAYS

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INTRODUCTION: MuSK Ab Myasthenia Gravis is a difficult diagnosis. The radio Immunoprecipitation assay (RIPA) detecting MuSK Ab is heavily relied on and seen as the gold standard test. We have developed another testing platform using surface plasmon resonance (SPR) technology. For several years, we have been using both test platforms in parallel.

OBJECTIVE: To measure the clinical sensitivity and specificity for two different MuSK Ab assays; the gold-standard RIPA assay and the new SPR assay.

METHODS: To assess clinical utility, we are describing a retrospective clinical evaluation of 987 AchR Ab negative samples that have been measured for MuSK Ab by the two different methods.

RESULTS: 132 of the 987 were either positive or borderline by one of the methods. Every final diagnosis of the patients associated with these samples was reviewed in detail. Also, 167 randomly selected patients who tested negative with both tests were reviewed.
The RIPA assay showed to be 49% to 58% sensitive depending on the criteria of diagnosis used and 89-92% specific. The SPR assay is 68-79% sensitive and 67% specific. If both assays are in congruence the specificity is 100%

SUMMARY/CONCLUSION: The RIPA assay has moderate sensitivity and good specificity while the SPR method has good sensitivity and moderate specificity. If only the RIPA is positive the confidence is high. If only SPR is positive, MuSK MG should be evaluated alongside alternative diagnosis and the test can be repeated. Also, SPR can follow antibody titer which is very useful in measuring treatment response. A prospective study is needed.

PERSPECTIVES ON MYASTHENIA GRAVIS: THE IMPACT ON QUALITY OF LIFE, PRODUCTIVITY AND EMPLOYMENT IN THE UNITED STATES

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Michelle Mackechnie (Slough, United Kingdom)

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INTRODUCTION: Myasthenia gravis (MG) is a chronic, autoimmune neuromuscular disease that causes muscle weakness and fatigue. Symptoms may impact productivity, employment, and the ability to perform daily tasks.

OBJECTIVE: To understand the relationship between severity of MG and employment, productivity and quality of life (QoL) of patients in the United States (US).

METHODS: Data were drawn from the Adelphi MG Disease Specific Programme, a point-in-time real-world survey of MG treating physicians and patients in the US. Physicians completed patient records, including demographics and MGFA classification. Patients completed a form including employment status, the work productivity and activity impairment (WPAI) questionnaire, EQ-5D-5L, and MG-QoL-15r, a MG-specific QoL tool.

RESULTS: The analysis included 109 patients with MG (58% male), with a mean age of 55 years. Patients had a physician-reported MGFA classification, 66% (n=72) were class I-IIa and 34% (n=37) were class IIb-IVa. Of class I-IIa patients, 13% were retired, unemployed or on long-term sick leave due to their MG, compared to 43% of class IIb-IVa patients. Of those currently still working, class I-IIa (n=33) and IIb-IVa (n=13), the proportion of overall work impairment was 25% and 31%, respectively. EQ-5D-5L was significantly worse (lower) in class IIb-IVa, a score of 0.65, compared to 0.82 for class I-IIa (p<0.0001); MG-QoL-15r was also significantly worse (higher) in class IIb-IVa, a score of 16.2, compared to 8.0 for class I-IIa (p<0.0001).

SUMMARY/CONCLUSION: US patients with greater MG severity were less likely to be employed. Greater severity was also associated with reduced productivity and QoL.

Abstract #17

PERSPECTIVES ON MYASTHENIA GRAVIS: THE QUALITY OF LIFE AND PRODUCTIVITY OF CAREGIVERS

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INTRODUCTION: Myasthenia gravis (MG) is a chronic, autoimmune disease that causes muscle weakness and fatigue. MG affects patients' ability to perform daily tasks, often necessitating support from caregivers.

OBJECTIVE: To understand the impact of MG on the health and productivity of caregivers supporting patients with MG.

METHODS: Data were drawn from the Adelphi MG Disease Specific Programme, a point-in-time, real-world survey of MG treating physicians and patients' caregivers in the United States, France, Germany, Italy, Spain and the United Kingdom. Physicians completed patient record forms including support required. Caregivers completed a voluntary form recording their productivity, using the work productivity and activity impairment (WPAI) questionnaire, and health state, using the EuroQol visual analogue scale (EQ-VAS), which ranges from 0=worst possible health to 100=best imaginable health.

