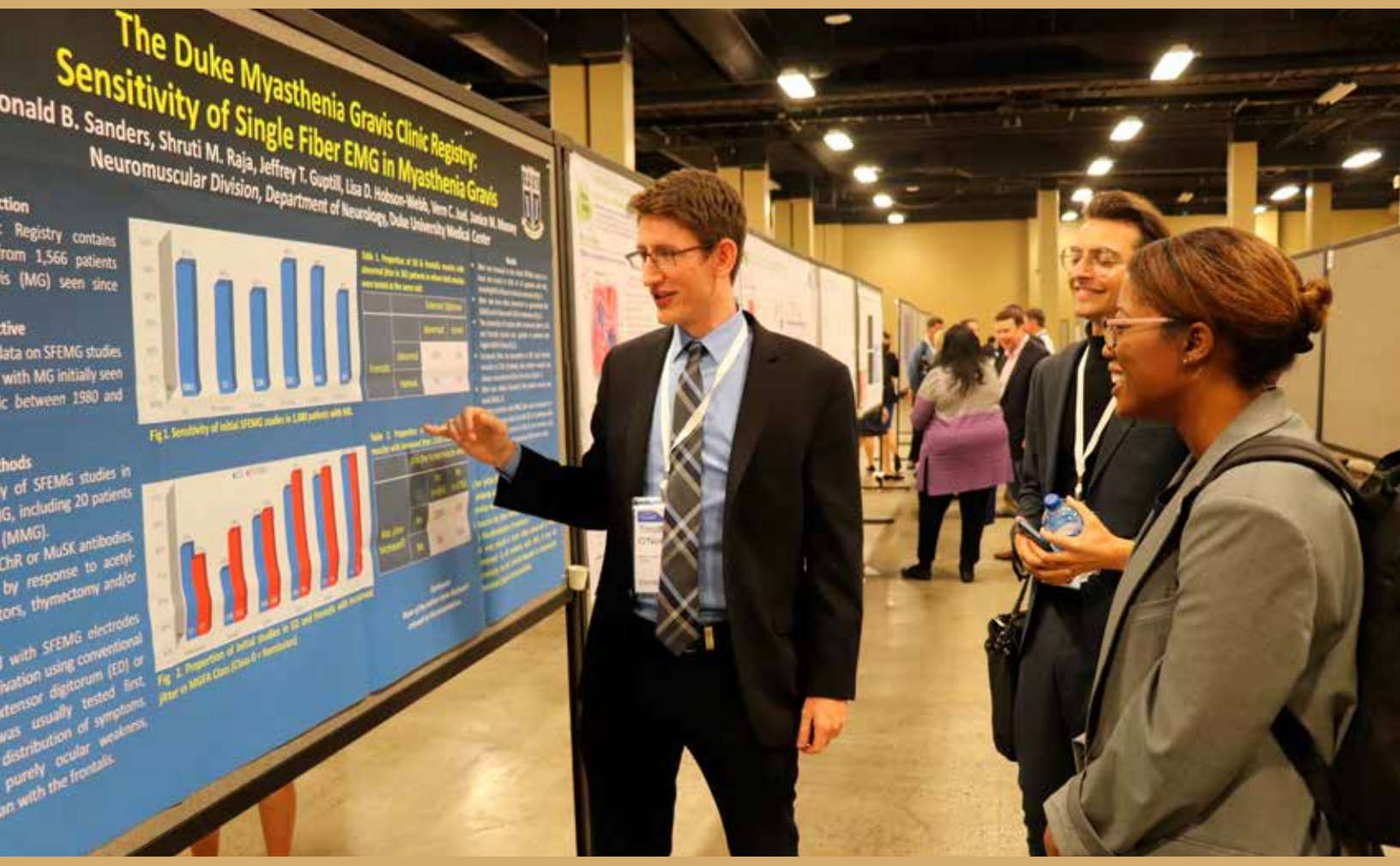
AANEM

ABSTRACT GUIDE



2023 AANEM Annual Meeting

AANEM
American Association of Neuromuscular & Electrodiagnostic Medicine

2023 ANNUAL MEETING
ABSTRACTS GUIDE

Abstracts present basic, clinical, technical, or developing research or case reports in one of the following areas: clinical neurophysiology, topics in nerve, topics in muscle, topics in neuromuscular junction, topics in anterior horn cell, musculoskeletal, practice issues, academic topics, pain, and therapies. The abstract committees review and score submissions. Abstracts are selected on the basis of their medical and scientific significance, timeliness, quality of data and methodology, adherence to specific format requirements, and other criteria.

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THE UTILITY OF ELECTRODIAGNOSTIC TESTING IN RHABDOMYOLYSIS

Michael Skolka (Rochester, MN), Margherita Milone (Rochester, MN), Ruple Laughlin (Rochester, MN), Teerin Liewluck (Rochester, MN)

INTRODUCTION: Rhabdomyolysis is an etiologically heterogeneous, acute necrosis of myofibers clinically characterized by transient weakness, myalgia, and marked creatine kinase (CK) elevation. Patients commonly undergo EDX testing searching for myopathic features.

OBJECTIVE: To identify rhabdomyolysis patients who have a high likelihood of myopathic EDX.

METHODS: Mayo Clinic's EMG database was reviewed to identify patients who underwent EDX for a single or recurrent episodes of rhabdomyolysis in the non-acute phase between January 2012 to January 2022. Patients' clinical profiles and laboratory results were reviewed.

RESULTS: Sixty-six patients were identified, 32 of whom had myopathic EDX. The median number of episodes of rhabdomyolysis was 1 and 2 in patients with and without myopathic EDX, respectively. Time from the last episode of rhabdomyolysis to EDX was not statistically significant between the 2 groups (16.3 versus 9.8 months; p=0.25). Diagnosis was reached in 15 (11 with myopathic EDX; p=0.04) of the 37 patients who underwent genetic testing, including 7 metabolic myopathies, 5 muscular dystrophies (3 LGMDR9 and 2 LGMDR12), and 3 RYR1-myopathies. The following parameters were more common in patients with myopathic EDX compared to patients with normal EDX: elevated baseline CK levels (n=15:3, p<0.001), objective weakness on exam (n=13:2, p<0.001), and identified non-metabolic myopathy as a cause of rhabdomyolysis (n=7:1, p=0.03).

SUMMARY/CONCLUSION: Rhabdomyolysis patients with weakness and elevated CK at baseline are more likely to have myopathic EDX and non-metabolic myopathies. EDX can be normal following rhabdomyolysis and does not exclude an underlying myopathy.

Michael Skolka, MD

Golseth Young Investigator Award Recipient

Resident and Fellow Member Award Recipient

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LONG-TERM SAFETY AND EFFICACY IN PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY 4 YEARS POST-TREATMENT WITH DELANDISTROGENE MOXEPARVOVEC IN A PHASE 1/2A STUDY

Jerry Mendell (Columbus, OH), Zarife Sahenk (Columbus, OH), Kelly Lehman (Columbus, OH), Linda Lowes (Columbus, OH), Natalie Reash (Columbus, MA), Megan Iammarino (Columbus, OH), Lindsay Alfano (Columbus, OH), Sarah Lewis (Cambridge, MA), Kathleen Church (Columbus, OH), Richard Shell (Columbus, OH), Rachael Potter (Cambridge, MA), Mark Hogan (Columbus, OH), Stefanie Mason (Cambridge, MA), Eddie Darton (Cambridge, MA), Louise Rodino-Klapac (Cambridge, MA)

INTRODUCTION: Delandistrogene moxeparvovec (SRP-9001) is an investigational rAAV vector-based gene therapy, designed to compensate for missing dystrophin in Duchenne muscular dystrophy by delivering a transgene encoding SRP-9001 dystrophin, an engineered dystrophin protein retaining key functional domains of the wild-type protein.

OBJECTIVE: Evaluate safety and functional outcomes 4 years post treatment with delandistrogene moxeparvovec in an open-label, phase 1/2a study (Study 101; SRP-9001-101; NCT03375164).

METHODS: Ambulatory patients (N=4; ≥4 to <8 years old) received a single IV infusion of delandistrogene moxeparvovec (2.0x1014 vg/kg; equivalent to 1.33×1014 vg/kg using qPCR with linear standard). The primary outcome was safety. Efficacy outcomes included change from baseline in North Star Ambulatory Assessment (NSAA) and timed function tests.

RESULTS: Treatment-related adverse events occurred mostly within the first 70 days of treatment, and all resolved. At 4 years post treatment, no new safety events were reported. NSAA scores improved, with a mean change from baseline at 4 years of 7.0 points. Similar trends were observed for time to rise, 4-stair climb, and 10- and 100-meter walk/run function tests. In post hoc analyses, delandistrogene moxeparvovec showed a statistically significant difference of 9.4 points (p=0.0125) in least-squares mean change from baseline to 4 years in NSAA versus a propensity-score-weighted external control cohort.

SUMMARY/CONCLUSION: Delandistrogene moxeparvovec was well tolerated 4 years post-treatment. Functional assessments demonstrated long-term sustained stabilization of motor function that was clinically meaningful, at ages where functional decline would be expected based on natural history.

Jerry Mendell, MD

Best Abstract Award Recipient

Disclosures:

Jerry Mendell - Received study funding from Sarepta Therapeutics; co-inventor of AAVrh74.MHCK7.micro-dys technology

Zarife Sahenk - Received grant support from Sarepta Therapeutics and the Parent Project Muscular Dystrophy

Kelly Lehman - Received an institutional grant from Sarepta Therapeutics

Linda Lowes - Receives salary support from Sarepta Therapeutics through Nationwide Children's Hospital

Natalie Reash - Receives salary support from Sarepta Therapeutics

Lindsay Alfano - Receives salary support from Sarepta Therapeutics through Nationwide Children's Hospital

Sarah Lewis - Employee of Sarepta Therapeutics and may have stock options

Rachael Potter - Employee of Sarepta Therapeutics and may have stock options

Stefanie Mason - Employee of Sarepta Therapeutics and may have stock options

Eddie Darton - Employee of Sarepta Therapeutics and may have stock options

Louise Rodino-Klapac - Employee of Sarepta Therapeutics and may have stock options; received grant support from Sarepta Therapeutics and the Parent Project Muscular Dystrophy and financial consideration from Sarepta Therapeutics and Myonexus Therapeutics; co-inventor of AAVrh74.MHCK7.micro-dys technology

THE ROLE OF ULTRASOUND IN DIAGNOSIS OF NERVE INJURY AFTER GUNSHOT WOUNDS AND BLAST INJURIES

Oksana Haiko (Kyiv, Ukraine), Liudmila Klymchuk (Kiyv, Ukraine), Roman Luchko (Kiev, Ukraine)

INTRODUCTION: Ultrasound is widely used in diagnosis of traumatic injuries of peripheral nerves.

OBJECTIVE: To study ultrasound features of the different types of nerve injury after gunshot wounds and blast injuries to improve diagnostics and substantiate tactics of treatment.

METHODS: An ultrasound examination was performed from March 2022 to November 2022 on 86 patients aged 20 to 55 years with gunshot (GS) and blast injuries (BI) of the peripheral nerve of the limbs (97 cases of nerve injury). All patients underwent ultrasound (US) on a LOGIQ P9 ultrasound device with 3-12 MHz and 8-18 MHz multifrequency transducer.

RESULTS: Eighty-two (84.5%) cases were diagnosed with injuries of the median/ulnar/radial nerves and 15 (15.5%) sciatic/peroneal/tibial nerves. Ulnar and peroneal nerve injuries prevailed. The site, severity (nerve injury in continuity, chronic nerve degeneration with loss of nerve fascicular architecture, partial and complete transection), and extent of the injury (in the case of neurotmesis the diastasis between the ends and the presence of a traumatic neuroma) were determined. Sunderland grade II-III injury were detected in 47.4%, grade IV-16.5%, grade V-15.5%, and Mackinnon-Dellon grade VI-20.6% of cases. Ultrasound characterization of nerve abnormalities was in agreement with intraoperative findings. The US correctly identified severity 95 out of 97 injured nerves, sensitivity 97.9%.

SUMMARY/CONCLUSION: US is an objective and highly informative method of diagnosing nerve injury after GS and BI, allowing early identification of severity of injury to guide surgical decision-making.

Oksana Haiko, MD, PhD, ScD

Best Abstract Runner Up Award Recipient

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A SURVEY OF NERVE CONDUCTION TECHNOLOGISTS' ROLE IN EMG LABS

Stephanie Harvey (Houston, TX), Thy Nguyen (Houston, TX)

INTRODUCTION: This study presents results from a survey of physicians who perform electromyography studies.

OBJECTIVE: We asked physicians whether technologists were employed in their lab and about training, additional responsibilities, and impact on productivity.

METHODS: This survey was considered Institutional Review Board (IRB) exempt by UT Houston and sent out anonymously via QR code or hyperlink to multiple forums in the fields of neurology, neuromuscular specialty, and electromyography.

RESULTS: The survey was initiated by 201 physicians. Fifty-one percent of respondents reported employing technologists in the electromyography lab. Labs reported number of employed technologists as 1 (41%), 2 (31%), 3 (11%), 4 (6%), and 5 or more (11%). Twenty-nine percent employed previously certified technologists, 26% were trained on site by a physician, 19% were trained by another technologist, 8% completed a technologist school/training program, and 18% responded with "other" (combination of ways). In addition to performing nerve conduction studies, respondents also reported additional duties: 31 scheduled patients, 17 authorized electromyography procedures, 19 coded procedures, 27 communicated with referring physicians, and 39 responded "other", such as performing electroencephalograms (EEGs). Finally, when asked about nerve conduction technologists' impact on productivity, 76% responded they can see more patients, 10% reported no change, 14% chose "other," and 0% said they have to see fewer patients.

SUMMARY/CONCLUSION: The data from this survey shows that the majority of physicians who employ technologists in their lab report a positive impact on productivity.

Stephanie Harvey, CNCT

Technologist Member Recognition Award Recipient

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PATIENT REPORTED IMPACT OF SYMPTOMS IN SPINAL BULBAR MUSCULAR ATROPHY

Abdullah Al Qahtani (Bethesda, MD), Angela Kokkinis (Bethesda, MD), Nuran Dilek (Rochester, NY), Kenneth Fischbeck (Bethesda, MD), Chad Heatwole (Pittsford, NY), Christopher Grunseich (Bethesda, MD)

INTRODUCTION: Spinal bulbar muscular atrophy (SBMA) is an inherited motor neuron disease caused by a CAC-repeat expansion. Variations in disease onset and progression have been observed. Evaluation of disease burden is important for assessing the efficacy of candidate therapeutics and may be useful for regulatory approval. In addition, the evaluation of disease burden provides valuable information for improving patient care.

OBJECTIVE: To determine the frequency and relative importance of symptoms experienced by patients with SBMA and to identify the modifiable factors that have the greatest effect on severity of symptoms.

METHODS: We conducted an international cross-sectional study of 232 patients with SBMA. Participants provided input regarding 18 themes and 208 symptoms that affect SBMA patients. Participants were asked about the relative importance of each symptom, and an analysis was done to determine how age, education, disease duration, CAG repeat length, and ambulation status relate to symptom prevalence.

RESULTS: Thigh or knee weakness (96.5%), fatigue (96.5%), problems with hands and fingers (95.8%), and limitations with walking were themes that had high prevalence in the study population. Ambulatory status was associated with 9 of the 14 themes and CAG repeat length and education were each associated with 4 of 14 themes. The prevalence of fatigue was reduced in those with lower CAG repeat length and increased with longer disease duration. Younger patients reported a higher prevalence of emotional issues.

SUMMARY/CONCLUSION: There is a diversity of themes that are important to patients with SBMA. These themes have a variable level of importance and represent factors for assessment in future therapeutic interventions.

Abdullah Al Qahtani, MD, MPH

President's Research Initiative Award Recipient

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ASSESSING REHAB NEEDS IN CHILDREN WITH SPINAL MUSCULAR ATROPHY STATUS POST ONASEMNOGENE ABEPARVOVEC-XIOI

Julia Shah (Seattle, WA), Jaclyn Omura (Seattle, WA), Molly Fuentes (Seattle, WA)

INTRODUCTION: In 2019, onasemnogene abeparvovec-xioi became the first FDA-approved gene replacement therapy (GRT) for children with spinal muscular atrophy (SMA). As children with SMA receive GRT at young ages and have the potential to achieve motor milestones such as ambulation which were previously impossible, there is a need to re-address functional status and therapy needs in this population.

OBJECTIVE: Assess developmental milestone achievement and therapy utilization for children with SMA who received GRT.

METHODS: Descriptive retrospective chart review of 16 patients at a tertiary pediatric hospital who meet the following inclusion criteria: 1) diagnosis of SMA and 2) received GRT between June 2016-June 2023.

RESULTS: Age of diagnosis ranged from 0 months to 22 months; median 2.5 months. GRT was administered between 1 -25 months of age; median 3.5 months. Age at the time of data collection ranged 12-71 months; median 33 months. All children could sit independently. Three children were ambulatory, and 13 children could say at least 1 word. In general, the median age for achievement of these milestones was delayed. Thirteen children received regular physical therapy, 10 received occupational therapy, and 8 received speech therapy services. Ten of the 16 had received birth-to-three services. If accepted, more detailed analysis of characteristics associated with milestone achievement and therapy utilization will be discussed.

SUMMARY/CONCLUSION: Most children with SMA who received GRT were delayed in achieving developmental milestones, yet therapy services were under-utilized. In the post-GRT era, it is crucial to monitor developmental progress in children with SMA and optimize their function with necessary therapy services.

Julia Shah, MD

President's Research Initiative Award Recipient

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OBJECTIVE PROGNOSTIC PARAMETERS FOR MANAGEMENT OF SPASTICITY: CLINICAL, ELECTRODIAGNOSTIC, AND SURGICAL STUDY

Naglaa Gadallah (Cairo, Egypt), Walid Abd Ghany (Cairo, Egypt)

INTRODUCTION: Intractable spasticity is considered as one of the most worldwide distributed disabling condition.

OBJECTIVE: Evaluation of the different EDX methods used in assessment of intractable spasticity in order to select the best objective and prognostic parameters to be used; and evaluation of different current modalities involved in treatment.

METHODS: A prospective open-label study; 57 adult patients were included. They underwent pre- and post-functional assessment and EDX assessment (Fmax/Mmax, Hmax/Mmax ratios, measuring agonist-antagonist co-contraction, spontaneous motor unit firing rate, and voluntary activity). Patients were divided according to the clinical assessment of spasticity severity into 4 groups: group 1, 27 patients for botulinum toxin injection; group 2, 12 patients for selective neurotomy; group 3, 5 patients for dorsal root entry zone lesioning; and group 4, 13 patients in a multimodality group. Intra-operative monitoring was used in all neurosurgical procedures. Patients had a minimum of 6 months follow up.

RESULTS: In groups 1 and 2, pain and spasm were significantly reduced (P 0.001) at the first month and significant improvement in disability score occurred at 6 months. In group 3 there was no change in disability score over 1 year follow-up period; patients had the same degree of dependence but care was given with more ease.

SUMMARY/CONCLUSION: EDX offers an easy and valid objective method for evaluating the severity of spasticity. Botulinum toxin type-A gave good results, provided that spasticity is focal and moderate (Hmax/Mmax < 0.5). Selective peripheral neurotomy showed the best results in this study in both physical and functional outcomes.

Naglaa Gadallah, MD

President's Research Initiative Award Recipient

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TRANSCRANIAL DIRECT CURRENT STIMULATION IN MULTIPLE SCLEROSIS: EXPLORING NOVEL ROUTES

Hala Elhabashy (Cairo, Egypt), Noha Elsawy (Cairo, Egypt), Ahmed Dahshan (Cairo, Egypt), Shahenda Almenabawy (Cairo, Egypt)

INTRODUCTION: Multiple sclerosis (MS) is a disabling chronic inflammatory demyelinating disorder of the central nervous system (CNS). Patients with MS usually suffer from severe physical, cognitive, social, and other neurological disabilities. Since a complete cure has not yet been established, the goal became focused on finding modalities to alleviate some of these disabilities.

OBJECTIVE: To investigate whether anodal transcranial direct current stimulation (tDCS) has an effect on spasticity, fatigue, pain, depressive symptoms, memory, learning, and attention in MS patients.