RESULTS: 293 physicians completed records for 1,234 patients, while 38 caregivers provided a self-completed form. Physicians reported that 38% (n=464) of patients with MG needed ≥1 caregiver, with 87% (n=405) of these patients having a family member as a caregiver. Of those with a caregiver, walking was the highest reported problem needing support (49%), followed by shopping (33%) and emotional support (32%). Caregiver-reported mean EQ-VAS was 78.5. The mean number of hours per week spent caring for patients was 30.4, and 19% of caregivers reported reducing working hours, stopping or changing work due to caregiving, while 39% of their non-work activities were impaired.

SUMMARY/CONCLUSION: Many patients with MG require a caregiver, often a family member, to help with activities of daily living. This negatively impacted caregivers' work and non-work activities.

Abstract #18

CONTRASTING VIEWS OF MYASTHENIA GRAVIS DISEASE ASSESSMENT: INSIGHTS FROM A MOBILE HEALTH CO-DESIGN PROCESS INVOLVING PEOPLE LIVING WITH MYASTHENIA GRAVIS AND HEALTHCARE PROFESSIONALS

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INTRODUCTION: People living with myasthenia gravis (MG; PLWMG) identified an opportunity to improve communication about ongoing MG disease experience with their healthcare professional (HCP), particularly in the absence of validated biomarkers for MG disease activity.

OBJECTIVE: To explore the disease assessment perspectives of HCPs and PLWMG as part of a mobile health (mHealth) app co-design process.

METHODS: The co-design process obtained separate input from PLWMG and HCPs. Each workstream provided independent feedback on disease assessment and management that an mHealth intervention could address, which was cross-compared. Five PLWMG from three countries participated in four workshops. HCP engagement involved 20 interviews with neurologists specialising in MG.

RESULTS: PLWMG framed disease assessment subjectively, in terms of their personal experience and how MG impacts their daily activities, whereas HCPs referred to objective measures such as clinical or muscular scores, e.g. Quantitative Myasthenia Gravis score (QMG). However, PLWMG view their MG Activities of Daily Living responses as objective, whereas HCPs see them as subjective data. HCPs recognise the value of change in patient-reported scores over time, reflecting relative changes in disease activity, rather than using them as absolute markers to quantify symptoms.

SUMMARY/CONCLUSION: The co-design process revealed a disconnect between HCPs and PLWMG in their understanding of 'disease control', which may influence care decisions, impacting quality of life. For any assessment tool, these differing views need to be considered. An mHealth MG disease management tool (app) is in development to support PLWMG agency in the management of their own disease through recognising and communicating MG manifestations to HCPs.

Abstract #19

REAL-WORLD USE OF ECULIZUMAB IN GENERALIZED MYASTHENIA GRAVIS IN THE US: RESULTS FROM A PILOT RETROSPECTIVE CHART-REVIEW STUDY

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INTRODUCTION: Eculizumab is approved for AChR antibody-positive gMG in the US, but published data on its real-world use and effectiveness are limited.

OBJECTIVE: To examine real-world experience with eculizumab in patients with generalized myasthenia gravis (gMG) in the US.

METHODS: Data were retrospectively abstracted by physicians from their patients' electronic medical records. Patients with gMG aged ≥18 years who had received eculizumab for ≥6 months were eligible for inclusion. Patient outcomes for two consecutive periods were analyzed: 6 months before eculizumab initiation and ≥6 months during eculizumab treatment. Outcomes included MG-related crisis, exacerbation, and hospitalization. Descriptive statistical analyses for each period are presented.

RESULTS: In 84 patients with gMG, mean (SD) age was 46.3 (19.2) years and 55% were female; 74% were white and 16% black/African American. At eculizumab initiation the median MG Activities of Daily Living score was 8. Most patients were categorized as having Myasthenia Gravis Foundation of America Class II–III disease (71%). In the 6-month period before eculizumab initiation and the ≥6-month period during eculizumab treatment, MG crisis occurred in 25% and 1% of patients respectively; MG exacerbations in 38% and 10% respectively; MG crisis-related hospitalizations in 21% and 1%, respectively; and MG exacerbation-related hospitalizations in 15% and 4%, respectively.