METHODS: Five consecutive daily sessions of 20 minutes' duration of active anodal tDCS over the ipsilesional motor cortex were given to 10 relapsing-remitting MS (RRMS) patients with at least 1 spastic lower limb (active group) who were compared with other 10 RRMS patients who received placebo sessions (sham group). The primary outcome was to measure the effect on spasticity by clinical assessment using Modified Ashworth Scale (MAS) and neurophysiological assessment (H reflex latency and H/M amplitude ratio). Secondary outcomes were the effects on fatigue, pain, depressive symptoms, memory, and attention using appropriate scales.

RESULTS: Active sessions of anodal tDCS of 2 mAmp intensity for 20 minutes over the primary motor cortex (M1) of the ipsilesional hemisphere once daily for 5 consecutive days decreased H/M amplitude ratio, FSS, and VAS and improved the depressive symptoms, verbal learning and memory, visuospatial learning and memory, and sustained attention of the patients.

SUMMARY/CONCLUSION: Anodal tDCS could ameliorate various disabling symptoms experienced by patients with MS, if administered properly, which would consequently improve their quality of life and lessen the burden over their caregivers.

Hala Elhabashy, MD

President's Research Initiative Award Recipient

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VIRTUAL EXERCISE GROUP PROGRAMS FOR REHABILITATION OF VETERANS WITH AMYOTROPHIC LATERAL SCLEROSIS

Hallie Walsh (Rochester, MN), Virginia Kudritzki (Seattle, WA), Heajun Chun (Buckley, WA), Ileana Howard (Woodinville, WA)

INTRODUCTION: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease in which muscle weakness is a prominent symptom and which impacts the veteran population at nearly twice the rate of civilians. Prior studies have demonstrated the benefit of exercise for this patient population, but access for persons with ALS to these specialized programs is limited both by geography and disability.

OBJECTIVE: To describe the implementation and effectiveness of a virtual group exercise program for persons with ALS in the Veterans Health Administration.

METHODS: A telehealth-based group exercise program was offered twice a week, which included cardiovascular, respiratory, balance, stretching, and resistance exercises. Outcomes assessed included pain, fatigue and rate of perceived exertion (RPE) levels, Fatigue Severity Scale (FSS), ALS Functional Rating Scale (ALSFRS), ALS-Specific Quality of Life (ALS-SQOL), 2-minute step test, forced vital capacity (FVC), and 5x sit to stand test.

RESULTS: A total of 6 veterans enrolled in the group exercise class during the initial 3 months. While ALS-FRS scores and pulmonary function tests decreased during the treatment period, quality of life scores improved for participants and for most participants fatigue was minimally impacted or improved. There were no adverse events during the class sessions.

SUMMARY/CONCLUSION: A virtual group exercise program is a safe, efficient, and effective means of delivering exercise for veterans with ALS and may improve accessibility to specialty care for this population.

Hallie Walsh, BA

President's Research Initiative Award Recipient

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EVALUATION OF NEUROMUSCULAR PROVIDER PERCEPTIONS AND OFFICE SETUP FOR EVALUATING PATIENTS WITH DISABILITIES

Adeel Zubair (Milford, CT), John Paul Mikhaiel (New Haven, CT), Seth Keller (Lumberton, NJ)

INTRODUCTION: Neuromuscular diseases are prevalent in the general population; patients can often develop disabilities because of these conditions. These disorders can also affect individuals with intellectual and developmental disabilities (IDD). The Americans with Disabilities Act (ADA) stipulates that reasonable accommodations are necessary to ensure individuals with disabilities receive equitable care.

OBJECTIVE: To assess provider comfort and available resources for providing care to patients with disabilities resulting from neuromuscular conditions and in patients with IDDs.

METHODS: A survey regarding perceptions and resources for evaluating patients' disabilities secondary to their neuromuscular disorders as well as patients with IDDs was created and sent out to 457 neuromuscular physicians across the United States; 29 emails were undeliverable and 28 responses were received.

RESULTS: Of the respondents, 82.1% reported that patients with IDDs made up less than 20% of their practice. Most offices had automatic doors (78.6%), grab bars in bathrooms (78.5%), and ramps for entryways (85.7%) but the minority had patient lifts (35.7%); 30.8% of EMG rooms were not set up to handle patients with disabilities. Most physicians felt comfortable managing patients with disabilities in clinic (82.1%); 10.7% felt that they lacked the tools necessary to provide care to this group.

SUMMARY/CONCLUSION: While most providers have access to resources and comfort in treating these patients, gaps continue to exist. Health systems and offices should aim to provide accessibility options to all patients seen. The continued lack of supports for many with disabilities perpetuates long standing health challenges as well as marginalization of those with disabilities.

Adeel Zubair, MD

President's Research Initiative Award Recipient

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IMPACT OF EDARAVONE ON THE AMYOTROPHIC LATERAL SCLEROSIS COURSE AT TTUHSC EL PASO CLINIC: A PROSPECTIVE COHORT STUDY

Ryan Floresca (El Paso, TX), Rui Tang (El Paso, TX), Ahmed Khan (El Paso, TX), Darine Kassar (El Paso, TX), Arada Wongmek (El Paso, TX), Isabel Narvaez Correa (El Paso, TX)

INTRODUCTION: Edaravone (Radicava) is an FDA-approved drug for ALS and helps decrease the neurological decline by reducing oxidative stress in neurons. The study in Japan showed benefit in patients using edaravone vs placebo by decrease in the decline in Amyotrophic Lateral Sclerosis Functional Rating Scale-revised (ALSFRS-R) score by 2.5 points over 6 months period. The purpose of our study is to compare the effect of edaravone vs edaravone/riluzole on patients with ALS followed at TTUHSC-El Paso ALS clinic.

OBJECTIVE: To compare the decline in ALSFRS-R and forced vital capacity (FVC) in subjects being treated with either riluzole or both edaravone and riluzole.

METHODS: Thirty total patients from the ALS clinic were followed from 2017-2022: 12 taking edaravone and riluzole, 18 taking riluzole only. ALSFRS-R and FVC were compared using ANOVA at the initial visit and 6 months later for the 2 different groups.

RESULTS: There was no statistically significant difference for the ALSFRS-R score at the first visit between patients who took the combined drug vs riluzole alone (p=.652). A similar trend is seen for the FVC score (p=.104) at initial visit. Correspondingly, no statistical significance was found at the 6-month visit ALSFRS-R score (p=.658) and FVC (p=.335).

SUMMARY/CONCLUSION: There was a lower decline of the ALSFRS-R score and FVC in those receiving edaravone and riluzole, however, it's statistically insignificant. This is likely due to small sample size and other factors: time between onset of symptoms to diagnosis and initiation of treatment. Minimizing these factors can be helpful in gathering data and detecting a true effect of edaravone.

Ryan Floresca, BS

President's Research Initiative Award Recipient

CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY IS ASSOCIATED WITH DECREASED EXECUTIVE FUNCTIONING IN CANCER SURVIVORS

Brendan McNeish (Pittsburgh, PA), Kim Dittus (Burlington, VT), Jurdan Mossburg (Burlington, VT), Nicholas Krant (Burlington, VT), Jack Steinharter (Burlington, VT), Kendall Feb (Burlington, VT), Hunter Cote (Burlington, VT), Rebecca Reynolds (Burlington, VT), Michael Hehir (South Burlington, VT), James Richardson (Ann Arbor, MI), Noah Kolb (Charlotte, VT)

INTRODUCTION: Cancer survivors with chemotherapy-induced peripheral neuropathy (CIPN) are at risk for chemotherapy-related declines in executive function. Despite emerging evidence that executive function is an independent risk factor for balance and falls in cancer survivors, little is known about the differences in executive function in cancer survivors with and without CIPN.

OBJECTIVE: To compare measures of executive function in chemotherapy-treated cancer survivors with and without CIPN.

METHODS: This cross-sectional study enrolled 50 chemotherapy-treated cancer survivors (65.6±11.5 years, 90% women) at a single time point post chemotherapy. Twenty-two (44%) participants had CIPN as defined by patient reported distal paresthesias or numbness that began with chemotherapy and was present at study enrollment. Measures of executive function included Trail Making Test Part B (TMT-B), Stroop Color and Word Test (SCWT), and rapid reaction accuracy.

RESULTS: Cancer survivors with CIPN (CIPN+) had decreased executive function compared to survivors without CIPN (CIPN-) on TMT-B (CIPN+: 84.9s±44.1s, CIPN-: 59.1s±22.5s, p=0.01), SCWT (CIPN+: 178.1s±55.4s, CIPN-: 152.7s±29.5s, p=0.04), and rapid reaction accuracy (CIPN+: 60.3%±12.9%, CIPN-: 70.6%±15.7%, p=0.01). Importantly, the association between CIPN and decreased executive function remained in multivariable models after adjusting for age, gender, depression, and benzodiazepine use for TMT-B (ß:18.7, p=0.046) and rapid reaction accuracy (ß:-.088, p=0.018), but not SCWT (ß:9.52, p=0.233).

SUMMARY/CONCLUSION: CIPN is associated with decreased executive function in chemotherapy-treated cancer survivors. Future research to further understand the association, causality, and risk factors is required. Regardless, current clinical approaches to caring for this growing population should not assume that the well-known increased fall risk is solely related to CIPN.

Brendan McNeish, MD

President's Research Initiative Award Recipient

ARE NEUROMUSCULAR DISEASES ASSOCIATED WITH A GREATER LEVEL OF NEURO-PSYCHIATRIC CONDITIONS?

Mohsen Ahmed (South Setauket, NY), Afaaq Ahmed (Pikeville, KY), Nabeel Ahmed (South Setauket, NY), Sarah Shoeb (Newark, NJ), Nizar Souayah (Westfield, NJ)

INTRODUCTION: Neuromuscular diseases (NMD) have been shown to contribute to a greater level of morbidity and mortality among patients. However, the impact of NMD on the prevalence and outcomes of patients hospitalized with neuro-psychiatric conditions (NP) has not been established.

OBJECTIVE: To characterize the prevalence and outcomes of NP among those hospitalized with NMD and without NMD.

METHODS: A retrospective analysis of 28,476,826 hospitalizations from 2016 to 2019 was conducted using the National Inpatient Sample database. 580,403 cases of NMD (2%) and 5,923,476 (21%) cases of NP were reported. NP cases include those with mood, psychotic, and neurodegenerative disorders. NMD and non-NMD among those with NP are grouped as npNMD and npnNMD respectively. Incidence of NP, mortality, length of stay, and patient demographics were compared in the analysis.