SUMMARY/CONCLUSION: These results suggest that real-world eculizumab treatment is associated with substantial reductions in MG crises/exacerbations and related hospitalizations in patients with gMG, consistent with outcomes of the Phase 3 REGAIN study and its open-label extension. A larger real-world study of longer duration is underway to confirm these findings.

REAL WORLD IVIG USAGE IN US ADULTS WITH GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: Intravenous immunoglobulin (IVIG) is thought to be an expensive and commonly used immunotherapy treatment in adult US patients with generalized myasthenia gravis (gMG). There is limited longitudinal data on IVIG treatment usage in gMG, especially as a maintenance treatment.

OBJECTIVE: Evaluate IVIG usage over a 3-year period post IVIG initiation in adults with gMG.

METHODS: Adults with ≥1 diagnostic claim for MG were identified using Symphony Health's Integrated Dataverse (IDV)®, 01/01/2014–12/31/2019, unprojected de-identified patient Rx and medical claims, Jan 2020 dataset. From this cohort, patients who initiated IVIG therapy in 2015-2016 period were included in the analysis. IVIG episodes were defined as ≥1 IVIG claims filed consecutively with ≤5 days between each claim. Outcomes included the number and proportion of patients with 1, 2 to 3, 4 to 5, or ≥6 episodes in each 12-month period over 3 years following IVIG initiation.

RESULTS: A total of 1 331 patients met the inclusion criteria. In the 12 months following IVIG treatment initiation, a large proportion (46.3%) had ≥6 episodes of IVIG infusion, followed by 1 episode (26.4%), 2 to 3 episodes (16.6%) and 4 to 5 episodes (11.1%). In second year, 50.1% patients did not receive any IVIG treatment. Over half (66%) of patients with ≥6 episodes in the 12 months following treatment initiation also experienced ≥6 episodes during the second year.

SUMMARY/CONCLUSION: Approximately half of the patients dropped off IVIG treatment after the first year, and patients with more frequent maintenance therapy (≥6 episodes) were more likely to continue with IVIG over time.

Abstract #21

CUMULATIVE BURDEN OF REFRACTORY GENERALIZED MYASTHENIA GRAVIS AND THE THERAPEUTIC EFFECTS OF ECULIZUMAB: AN EXPLORATORY ANALYSIS

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INTRODUCTION: Typical outcome measures for generalized myasthenia gravis (gMG) assess disease burden at pre-specified timepoints. However, evaluation of outcome measures integrated over time may provide meaningful insights into cumulative functional impairment and treatment effects.

OBJECTIVE: To measure cumulative disease burden in patients receiving eculizumab or placebo during the REGAIN study (NCT01997229), using exploratory area-under-the-curve (AUC) outcome analyses.

METHODS: REGAIN assessed eculizumab (n=62) vs. placebo (n=63) in adults with refractory gMG over 26 weeks. Efficacy was evaluated using Myasthenia Gravis-Activities of Daily Living (MG-ADL), Quantitative Myasthenia Gravis (QMG) and 15-item Myasthenia Gravis Quality of Life (MG-QOL15) total scores. Normalized AUC scores were calculated (trapezoidal rule), integrating serial assessments of changes from baseline at pre-specified and unscheduled study visits through Week 26. LOCF was used for the few missing assessments. Least-squares mean (LSM) AUCs were compared between treatment groups using ANCOVA.

RESULTS: The 26-week AUC changes from baseline demonstrated significantly greater reductions for eculizumab vs. placebo for MG-ADL [LSM (SEM) −101.1 (10.67) vs. −56.2 (10.56), 1.8-fold improvement, p=0.0034]; QMG [−101.2 (13.24) vs. −44.7 (13.12), 2.3-fold improvement, p=0.0029]; and MG-QOL15 [−245.4 (31.28) vs. −121.0 (30.99), 2.0-fold improvement, p=0.0056]. These AUC differences represent clinically meaningful average eculizumab treatment effects of 1.7, 2.2, and 4.8 points for MG-ADL, QMG, and MG-QOL15 measures, respectively, over the entire treatment period.

SUMMARY/CONCLUSION: This exploratory AUC-based analysis supports eculizumab's effectiveness vs. placebo in improving gMG outcomes. Further analyses are required to understand how this approach may provide a measure of cumulative disease burden and supplement traditional timepoint-focused analysis.

Abstract #22

DISCOVERY PHASE STUDY FOR TREATMENT-PREDICTIVE BIOMARKERS OF MG

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INTRODUCTION: There are no markers of treatment response to therapies for MG. This situation compromises selection of therapy, patient stratification based on disease severity, and counseling of patients regarding their expectations for the course of MG.

OBJECTIVE: To identify candidate biomarkers which predict treatment response.

METHODS: We applied ultra-performance liquid chromatography coupled with electro-spray quadrupole time of flight mass spectrometry to obtain comparative metabolomic and lipidomic profiles from sera obtained at baseline of the MGTX trial and compared profiles of 115 subjects judged to be treatment-responsive using the minimal manifestation status (MMS), MG-ADL, QMG, or a composite measure of responsive or non-responsive at 6 months.

RESULTS: Using a rigorous definition of unequivocal treatment response at 6 months we identified a composite of metabolites and lipids at baseline that predicted treatment response with an area under of a receiver operator curve (AUC) of 0.9 and confidence interval of 0.79 to 1 (N=68), while using QMG, MG-ADL, and MMS provided progressively lower AUC values. The lipids and metabolites identified were similar when QMG and our specific response definition was used, but distinctly different for MG-ADL.

SUMMARY/CONCLUSION: We have defined lipids and metabolites that can now undergo validation as treatment-predictive markers for patients undergoing corticosteroid therapy. Metabolic phenotyping suggests that the biological correlate of improvement based on MG-ADL and QMG are distinctly different and this challenges how these assessments should be used as clinical outcome measures. Supported by U54 NS115054 MGNet Rare Disease Network

Disclosures:

PRESYNAPTIC CONGENITAL MYASTHENIC SYNDROMES WITH LAMBERT-EATON SYNDROME-LIKE ELECTROPHYSIOLOGY

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INTRODUCTION:
Congenital myasthenic syndromes (CMS) caused by mutations in genes encoding proteins of the nerve terminal, including VAMP1, MUNC13-1 and SYT2 (dominant and recessive) can have electrophysiology features that resemble Lambert-Eaton myasthenic syndrome (LEMS). CMS resulting from mutations in genes associated with proteins outside the nerve terminal, such as AGRN and LAMA5, can also present a LEMS-like electrophysiology. The clinical significance of this finding is uncertain.

OBJECTIVE:
To determine the significance of LEMS-like electrophysiology in presynaptic CMS.

METHODS:
Clinical evaluation and electrodiagnostic studies in three CMS patients with mutations in LAMA5 and SYT2 (dominant and recessive).

RESULTS:
Patient 1- 28-year-old female with lifelong history of weakness, fatigability, and severe bulbar deficit linked to a homozygous LAMA5 mutation. Her compound muscle action potential (CMAP) amplitudes showed 244% facilitation after exercise and she had an excellent response to 3,4 diaminopyridine (3,4 DAP).

Patient 2- 27-year-old male with a lifelong weakness and fatigability, bulbar deficit, and a heterozygous mutation in SYT2. His baseline CMAP amplitudes were about 30% of normal and showed 300% facilitation after exercise. He had a good response to (3,4 DAP).

Patient 3- 4-year-old female with prenatal onset of severe weakness and bulbar deficit caused by a homozygous SYT2 mutation. Her baseline CMAP amplitudes were about 0.1 mV and showed more than 1000% facilitation with 50Hz stimulation. She had an excellent response to 3,4 DAP.

SUMMARY/CONCLUSION:
1. A LEMS-like electrophysiology predicted a good response to 3,4 DAP.
2. A LEMS-like electrophysiology may uncover important molecular interactions at the neuromuscular junction.