RESULTS: The prevalence of NP was significantly higher in NMD compared to non-NMD patients (38.3% vs 20.4%; p<0.001). npNMD had a significantly higher number of patients with schizophrenia (3.4% vs 2.5%; p<0.001), bipolar disorders (3.7% vs 2.8%; p<0.001), depression (19% vs 12%; p<0.001), and dementia (19.3% vs 5.2%; p<0.001) when compared to npnNMD. npNMD also had a significantly higher mean age (71 vs 61 years; p<0.01), length of stay (6.3 vs 5.8 days; p<0.01), and mortality (3.1% vs 2.1%; p<0.001). npNMD had significantly higher autoimmune disease, peripheral vascular disease, hypertension, and diabetes than npnNMD.

SUMMARY/CONCLUSION: These results suggest that NMD may be directly correlated with the prevalence of NP and hospital resource utilization. Further studies are needed to characterize an NMD-NP relationship while accounting for potential confounding variables.

Mohsen Ahmed, BS

President's Research Initiative Award Recipient

Medical Student Research Award Recipient

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AN ULTRA-RARE GENETIC CAUSE OF GLOBAL DEVELOPMENTAL DELAY AND SEVERE HYPOTONIA

Tyler Cook (Richmond, VA), Mathula Thangarajh (Glen Allen, VA)

INTRODUCTION/BACKGROUND: We present an infant in whom an ultra-rare cause of hypotonia was established.

CASE REPORT: A 5-month-old male infant boy was evaluated for severe hypotonia and delayed motor milestones including inability to maintain head control and inability to sit unsupported. Initial neurological examination was concerning for moderate head lag, lack of antigravity strength in upper extremities, inability to bear weight, truncal and appendicular hypotonia, and easily elicitable deep tendon reflexes. Genetic testing for spinal muscular atrophy, chromosomal microarray was negative. Metabolic evaluation and brain MRI were negative. The infant continued to show poor gains in motor and language development. Three months after initial evaluation, at 8 months of age, he was noted to pseudostrabismus. At 19 months of age, he was noted to have expressive language delay which prompted whole exome sequencing. A heterozygous pathogenic mutation in the PURA (c.733 C>T) was detected. PURA codes for the multifunctional Pur-alpha protein that is involved in DNA replication, transcription, translation, and RNA processing. Mutations in PURA gene have been associated with neurodevelopmental disorders, developmental delay, epilepsy, congenital heart block, and skeletal deformities. Endocrinology and cardiac evaluations revealed normal thyroid and gonad functions, and normal cardiac function. At the last clinic follow-up at 24 months of age, he was noted to be making motor gains. He demonstrated better head control and ability to sit without assistance. He was also begun on pyridostigmine to counter fatiguability.

SUMMARY/CONCLUSION: PURA-related syndrome accounts for 1% of developmental delay and approximately 500 patients worldwide have genetically confirmed PURA-related developmental syndrome, making this condition ultra-rare.

Tyler Cook, MS

Medical Student Research Award Recipient

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A CASE OF SLOWLY PROGRESSIVE ASCENDING WEAKNESS AFTER COVID-19 VACCINE

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INTRODUCTION/BACKGROUND: Neurological complications after vaccination, including against SARS-CoV-2, seem to implicate the vaccine, but causation vs association is difficult to ascertain. We report a novel case of a yearlong relentlessly ascending weakness in a previously healthy woman that ensued 2 weeks after receiving the COVID-19 vaccine's first dose.

CASE REPORT: An otherwise healthy 61-year-old female presented with progressively worsening weakness of ascending pattern. The weakness began 2 weeks after receiving COVID-19 mRNA vaccine's first dose. She was initially misdiagnosed with multiple sclerosis and received ocrelizumab without improvement. Now 1 year after symptom onset, her exam demonstrated 4/5 strength on MRC scale in the upper extremities, 1/5 in the lower extremities, diffusely diminished reflexes, no Babinski, some accessory-respiratory muscle use, and mildly decreased sensation to vibration and temperature in her lower extremities. She eventually developed respiratory failure and required tracheostomy placement. MRI of the brain and spinal cord as well as cerebrospinal fluid (CSF) analysis proved unyielding. A trial of IVIg yielded no symptomatic improvement. NCSs revealed evidence for a generalized predominantly-motor axonal peripheral neuropathy and widespread muscle denervation concerning for progressive muscular atrophy (PMA), among other less likely differential diagnoses such as motor-predominant chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy without conduction block.

SUMMARY/CONCLUSION: Patients presenting with primary motor weakness are sometimes difficult to differentiate. After extensive workup of our patient, a diagnosis of primary PMA was favored primarily due to the course of her illness, the predominantly motor deficits on the NCS, and failure of IVIg. Theories such as anti-idiotype antibody formation after vaccination may provide etiological explanation.

Jonathan Espinosa, BSA

Medical Student Research Award Recipient

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CLINICAL AND DIAGNOSTIC FEATURES OF SMALL FIBER NEUROPATHY WITH FIBROBLAST GROWTH FACTOR RECEPTOR 3 ANTIBODIES

Margarita Fedorova (Saint Louis, MO), Jafar Kafaie (Saint Louis, MO)

INTRODUCTION: Small fiber neuropathy (SFN) is a disorder characterized by damage to small-diameter sensory and/or autonomic nerve fibers. The clinical presentation of SFN is often non-specific, with symptoms including burning pain, numbness, tingling, and sensory loss. Diagnosis is typically made through a combination of clinical evaluation, nerve conduction studies, and skin biopsy. A subset of SFN patients may test positive for antibodies against fibroblast growth factor receptor 3 (FGFR3), a receptor involved in the regulation of cellular growth and differentiation.

OBJECTIVE: This retrospective study aims to explore clinical and diagnostic characteristics of SFN patients with FGFR3 antibodies.

METHODS: We reviewed SFN patients at Saint Louis University School of Medicine (2015-2023) and explored FGFR3 antibody associations with symptoms, lab results, and comorbidities.

RESULTS: We examined 63 SFN patients (age 11-79, average 52)with positive FGFR3 antibodies. Most were women (66.6%). Common symptoms included neuropathic pain (76%) and autonomic manifestations (57%). Some had prior autoimmune (22%) or chronic pain conditions (16%, including 7/10 with fibromyalgia). Seventy-three percent had other antibodies, most commonly trisulfide heparin disaccharide (43%), antinuclear (30%), and histone H3 (12.6%). Physical exam revealed diminished pinprick (66.6%), temperature (55.5%), and vibration (57.8%). Skin biopsy was performed in 25 patients and was confirmatory in 64%.

SUMMARY/CONCLUSION: In this review, we highlight features of immune-mediated SFN with positive FGFR3, such as prevalent autonomic manifestations and concomitant large fiber findings. Further studies are needed to elucidate the mechanisms underlying the association between FGFR3 antibodies and SFN, as well as to explore the potential clinical implications of these findings.

Margarita Fedorova, BA

Medical Student Research Award Recipient

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URINE SECRETORY PHOSPHOLIPASE A2 IN DEMYELINATING DIABETIC DISTAL SYMMETRIC POLYNEUROPATHY

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INTRODUCTION: Motor nerve conduction velocity (CV) slowing in diabetic distal symmetric polyneuropathy (DSP) exceeds what is expected from pure axonal loss and can be attributed to additional acquired demyelination.

OBJECTIVE: To develop a new strategy to identify acquired demyelination in diabetic distal symmetric polyneuropathy (DSP).

METHODS: We prospectively studied CV and urine secretory phospholipase A2 (sPLA2) activity in 90 diabetic DSP patients divided into 2 groups A and B with and without at least 1 motor nerve with CV slowing in the demyelination range. sPLA2 activity was tested in 46 healthy controls. In parallel, we studied CV in these diabetic patients using a regression analysis that we developed and validated with data from 114 CIDP patients.

RESULTS: Mean urine sPLA2 activity was significantly higher in diabetic groups compared to healthy controls (942.9±977.97 vs 591.6±390.15, pmol/min/ml, $p<0.05$) and was significantly higher in group A compared to B (1328.3±1274.21 vs 673.8±576.93, pmol/min/ml, $p=0.0014$). The number of patients with elevated sPLA2 activity and more than 2 motor nerves with CV slowing in the AAN or regression analysis ranges was significantly higher in patients of group A compared to group B (35.1%vs5.7%, $p=0.0005$). Furthermore, 13.5% in diabetic DSP group A and no patient in diabetic DSP group B fulfilled an additional criteria of more than 1 motor nerve with CV slowing in the demyelinating range with the corresponding F response in the demyelinating range by AAN criteria.

SUMMARY/CONCLUSION: We used the combination of a novel electrodiagnostic strategy and a urine biological marker of inflammation to identify a subgroup of diabetic DSP with significant contribution of acquired demyelination and neuroinflammation to diabetic nerve injury.

Kazim Jaffry, BA

Medical Student Research Award Recipient

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COMPARING MORTALITY AND MORBIDITY IN STANDARD TREATMENT PROTOCOLS FOR GUILLAIN-BARRE SYNDROME

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INTRODUCTION: Intravenous immunoglobulin (IVIg) and plasmapheresis are the standard treatment of Guillain-Barre syndrome (GBS).

OBJECTIVE: To investigate the differences in outcomes of adult GBS patients treated with IVIg vs plasmapheresis.

METHODS: We utilized the New York Statewide Planning and Research Cooperative System (SPARCS) database to implement a retrospective data analysis. Mortality was considered if the patient expired or was sent to a hospice.

RESULTS: We identified 13,210 adult patients with GBS of which 711 (5.38%) expired and 3,699 (28.7%) were disabled. Three hundred forty (2.6%) were treated with both IVIg and plasmapheresis. 2,439 were treated with only IVIg of which 92 expired and 887 were treated with only plasmapheresis of which 94 expired. The death rate was significantly lower in the IVIg group (3.8% vs 10.6%; p<0.001). There is no significant difference regarding gender (M/F: 56.0%/44.0% vs 59.4%/40.6%; p=0.079) or rate of disability (40.7% vs 41.1%; p=0.804) between the 2 groups. The mean age was significantly lower in the IVIg group (54.42±18.40 vs 56.02±17.61; p=0.022). The mean length of stay in days and the rate of mechanical ventilation were significantly lower in the IVIg group, respectively (11.24±14.99 vs 22.22±28.97; p<0.001) and (11.2% vs 32.1%; p<0.001). Multivariate binomial logistic regression found that sole IVIg use was significantly associated with a lower likelihood of mortality (OR: 0.670; 95% CL: 0.531-0.846; p<0.001).

SUMMARY/CONCLUSION: IVIg usage was significantly associated with less mortality, lower rate of placement on mechanical ventilation, lower age, and lower length of hospitalization stay in comparison to plasmapheresis.

Kazim Jaffry, BA

Medical Student Research Award Recipient

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TEMPORAL CHANGES IN TRENDS AND OUTCOMES FOR MULTIFOCAL MOTOR NEUROPATHY

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INTRODUCTION: Multifocal motor neuropathy (MMN) is a rare condition that has few large scale studies investigating outcomes.

OBJECTIVE: To assess significant differences in trends and outcomes in patients with MMN.

METHODS: We conducted a retrospective analysis of data from the New York Statewide Planning and Research Cooperative System (SPARCS) database. We investigated outcomes in 2 groups of adult patients diagnosed with MMN from years 2001-2005 (M1) and 2014-2018 (M2). We identified MMN patients through ICD-9 and ICD-10 codes. ICD-9 patients were identified through specific diagnostic criteria that excluded chronic inflammatory demyelinating polyneuropathy (CIDP) diagnosis and steroid treatment.

RESULTS: We identified 162 and 491 patients with MMN in M1 and M2, respectively. There was a significant difference in gender (M1 M/F: 50.6%/49.4% vs M2 M/F: 60.5%/39.5%; p=0.027), showing male majority in M2. No significant difference was seen with mean age (61.44±19.40 vs 58.83±16.53; p=0.126). There was a significant increase in mean length of hospitalization stay in M2 compared to M1 time period (11.37±15.48 vs 8.70±11.60; p=0.019) associated to a significant increase in disability rate in M2 time period (26.3% vs 17.3%; p=0.020). Multivariate logistic regression of comorbidities found that hypertension, peripheral vascular disease, depression, and pneumonia increased the likelihood of disability. Interestingly, the Guillain-Barre syndrome incidence rate among all patients from 2000-2018 was 10.1%.

SUMMARY/CONCLUSION: There was a significant increase in mean hospitalization stay and disability rate in MMN in 2014-2018 compared to 2001-2005 time period. Patients with select comorbidities are likely to develop disability related to MMN.

Kazim Jaffry, BA

Medical Student Research Award Recipient

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IDENTIFICATION OF TRENDS AND CLINICAL OUTCOMES IN PEDIATRIC BOTULISM

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INTRODUCTION: The pediatric cohort is the most vulnerable to botulism infection and often requires intensive treatment due to severity and complication risk.

OBJECTIVE: To investigate trends and outcomes of pediatric patients with botulism.

METHODS: We conducted a retrospective analysis of data from the New York Statewide Planning and Research Cooperative System (SPARCS) database comparing outcomes in 2 groups of adult patients diagnosed with botulism from years 2005-2009 (B1) to 2014-2018 (B2). Demographics and trends in hospitalization length of stay, mechanical ventilation, disability, and death were investigated.

RESULTS: We isolated 26 and 54 patients in B1 and B2, respectively. There was no significant difference in gender (B1: M/F: 38.5%/61.5% vs B2: M/F: 50.0%/50.0%; p=0.332), length of hospitalization stay (B1: 14.53±9.00 vs B2: 12.59±7.63; p=0.428), or rate of subsequent disability (B1: 30.8% vs B2: 25.9%; p=0.650). One patient, who was placed on a mechanical ventilator, died in 2018. The rate of placement on mechanical ventilation was significantly different from B1 to B2 (B1: 57.7% vs B2: 14.8%; p<0.001). When assessing all pediatric patients from 2000-2018 (133 patients), a longer length of hospitalization stay was associated with a higher likelihood of subsequent disability ($\bar{x}$=14.75 days; OR: 1.053; 95% CL: 1.002-1.107; p=0.043).

SUMMARY/CONCLUSION: Despite the significant reduction of mechanically ventilated patients with pediatric botulism, no significant reduction in disability, length of stay was observed between the 2015-2018 and 2006-2009 time periods.

Kazim Jaffry, BA

Medical Student Research Award Recipient

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THE "ROGUE WAVE SIGN" AS AN INDICATOR OF AN ENTRAPMENT MONONEUROPATHY: A CASE REPORT

Angela Ballesteros (Mission, TX), Bernardo Gonzalez (Amarillo, TX), Jodi Goldman (Amarillo, TX), Brendan Mackay (Lubbock, TX), Bei Zhang (Lubbock, TX), John Norbury (Lubbock, TX)

INTRODUCTION/BACKGROUND: Identifying and evaluating entrapment mononeuropathies has been historically accomplished with a detailed history and physical exam and the use of EDX studies. Neuromuscular ultrasound (NMUS) has shown to be a complementary tool to EDX when faced with entrapment mononeuropathies in being able to provide an accurate diagnosis and visualization of the nerve and surrounding tissue. It has also been shown to appropriately localize ulnar neuropathies in nonspecific EDX evaluations.

CASE REPORT: A 34-year-old woman with a history of ulnar transposition and a wrist fracture that was addressed surgically in 2016 presented with pain, numbness, and weakness in an ulnar distribution. An EDX study done in November 2022 showed an ulnar mononeuropathy at the elbow. NMUS done in February 2023 showed increased swelling and hypoechogenicity 3 cm anterior to the medial epicondyle, a "rogue wave" sonographic finding in which a subtle change in echogenicity passed across the screen from lateral to medial at the area of maximum tenderness to sonopalpation. At the location where the wave "hit" the nerve, there was a change in echotexture and a sharp change in the nerve's course.

SUMMARY/CONCLUSION: The "rogue wave sign" may represent a novel sonographic finding where subtle changes in tissue echotexture surrounding the nerve can assist in precisely localizing entrapment in complex cases. A possible mechanism for this would be a plane of scar tissue/fascial plane which passes perpendicular to the nerve during scanning in the transverse plane. A case series with associated surgical findings is needed to confirm the clinical utility of this sign.

Angela Ballesteros, BS

Medical Student Research Award Recipient

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WHAT IS THE MOST EFFECTIVE USE OF BISPHOSPHONATES TO OPTIMISE BONE HEALTH IN PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY?

Nikhita Valipe (Glasgow, United Kingdom)

INTRODUCTION: Duchenne muscular dystrophy (DMD) is the most common inherited muscular dystrophy. It is characterised by progressive muscle dysfunction in children with early loss of ambulation and cardiorespiratory manifestations which result in a low life expectancy. Corticosteroids are gold-standard to improve quality of life and life expectancy, but long-term use causes osteoporosis, deteriorating ambulation. While bisphosphonates are effective in preventing osteoporosis from other causes, including in children, no protocol exists for their use in DMD.

OBJECTIVE: Critically review and compare the efficacy of bisphosphonates in promoting bone health in DMD to suggest a treatment protocol.

METHODS: Primary research publications reporting the effects of bisphosphonates on bone mineral density (BMD), fractures, and beta-c-terminal telopeptide (βCTX) in DMD patients were identified from 3 database searches. Results of alendronate, zoledronic acid, pamidronate, and risedronate use were compared.

RESULTS: Zoledronic acid was most effective for improving BMD. All were equally effective for fracture-related and βCTX outcomes. Alendronate and zoledronic acid, with respective doses of 17.5-70 mg/week and 0.1 mg/kg/year, are the preferred oral and intravenous bisphosphonate respectively due to a higher quantity of evidence available. Unless contraindicated, a low dose of alendronate is recommended initially, progressing to a higher dose and then to zoledronic acid if ineffective. A drug holiday can be offered after 10 years if BMD is satisfactory.

SUMMARY/CONCLUSION: Bisphosphonates are effective in preventing bone health deteriorations in DMD. This paper suggests a protocol for their use in DMD based on current evidence. More research needs to be carried out on long-term and prophylactic use to complete this protocol.

Nikhita Valipe

Medical Student Research Award Recipient

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WHAT A WASTE! (OF THENAR MUSCLE): A SERVICE IMPROVEMENT AUDIT

Lisa McReynolds (Swansea, United Kingdom)

INTRODUCTION: CTS is the most common form of peripheral entrapment neuropathy and affects 281/100000 patients in the UK population annually. The demand for efficient and effective treatment is great. NCS are performed to diagnose CTS, with escalation of those presenting with thenar muscle atrophy (TMA).

OBJECTIVE: To assess the quality of documentation of TMA in referral letters by hospital physicians (HP) and general practitioners (GP). Based on information from the referral letter only to improve patient-centered care by streamlining clinically urgent referrals to reduce waiting times in Northern Ireland in severe cases of suspected CTS.

METHODS: There were 106 patient referrals included. All patients had NCS performed in a singular CTS clinic. Inclusion criteria consisted of the length of time on CTS waiting list (in months) from initial referral to NCS and documentation of TMA in referral letters.

RESULTS: One hundred six CTS referrals were reviewed (79 GP, 27 HP). The mean time on NCS waiting list for CTS was 13 months (range 11-28 months). Thirteen referral letters (12.3%) mentioned findings of TMA (12 GP, 1 HP). Overall, 7 patients (6.6%) were positive for TMA (5 GP, 2 HP) with waiting times for NCS in range of 12-28 months (mean 17.1 months).

SUMMARY/CONCLUSION: Referral letters lacking documentation of TMA have led to incomplete prioritisation of urgent patients presenting on the NCS waiting list leading to inappropriate waiting times and consequently TMA in this small study cohort. A standardised referral form could improve referrals to NCS in Northern Ireland and improve waiting times of severe CTS in the population.

Lisa McReynolds, MBBCH

Medical Student Research Award Recipient

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PERFORMANCE OF ACADEMIC AND NON-ACADEMIC CENTERS IN TREATMENT OF GUILLAIN-BARRE SYNDROME

Mohsen Ahmed (South Setauket, NY), Sarah Shoeb (Newark, NJ), Nabeel Ahmed (Stony Brook, NY), Afaaq Ahmed (Pikeville, KY), Nizar Souayah (Westfield, NJ)

INTRODUCTION: Outcomes between academic (AA) and non-academic (nAA) centers for general in-patient and post-operative patients have been well characterized in the literature. However, studies have not compared outcomes for treatment of Guillain-Barre syndrome (GBS), which is especially relevant since the onset of the SARS-CoV-2 pandemic.