Abstract #24

EFFECT OF EFGARTIGIMOD, A NEONATAL FC RECEPTOR BLOCKER, ON HUMORAL VACCINE RESPONSES IN AUTOIMMUNE PATIENTS

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INTRODUCTION: Immunosuppressive agents used to treat generalized myasthenia gravis (gMG) have been associated with an increased risk of infection and reported to impair immunogenicity to vaccines, specifically the recently developed SARS-CoV-2 vaccines. MG has also been suggested as a risk factor for severe Covid. Efgartigimod, a modified human IgG1 Fc fragment with increased affinity for neonatal Fc receptor (FcRn), blocks FcRn-mediated IgG recycling, leading to a rapid reduction of IgG. It is being evaluated in multiple autoimmune diseases, including gMG.

METHODS: We identified patients who were treated with efgartigimod that had been vaccinated prior to or during clinical studies in gMG (n=12) and pemphigus (n=15). Protective IgG antibody serum titers were measured for several pathogens in pemphigus patients throughout the study, regardless of vaccination history. Patients with gMG were vaccinated during the clinical studies and IgG levels were monitored to evaluate immune response.

RESULTS: gMG patients were vaccinated during and prior to efgartigimod treatment, at variable time points. Most patients received an influenza vaccine, and one also received a pneumococcal vaccine. Clear immune responses were seen to all pneumococcal and most influenza strains, except in one patient. The response persisted even with additional efgartigimod treatment. In the pemphigus study, anti-vaccine antibody titers followed the total IgG reduction but remained above determined protective levels in most cases, returning to baseline with treatment cessation.

SUMMARY/CONCLUSION: The data from these studies indicate that vaccination during or prior to efgartigimod treatment, does not hinder the ability of gMG patients to mount an immune response to those vaccines studies.

Abstract #25

EFGARTIGIMOD TREATMENT OF PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS DEMONSTRATES CONSISTENT IMPROVEMENTS ACROSS ALL MUSCLE SUBGROUPS AND REGARDLESS OF BACKGROUND IMMUNOSUPPRESSIVE THERAPY

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INTRODUCTION: Efgartigimod, a human IgG1 antibody Fc-fragment, demonstrated clinical improvement in patients with generalized myasthenia gravis (gMG) by blocking FcRn and decreasing IgG, including pathogenic IgG. Here we assess the effect of efgartigimod on muscle groups by analysing the subdomains of MG-ADL and QMG, as well as the effects of concomitant gMG therapy.

METHODS: The ADAPT study evaluated efgartigimod in patients with gMG randomized 1:1 to receive cycles of four weekly 10 mg/kg infusions of efgartigimod or placebo; subsequent treatment cycles initiated according to clinical response. Individual items of MG-ADL and QMG were grouped by Bulbar, Ocular, Respiratory, and Limb/Gross motor subdomains, and analyzed over cycles 1 and 2 in patients with a baseline score of >0 in each respective subdomain. MG-ADL responder status (≥2-point improvement for 4 consecutive weeks) was also assessed across concomitant acetylcholinesterase inhibitors, steroids and non-steroidal immunosuppressives (NSIST) subgroups.

RESULTS: In 129 AChR-Ab+ subjects, statistically significant mean differences between arms were noted across MG-ADL subdomains; Bulbar (-1.22, 95%CI [-1.71 to -0.73], p<0.001); Ocular (-0.64, [-1.11 to -0.17], p=0.008), Respiratory (-0.34, [-0.59 to -0.09], p=0.008), and Limb/Gross Motor (-0.79, [-1.22 to -0.36], p<0.001) at week 4 of cycle 1. Similar improvements were noted in cycle 2 and in QMG subdomains in cycles 1 and 2. Consistent and statistically significant improvements in MG-ADL responder status were seen in patients with/without concomitant NSIST, concomitant steroid and in patients only receiving acetylcholinesterase inhibitors.

SUMMARY/CONCLUSION: Efgartigimod demonstrated rapid and consistent improvements across concomitant background therapies, and across ocular, respiratory, bulbar and limb/gross motor muscle groups.