OBJECTIVE: To characterize and compare outcomes between AA and nAA for the treatment of GBS.

METHODS: A retrospective analysis of 96,880 hospitalizations for GBS from 2016 to 2020 was conducted using the National Inpatient Sample database. 71,765 (74%) and 25,115 (26%) cases of GBS were treated at AA and nAA respectively. Mean length of stay was 9.6 days with 2830 (2.9%) deaths reported. Mortality, length of stay, patient demographics, and comorbidities were compared between AA and nAA groups.

RESULTS: Mean length of stay was significantly higher (10.1 vs 8.2 days; $p<0.01$) with no difference in mortality between AA and nAA (3.0% vs 2.7%; $p>0.01$). A significantly younger average age (57.1 vs 60.2 years; $p<0.01$) and lower prevalence of diabetes (26% vs 29%; $p<0.01$), hypertension (60.8% vs 63.3%; $p<0.01$), and peripheral vascular disease (5.1% vs 5.7%; $p<0.01$) was observed for AA. Significantly higher numbers of minority patients were treated at AA than in nAA (29.1% vs 21.6%; $p<0.01$). AA status ($p<0.01$; OR: 1.2; 95%CI 1.1, 1.4) and low-income status ($p<0.01$; OR: 1.5; 95%CI 1.3, 1.6) were significant predictors of mortality.

SUMMARY/CONCLUSION: These results suggest a significantly higher length of stay but no difference in mortality for AA compared to nAA for treatment of GBS despite AA having patients with significantly less comorbidities.

Mohsen Ahmed, BS

Medical Student Research Award Recipient

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OUTCOMES FOR PATIENTS WITH NEUROMUSCULAR DISEASE FOLLOWING INVASIVE NEUROLOGICAL PROCEDURES

Mohsen Ahmed (South Setauket, NY), Sarah Shoeb (Newark, NJ), Nabeel Ahmed (Stony Brook, NY), Afaaq Ahmed (Pikeville, KY), Nizar Souayah (Westfield, NJ)

INTRODUCTION: Patients with neuromuscular disease (NMD) have been shown to carry a higher morbidity and mortality, and experience more complications after invasive procedures. However, no studies have been conducted to characterize outcomes among those with NMD after invasive neurological procedures.

OBJECTIVE: To define outcomes of patients with NMD compared to patients without NMD following invasive neurological procedures.

METHODS: A retrospective analysis of 159,595 hospitalizations from 2016 to 2019 for invasive neurological procedures was conducted using the National Inpatient Sample database. The mean age was 58.8 years, with 85,046 (53.3%) males and 8,766 (5.5%) deaths reported. Select patient demographics and comorbidities were included in our comparative analysis.

RESULTS: The NMD group showed a significantly lower mortality (2.3% vs 5.6%; $p<0.001$) and intra/post-operative cerebrovascular infarction (0.1% vs 0.3%; $p<0.001$) when compared non-NMD. There was a significantly lower amount of diabetes (17% vs 20.6%; $p<0.001$), obesity (11.1% vs 15.3%; $p<0.001$), hypertension (48.6% vs 56.7%; $p<0.001$), chronic lung disease (11.8% vs 14.6%; $p<0.001$), and peripheral vascular disease (2.9% vs 3.9%; $p<0.001$) in the NMD group. Patients with NMD had a significantly higher mean age (62.5 vs 58.6 years; $p<0.001$) but lower average length of stay (5.0 vs 8.2 days; $p<0.001$). The most common diagnosis for non-NMD and NMD was neoplasm of the brain (7.3%) and neuroleptic induced parkinsonism (45%) respectively.

SUMMARY/CONCLUSION: These results suggest that patients with NMD undergoing invasive neurological procedures may have significantly lower rates of mortality, complications, and comorbidities. However, further investigation is required to account for potential confounding variables such as income and insurance status.

Mohsen Ahmed, BS

Medical Student Research Award Recipient

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ULTRASOUND AS A DIAGNOSTIC MODALITY FOR WRIST PAIN IN A NONVERBAL PATIENT WITH AUTISM SPECTRUM DISORDER

Nicole Zougheib (Southampton, NJ), Usman Yaqoob (Rockaway, NJ), Isaac Soliman (Kinnelon, NJ), Altamash Raja (Sewell, NJ)

INTRODUCTION/BACKGROUND: Remnant structures within the carpal tunnel have shown incidence of contributing to carpal tunnel syndrome (CTS). Prompt recognition of this is difficult in non-verbal patients. In these instances, diagnostic ultrasound may be the most effective tool to discern underlying pathology.

CASE REPORT: A 19-year-old nonverbal female presented to clinic with her mother after 1 month of guarding both hands, more apparent on the right. The mother noted hand weakness and difficulty performing fine motor tasks. Prior wrist x-rays were unremarkable. Physical exam was limited due to patient cooperation but on inspection the patient's hands were freely moving, with antigravity strength grossly. A recommendation was made to treat pain with Tylenol, improving symptoms in 2 weeks. For the second appointment, Xanax 0.5 mg, 30 minutes prior and immediately before evaluation was administered. Again, patient deferred physical examination but limited diagnostic ultrasound of the volar wrists was obtained. Adjacent to the entire course of the median nerve was an anechoic, pulsating structure with internal Doppler flow that was slightly compressible. The median nerve appeared with normal echotexture and size. Diagnosis of CTS was given and she was treated with nighttime wrist splinting, improving over the next few weeks.

SUMMARY/CONCLUSION: In this case, autism spectrum disorder was severe and neither proper physical examination nor electrodiagnostics could be conducted. Ultrasound allowed the providers to diagnose secondary to an anatomical risk factor that crowds the carpal tunnel predisposing to median neuropathy. This novel use of ultrasound provides clinicians with another tool for diagnosing CTS in challenging patient populations.

Nicole Zougheib, MBA

Medical Student Research Award Recipient

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CLINICAL DISPARITIES BETWEEN CAUCASIANS AND AFRICAN AMERICANS WITH CHARCOT-MARIE-TOOTH DISEASE TYPE 1A

Olivia Pakula (Detroit, MI), Ryan Castoro (Detroit, MI)

INTRODUCTION: Charcot-Marie-Tooth disease type 1A (CMT1A) is an inherited dysmyelinating sensorimotor polyneuropathy that affects 1:5000 individuals worldwide. To our knowledge, no studies have attempted to determine differences in clinical care or biomarkers of CMT1A among different ethnicities.

OBJECTIVE: To identify differences in disease history, electrophysiology, ultrasonography, and clinical exam findings among African-American and Caucasian individuals with CMT1A.

METHODS: Five first-generation diagnosed African American individuals with CMT1A were gender, age, and body mass index (BMI) matched with 5 first-generation diagnosed Caucasian individuals with CMT1A. CMT neuropathy score, NCS, and median and ulnar nerve ultrasound was performed in all cases.

RESULTS: The mean age at enrollment was 45.6 =/- 14.0 years for Caucasians and 46.2 +/-9.1 years; p=0.938. The average age of diagnosis for Caucasian individuals was 24.6+/-11.5 years and was 39.6 =/-8.6 year; p<0.0212, in African Americans. There were no statistical differences in age of symptom onset, CMT neuropathy score, median or ulnar nerves cross-sectional area at the wrist or forearm, nor NCS studies.

SUMMARY/CONCLUSION: Here, we demonstrate that among individuals with CMT1A there is a significant difference among Caucasians and African Americans in the mean age of diagnosis, despite no differences in age at symptom onset, overall symptoms, or exam. This study highlights the need for improved recognition of inherited peripheral nerve disease among the African American community.

Olivia Pakula, BA

Medical Student Research Award Recipient

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JUVENILE MYASTHENIA GRAVIS IN NORTH TEXAS: CLINICAL FEATURES, TREATMENT RESPONSE, AND OUTCOMES

Marilyn Lu (Dallas, TX), Joan Reisch (Dallas, TX), Susan Iannaccone (Dallas, TX), Kaitlin Batley (Dallas, TX)

INTRODUCTION: Juvenile myasthenia gravis (JMG) is a rare autoimmune disease that causes fatigable muscle weakness in children ages <18 years. There is currently no curative treatment or internationally accepted standard of care for JMG. It is not fully understood what characteristics are associated with treatment-responsive or refractory disease course.

OBJECTIVE: To investigate relationships between clinical presentation, antibody status, disease onset severity, electrodiagnostic evaluation, and therapy response in JMG.

METHODS: This study was a retrospective chart review. Congenital myasthenic syndromes were excluded. Data on demographics, treatments, and outcomes were collected. Disease severity was evaluated using Myasthenia Gravis Foundation of America (MGFA) clinical classifications.

RESULTS: We identified 84 JMG patients at Children's Medical Center Dallas between January 2014 and February 2022. Fifty-two percent of patients presented with ocular JMG (median onset age 4.5 years) and 48% generalized JMG (median onset age 11.5 years). Eighty-one percent tested positive for acetylcholine receptor antibodies. Patients were 17% non-Hispanic White, 29% Hispanic, 39% Black, 12% Asian. There was a significant difference in average MGFA scores between ethnicities (p=0.0474) and age groups (p=0.0036), with post-pubertal patients having higher average MGFA scores than pre-pubertal patients. There was no significant difference in average MGFA scores between different antibody types or thymectomy pathologies. Seventy-one percent of patients who underwent thymectomy experienced a decrease in MGFA scores post-procedure.

SUMMARY/CONCLUSION: Our study showed significant differences in disease severity between ethnicities and age groups. Most patients who underwent thymectomy showed clinical improvement. These outcomes highlight the need for additional therapies in JMG treatment and the importance of extending clinical trials to pediatric populations.

Marilyn Lu, BA

Medical Student Research Award Recipient

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DEEP BRAIN STIMULATION FOR THE MANAGEMENT OF AIFM1-RELATED DISABLING TREMOR: A CASE SERIES

Jude Tunyi (Columbus, OH), Nicolas Abreu (New York, NY), Richa Tripathi (Atlanta, GA), Emily De Los Reyes (Columbus, OH)

INTRODUCTION/BACKGROUND: The apoptosis-inducing factor mitochondria associated 1 (AIFM1) gene encodes a mitochondrial protein that acts as a flavin adenine dinucleotide-dependent nicotinamide adenine dinucleotide oxidase and apoptosis regulator. Monoallelic pathogenic AIFM1 variants result in a spectrum of X-linked neurological disorders, including Cowchock syndrome. Common features in Cowchock syndrome include a slowly progressive movement disorder, cerebellar ataxia, progressive sensorineural hearing loss, and sensory neuropathy.