PATHOGENIC TH17 CELLS IN AUTOIMMUNE MYASTHENIA GRAVIS EXHIBIT A PRO-INFLAMMATORY TRANSCRIPTOMIC SIGNATURE THAT PROMOTE DISEASE PATHOGENESIS

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Introduction: Accumulating evidence suggests a critical role for Th17 cells in myasthenia gravis (MG) immunopathogenesis. A subset of Th17 cells co-produce IFN-g and IL-17 (pathogenic Th17 cells) and are implicated as a driver of autoimmunity. We previously demonstrated an association between MG disease severity and pathogenic Th17 cell frequencies. However, the molecular signatures that differentiate pathogenic and non-pathogenic Th17 cells in MG remain undefined.
Methods: To explore gene signatures associated with pathogenic and non-pathogenic Th17 cells, we performed single-cell RNA sequencing (scRNA-seq) analysis on PBMCs from 3 MG patients with known pathogenic Th17 cells, as validated by flow cytometry. PBMCs were differentiated under Th17 polarizing conditions and activated (OX40+CD25+) CD4 T cells were flow-sorted prior to scRNA-seq and followed data analysis.
Results: Using scRNA-seq, we identified single CD4 T cells with four cytokine profiles: IFN-g+IL-17+, IFN-g+IL-17-, IFN-g-IL-17+, and IFN-g-IL-17-. Compared with the other subsets, pathogenic Th17 cells demonstrated significant upregulation of genes associated with cytolysis (GZMK, GZMA), inflammation (IL-9, IL-22), and chemotaxis (CXCL3, CCL4, CCL5). Additionally, pathogenic Th17 cells exhibited higher levels of activation and proliferative capacity. Pseudo-time trajectory analysis demonstrated that pathogenic Th17 cells highly upregulated expression of IL-23R and originate from non-pathogenic Th17 cells.
Conclusions: Our early investigation shows that Th17 cells in human MG exhibit plasticity and that pathogenic Th17 cells have a unique pro-inflammatory gene signature compared to non-pathogenic Th17 cells. Future investigation is needed to determine whether the unique pathogenic Th17 cell signature could serve as a disease biomarker or be targeted with future therapeutics.

SAFETY AND TOLERABILITY OF SARS-COV-2 VACCINATION IN PATIENTS WITH MYASTHENIA GRAVIS: A SINGLE CENTER EXPERIENCE.

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Introduction:
SARS-CoV-2 vaccination was recommended for patients with myasthenia gravis primarily based on expert consensus. Patients on immune modulatory therapy, and those with myasthenia gravis, were not included in the pivotal vaccine trials so safety and tolerability was not known for these patients. We systematically collected information about safety and tolerability of SARS-CoV-2 vaccination in our myasthenia gravis patient cohort.

Methods:
As vaccine roll out started in December 2020, patients were asked to inform the study team about their vaccination status. Data was collected one of two ways using the same questionnaire, and data was recorded in the electronic medical records. Data was prospective when patients informed the clinic of scheduled date of vaccination; in such instances, study staff called patients within the first week of receiving each vaccination dose. In instances where patients did not contact the study team, data was collected retrospectively at the time of routine clinic visits.

Results:
To date, we have recorded information on 145 administered vaccine doses in 82 patients. This includes 81, 62 and 2 administered doses of the Pfizer-BioNTech, Moderna and Johnson & Johnson vaccines respectively. The majority of patients reported no or mild side effects, including mild injection site pain, malaise or generalized body aches, and did not experience worsening of their myasthenia. One patient who had been well-controlled on prednisone monotherapy experienced progressive ptosis, diplopia and dysphagia two days after receiving his second dose of the Pfizer-BioNTech vaccine and was admitted to the hospital for impending myasthenic crisis. He was treated with plasmapheresis and had rapid initial recovery but had subsequent worsening requiring maintenance intravenous immunoglobulin (IVIg) therapy and higher prednisone dose. A second patient who was on prednisone and chronic IVIg developed myasthenia exacerbation 3 days after receiving his second dose of Pfizer-BioNTech vaccine and improved with increased frequency of IVIg and higher prednisone dose. All other patients experienced mild side effects similar to those reported in the vaccine clinical trials and had no significant worsening of their myasthenia gravis symptoms.