CASE REPORT: We identified a novel maternally inherited hemizygous missense AIFM1 variant, c.1369C>T p.(His457Tyr), in 2 brothers with clinical features consistent with Cowchock syndrome using nextgeneration sequencing. Both individuals had a progressive complex movement disorder phenotype, including disabling tremor poorly responsive to medications.

SUMMARY/CONCLUSION: Deep brain stimulation (DBS) of the ventral intermediate thalamic nucleus ameliorated contralateral tremor and improved their quality of life. This suggests the beneficial role for DBS in treatment-resistant tremor within AIFM1-related disorders.

Jude Tunyi, BS

Medical Student Research Award Recipient

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THE PROVIDER'S PERSPECTIVE ON NEWER THERAPEUTICS FOR THE TREATMENT OF GENERALIZED MYASTHENIA GRAVIS: A CROSS-SECTIONAL SURVEY

Huang He Ding (Glen Allen, VA), Kelly Gwathmey (Charlottesville, VA)

INTRODUCTION: Generalized myasthenia gravis (gMG) is an autoimmune disease that results in impaired neuromuscular junction transmission resulting in muscle weakness. Recently, newer, more-targeted therapeutics, such as complement inhibitors and neonatal Fc receptor (FcRn) inhibitors, have been approved by the FDA for the treatment of gMG. It is unclear where these novel therapies fit in our current treatment paradigm.

OBJECTIVE: To study neuromuscular specialists' opinions on the role of newer therapeutics in gMG.

METHODS: Neuromuscular specialists were recruited from 3 neuromuscular websites to complete a 10-question survey sharing their perspectives regarding the current gMG treatment algorithm.

RESULTS: Eighty-one physicians completed the survey. Azathioprine and mycophenolate mofetil were first-line immunosuppressant therapies, while IVIg was considered the optimal "bridge" therapy to oral immunosuppressants in unstable patients where high-dose corticosteroids are contraindicated. Rituximab was mostly used in refractory cases. FcRn inhibitors and complement inhibitors were typically reserved for refractory cases and as bridge therapy. Cost and lack of experience with these medications were the biggest drawbacks to using newer therapeutics. When considering starting a novel treatment, affordability and safety profile were major concerns, with the route of administration, time to symptom onset, and medication track record cited as lesser concerns.

SUMMARY/CONCLUSION: Despite recent advances in gMG treatment, usage of the newer therapeutics appears to be low and reserved primarily for the treatment-refractory population. These survey results reflect the continued uncertainty about the role of novel gMG therapies. With numerous additional therapeutics on the horizon, navigating the evolving landscape will become increasingly challenging.

Huang He Ding, BS

Medical Student Research Award Recipient

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REGIONAL DISPARITIES IN TREATMENT OUTCOMES FOR PATIENTS WITH MYASTHENIA GRAVIS EXACERBATION

Afaaq Ahmed (Pikeville, KY), Mohsen Ahmed (South Setauket, NY), Sarah Shoeb (Newark, NJ), Nabeel Ahmed (Stony Brook, NY), Nizar Souayah (Westfield, NJ)

INTRODUCTION: Evidence shows that there are multi-level disparities within the US healthcare system between patients' race, gender, and socioeconomic status. However, regional disparities in outcomes of patients with myasthenia gravis (MG) have not yet been characterized.

OBJECTIVE: To investigate regional disparities in outcomes among patients hospitalized with MG exacerbation.

METHODS: A retrospective analysis on 29 million hospitalizations in 9 different hospital regions (New England (R1), Middle Atlantic (R2), East North Central (R3), West North Central (R4), South Atlantic (R5), East South Central (R6), West South Central (R7), Mountain (R8), and Pacific (R9)) in the US from 2016 to 2020 was conducted using the national inpatient sample. There were 93,240 hospitalizations for MG. Factors compared were income, mortality, comorbidities, discharge disposition, and mean ages.

RESULTS: R1 MG patients had significantly higher mortality (6.27%, $p<0.001$) and higher income (39.60%, $p<0.001$). R1 MG patients had significantly lower routine discharges (43.9%, $p<0.001$) and significantly higher mean age (65.79, $p<0.001$). R1 had significantly lower MG patients with chronic lung disease (19.80%, $p<0.001$), obesity (16.80%, $p<0.001$), and peripheral vascular disease (1.9%, $p<0.001$).

SUMMARY/CONCLUSION: Our study demonstrated a regional disparity in mortality among hospitalized MG patients within the New England region. Although R1 MG patients have a higher mean age, they also have significantly fewer comorbidities, and higher income patients still have higher mortality. More studies are needed to further characterize this relationship.

Afaaq Ahmed, BS

Medical Student Research Award Recipient

ADALIMUMAB-INDUCED MULTIFOCAL MOTOR NEUROPATHY - A DISABLING BUT REVERSIBLE PHENOMENON

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INTRODUCTION/BACKGROUND: Anti-tumor necrosis factor-alpha (anti-TNF-α) monoclonal antibodies are frequently used in patients with inflammatory bowel disease. Neuropathy is a rare adverse side effect of TNF-α antagonists with overall prevalence reported at 0.6% in 1 study. There have been 12 reported cases of infliximab-induced multifocal motor neuropathy with conduction block (MMN-CB), however only 1 prior reported case associated with adalimumab.

CASE REPORT: We report a case of a 36-year-old man with a 10-year history of Crohn's disease treated for the last year with adalimumab twice monthly, then subsequently increased to weekly 10 weeks prior to presentation of progressive painless left biceps and hand weakness. He underwent serial electrodiagnostic studies which showed a progressive motor neuropathy. MRI of the brain, cervical spine, and brachial plexus were unremarkable. Lumbar puncture revealed a mild albuminocytologic dissociation and serum labs excluded alternative inflammatory or infectious causes. Anti-GM1 antibodies were negative. The patient was diagnosed with presumed anti-TNF-α-induced MMN-CB, discontinued his medication, and underwent a 5-day course of intravenous immunoglobulin (IVIg, 0.4 gm/kg/day) with a rapid improvement of neurologic symptoms over the following 2 weeks and continued resolution over the last 2 years.

SUMMARY/CONCLUSION: In conclusion, the diagnosis of MMN-CB should be considered in patients presenting with asymmetric painless weakness who are currently being treated with anti-TNFα antibodies. Although it is a rare adverse side effect of the drug, this condition should be kept in mind as the prognosis is good with discontinuation of the drug and the use of IVIg infusions when needed.

Cole Denkensohn, MD

Resident and Fellow Member Award Recipient

A CASE OF HMGCR ANTIBODY POSITIVE NECROTIZING MYOPATHY AFTER COVID-19 MRNA VACCINATION

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OBJECTIVE: To present a case of immune mediated necrotizing myopathy (IMNM) after the Pfizer BNT162b2 COVID-19 mRNA vaccination.

BACKGROUND: Dermatomyositis and polymyositis are reported as uncommon, adverse effects following COVID-19 mRNA vaccination. However, COVID-19 vaccine related IMNM with positive anti-3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGCR) antibody, has rarely been previously reported.

CASE REPORT: A 56-year-old female with hyperlipidemia, on atorvastatin, presents with skin rash and proximal weakness after receiving the COVID-19 vaccination. Two days after the first vaccination dose, multiple well demarcated, red-purple patches appeared on her left trunk. The rashes extended to the extremities and face 1 day after receiving the second dose. Over the course of days, she developed weakness in proximal upper and lower extremities that progressed in severity. Creatine kinase level was elevated (12,694). EMG showed myopathic units in the deltoid and iliopsoas muscles. Left deltoid muscle biopsy demonstrated an active necrotizing myopathy lacking lymphocytic infiltrates. HMGCR antibody was elevated (185 units). Atorvastatin was discontinued and she was treated with IV Solu-Medrol, followed by oral prednisone taper, now taking mycophenolate. She slowly improved and regained the ability to ambulate independently after 1.5 years. Repeat HMGCR antibody was negative.

CONCLUSION: This case demonstrates a temporal association between the COVID-19 mRNA vaccination and IMNM. Our patient was on statin therapy without symptoms prior to vaccination. It is postulated that the COVID-19 mRNA vaccination could promote an autoimmune catalyst to trigger anti-HMGCR necrotizing myopathy with statin exposure.

Meghan Branston, DO

Resident and Fellow Member Award Recipient

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RISK OF INFECTION IN PATIENTS WITH MYASTHENIA GRAVIS WITH AND WITHOUT THYMOMA

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INTRODUCTION: Myasthenia gravis (MG) is treated with multiple immunosuppressive agents and is sometimes associated with thymoma, which may increase risk of infection further. Understanding infection risk may help with degree of immunosuppression and attempts to prevent infection with prophylactic vaccination/antibiotics.

OBJECTIVE: To assess risk of infection in patients with MG with thymoma compared to MG patients without thymoma.

METHODS: Retrospective analysis of all adult patients with AChR+ve MG at our center from 2015-2022 was performed. Rates of herpes zoster, pneumonia, urinary tract infection (UTI), meningitis, pneumocystis-jirovecii pneumonia, sepsis, cytomegalovirus (CMV) infections, and morbidity were analyzed in MG patients with or without a history of thymoma. We used descriptive statistics and propensity score (PS) matching for comparative analysis. Infections within 6 months of chemotherapy were excluded.

RESULTS: We identified 141 patients with AChR+ve MG, 30 with thymoma and 111 without thymoma. Baseline, the thymoma group had more females, more neurologic diagnoses, and higher immunosuppressant use, but similar age and comorbidity scores. The unadjusted rates of all infections during the follow-up period were 37% in the thymoma group and 11.7% in the non-thymoma group; this was significant in unmatched and basic-matched analyses (OR 16.1, 95% CI:2.04-744, p=0.002) but not after PS-matched analysis (OR 1.75, 95% CI:0.52-5.87, p=0.36). Rates of pneumonia and sepsis were significantly higher in thymoma group in unmatched, but not in PS-matched, analysis. Rates of CMV, zoster, UTI, and death were similar.