Conclusions:
For the majority patients in our cohort (98%), SARS-CoV-2 vaccination resulted in mild side effects very similar to those reported in the pivotal vaccine trials. Two patients however did have worsening of their myasthenia gravis, with one experiencing impending myasthenic crisis requiring hospitalization and emergent plasmapheresis. This is an ongoing effort and the total number is expected to increase by the time of presentation.

WHAT DOES IT MEAN TO BE BETTER? MINIMAL MANIFESTATIONS, MG-ADL, AND QMG

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Abstract:
INTRODUCTION: Defining rigorous measures of improvement are critical to enhance clinical trials.

OBJECTIVE: To determine a rigorous definition of treatment response using the outcome measures of the MGTX trial for use in biomarker discovery.

METHODS: Achievement of minimal manifestation status (MMS), QMG, and MG-ADL for all subjects who had provided biospecimens were used (N=115). Subject stratification was performed based on these clinical outcome measures at baseline and six months. We then defined responders as meeting the following conditions: QMG improved by >=3 or >=40%, ADL improved by >=2 or >=40% or if ADL is 0 at baseline and M6, then only use QMG improvement criteria of >=3 or >=40%. Non-responders were defined as QMG worsened or no change and ADL worsened or no change (did not apply when ADL is 0 at baseline and M6). There was no distinction made based on treatment group. All analysis was done in Excel.

RESULTS: Treatment response of greater than 40% improvement in QMG or ADL showed nonconcordance in 35 of 81 subjects, while those with no improvement or worsening in ADL or QMG were non-concordant in 12 of 31 subjects. 69 subjects were defined as responders and 14 as nonresponders. Of the 69 responders 43 had been defined as having MMS.

SUMMARY/CONCLUSION: Individual treatment response, even in rigorously assessed subjects in a clinical trial, demonstrates wide variations. In order to increase rigor of clinical trial performance and definition of biological markers, outcome measures require further refinement. Supported by U54 NS115054 MGNet Rare Disease Network

EFFICACY AND SAFETY OF RAVULIZUMAB, A LONG-ACTING TERMINAL COMPLEMENT INHIBITOR, IN ADULTS WITH ANTI-ACETYLCHOLINE RECEPTOR ANTIBODY-POSITIVE GENERALIZED MYASTHENIA GRAVIS: RESULTS FROM THE PHASE 3 CHAMPION MG STUDY

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Introduction
Ravulizumab is a potent terminal complement C5 inhibitor. Engineered to have a long half-life that permits a maintenance dosing interval of 8 weeks, ravulizumab is a convenient treatment option.

Objective
To evaluate the efficacy and safety of ravulizumab in adults with generalized myasthenia gravis (gMG).

Methods
In this multicenter, double-blind, phase 3 study (NCT03920293), adults with anti-acetylcholine receptor antibody-positive (anti-AChR+) gMG (Myasthenia Gravis Foundation of America Class II–IV) and Myasthenia Gravis Activities of Daily Living (MG-ADL) score ≥6 were randomized (1:1) to receive intravenous ravulizumab infusion (body weight-based dose regimen: 2400–3000 mg induction on Day 1, then 3000–3600 mg every 8 weeks beginning on Day 15) or placebo for 26 weeks. Stable standard-of-care therapy was permitted throughout the study. The primary efficacy endpoint was change from baseline to week 26 in MG-ADL total score. Secondary endpoints included change from baseline in Quantitative Myasthenia Gravis (QMG) total score.

Results
In total 175 patients were enrolled from 85 centers worldwide. Treatment with ravulizumab was associated with a statistically significant improvement in MG-ADL total score at week 26 (-3.1 vs -1.4 for placebo; $p<0.001$). Ravulizumab also demonstrated statistically significant improvements from baseline through week 26 in QMG total score ($p<0.001$ vs placebo). Improvements in MG-ADL and QMG scores were observed within 1 week, with maintenance of benefit at week 26. No notable differences in adverse events were observed between treatment groups.

Summary/Conclusion
Ravulizumab, administered every 8 weeks, provided rapid and sustained improvement in symptoms and was well tolerated in adult patients with anti-AChR+ gMG.