SUMMARY/CONCLUSION: The rates of all non-chemotherapy related infections in patients with MG and thymoma are higher compared to MG patients without thymoma but are similar after adjusting for comorbidities and observable confounders.

Katherine Clifford, MD

Resident and Fellow Member Award Recipient

Disclosures:

Ye Yuan - Employee of Atropos Health

Srikanth Muppidi - Served on advisory boards for Alexion, argenx, UCB/Ra, and Horizon Pharma

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SPINAL ARTERIOVENOUS FISTULA INITIALLY MISDIAGNOSED AS CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

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INTRODUCTION/BACKGROUND: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an immune-mediated neuropathy progressing for at least 2 months. EMG/NCS shows peripheral nerve demyelination. It presents with symmetric proximal and distal muscle weakness and motor greater than sensory symptoms. Spinal dural arteriovenous fistulas (SDAVF) can present with vague weakness and sensory symptoms. We present a unique case of SDAVF with notable EMG/NCS and MRI findings that contributed to misdiagnosis with CIDP.

CASE REPORT: A 62-year-old male presented with complaints of leg weakness and paresthesias for the past 2 years, but worsened over the last 2 months. Exam was significant for weakness of the bilateral lower extremities and absent patellar and Achilles reflexes bilaterally. Cerebrospinal fluid analysis revealed elevated protein. EMG/NCS showed borderline sensory responses in superficial peroneal nerves and absent F waves in the right tibial nerve. CIDP was suspected and the patient was treated with IVIg without improvement 1 month later. MRI of the thoracic spine and lumbar spine showed extensive abnormal signal and prominent vessels extending from T5 to the conus, suspicious for spinal dural arteriovenous fistula (SDAVF). Neurosurgery was consulted and the patient underwent surgical repair, gradually improving back to baseline after 6 months.

SUMMARY/CONCLUSION: This case demonstrated the importance of utilizing response to treatment (such as IVIg) as a diagnostic tool. Rather than anchoring on the diagnosis of CIDP and pursuing escalation of treatment (i.e., plasmapheresis), further imaging was done and SDAVF was diagnosed. This is particularly important because early diagnosis can prevent patients with SDAVF from progressing to severe myelopathy with paraplegia and sphincter dysfunction.

Gautham Upadrasta, MD

Resident and Fellow Member Award Recipient

SANDPAPER ARMS: A RARE NEUROLOGICAL PRESENTATION OF PRIMARY SJOGREN SYNDROME INITIALLY MISDIAGNOSED AS GUILLAIN-BARRE SYNDROME

Gautham Upadrasta (Bronx, NY), Ketevan Amirkhanashvili (Bronx, NY), Lauren Gluck (Bronx, NY)

INTRODUCTION/BACKGROUND: Sjögren syndrome (SS) is a known systemic disease that can have neurologic manifestations including central nervous system lesions and sensory neuronopathy or ganglionopathy. Symptoms include paresthesias, ataxia, difficulty with fine motor movements, reduced reflexes, and proprioceptive loss. Muscular strength is usually preserved and EMG/NCS shows widespread reduction of sensory potential amplitudes. We present a rare case of SS with absent sicca symptoms and notable EMG/NCS and MRI findings.

CASE REPORT: A 72-year-old woman presented with 2 weeks of lower extremity weakness. Exam revealed distal weakness, areflexia, and impaired proprioception. Autoimmune serum and cerebrospinal fluid (CSF) testing and malignancy screenings were all unrevealing. MRI was notable for multiple foci of periventricular T2 hyperintensity, along with non-enhancing lesions at the T3 and T6 levels. EMG was consistent with primarily axonal polyneuropathy. Given rapid progression of her symptoms, she received 5 days of IVIg for possible Guillain-Barre syndrome (GBS) with improvement. A few months later, she presented with a “sandpaper” sensation in her arms. Exam showed sensory changes from bilateral fingertips to elbows. NCS showed axonal polyneuropathy, primarily affecting sensory nerves consistent with sensory neuronopathy or ganglionopathy. Serum SSA antibody was positive. The patient underwent a salivary gland biopsy, which met histologic criteria for SS.

SUMMARY/CONCLUSION: It is important not to anchor on a diagnosis (in this case, GBS). Sjögren neuronopathy/ganglionopathy should be considered even in the absence of sicca symptoms. In 25-60% of cases of primary SS (pSS), neurological symptoms precede the diagnosis by an average of 2 years and can manifest as peripheral neuropathy or central nervous system lesions.

Gautham Upadrasta, MD

Resident and Fellow Member Award Recipient

CAUSES OF MONONEURITIS MULTIPLEX: A COMPREHENSIVE, STRUCTURED LITERATURE REVIEW

Colin Fry (Chicago, IL), Ryan Jacobson (Chicago, IL)

INTRODUCTION: Mononeuritis multiplex is a rare neuromuscular presentation characterized by injury to multiple, named nerves. It is known to have numerous causes and can be clinically severe. This can present diagnostic challenges to neuromuscular clinicians and trainees.

OBJECTIVE: To perform a structured literature review to delineate the various medical and neurological conditions that have been associated with a mononeuritis multiplex phenotype in order to guide teaching and clinical decision-making.

METHODS: We searched PubMed for the terms “mononeuritis multiplex,” “multiple mononeuropathies,” and “mononeuropathy multiplex” from the 30 year period spanning 1992 – 2022. Studies characterized as case reports or case series were selected. The reported causative diagnosis was recorded.

RESULTS: We identified 379 unique reports. The most common causes reported were eosinophilic granulomatosis with polyangiitis (71 reports, 78 unique patients), polyarteritis nodosa (19 patients, 19 studies), granulomatosis with polyangiitis (15 patients, 14 reports), microscopic polyangiitis (14 reports, 14 patients), and rheumatoid arthritis or vasculitis (14 reports, 13 patients). In addition, 32 reports (42 unique patients) with other, less categorizable vasculitides were found. In total, 120 different causes of mononeuritis multiplex were documented.

SUMMARY/CONCLUSIONS: Mononeuritis multiplex was associated with a multitude of underlying causes including inflammatory, immune, neoplastic, toxic, and infectious causes. Forms of vasculitis, especially eosinophilic granulomatosis with polyangiitis, were most commonly reported. Careful work-up for vasculitis therefore remains warranted in any case of apparent mononeuritis multiplex, with less attention towards a wide variety of rare, seldom-reported causes.

Colin Fry, MD

Resident and Fellow Member Award Recipient

ULTRASONOGRAPHIC AND ELECTRODIAGNOSTIC EVALUATION OF FOCAL MYOKYMIA WITH DEMYELINATING ULNAR NEUROPATHY

Trevor Logan (Lexington, KY), Rani Priyanka Vasireddy (Lexington, KY), Zain Guduru (Lexington, KY), Vishakhadatta Mathur Kumaraswamy (Lexington, KY)

INTRODUCTION/BACKGROUND: Myokymia involves continuous involuntary movements of muscles, with characteristic discharges on electromyography. It is associated with radiation-induced damage, demyelination, and peripheral nerve hyperexcitability syndromes. Here we describe a case of myokymia with demyelinating ulnar neuropathy.

CASE REPORT: Records of a patient at our institution were reviewed. A 20-year-old woman presented with continuous involuntary right hand movements previously diagnosed as chorea. The movements persisted in sleep and were painful. They were high-frequency, involuntary, non-rhythmic, non-distractible, and restricted to the ulnar-innervated intrinsic hand muscles. They appeared to dampen with action. Brain and spine imaging, and tests including voltage-gated potassium channel antibodies, had been unrevealing. Electrodiagnostic studies showed a partial conduction block in the ulnar nerve across the forearm, and florid myokymic discharges in the ulnar-innervated hand muscles. Impressive muscle contractions were visualized on ultrasound examination, which also showed a longitudinal pulsatile structure curving across the ulnar nerve at the cubital tunnel, continuously indenting and slightly displacing the nerve. This raised concern for compressive demyelination, but the nerve was normal in size and echogenicity. We intend to include viewable QR-code links to the ultrasound recordings, superposed with the needle EMG recordings and video of the clinical movements. Ganglioside antibody testing is awaited, for consideration of multifocal motor neuropathy. Contrasted MRI is planned to further investigate the vascular structure opposed to the nerve, especially since we later uncovered a prior history of multiple glomus tumors.

SUMMARY/CONCLUSION: This unusual case demonstrates the utility of electrodiagnostic studies and ultrasound in a patient with focal myokymia mistaken for chorea.

Trevor Logan, MD, PhD

Resident and Fellow Member Award Recipient

TARSAL TUNNEL SYNDROME SECONDARY TO POST-TRAUMATIC CYST

Laura Pinzón (Bogotá D.C, Colombia)

INTRODUCTION/BACKGROUND: Tarsal tunnel syndrome (TTS) is a tibial nerve entrapment neuropathy that is associated with compression of the structures within the tarsal tunnel. It is rare and usually related to structural causes. There is no specific test for its diagnosis and it is frequently confused with mechanical metatarsalgia.

CASE REPORT: A 65-year-old male patient with a 7-month evolution of paresthesia in the plantar surface of left hallux with subsequent appearance of pain over the first metatarsal head is presented. He had a history of grade II ankle sprain 30 years ago. On physical examination, he had hypoesthesia in the left hallux and pain during walking on tiptoes. It had initially been managed as a case of mechanical metatarsalgia. The EDX study showed an absence of sensory response in the left medial plantar nerve and low-amplitude compound muscle action potential (CMAP) to the abductor hallucis (AH). The EMG revealed denervation potentials and reduced recruitment in the AH. Ultrasound was performed where 2 cystic hypoechoic images were evidenced at the medial retromalleolar level that generated compression on the left tibial nerve.

SUMMARY/CONCLUSION: The diagnosis of TTS requires high clinical suspicion and compatible symptoms. It should be suspected in all patients with sensory symptoms in the foot. The findings in the EDX study are not always evident, but may be associated with lack of sensory responses from the plantar nerves and denervation in the abductor hallucis. In these cases, neuromuscular ultrasound is a useful complement to identify intrinsic anatomical causes at the level of the tarsal tunnel.

Laura Pinzón, MD

Resident and Fellow Member Award Recipient

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NEUROMUSCULAR ULTRASOUND AS A COMPLEMENTARY TOOL IN NEUROPHYSIOLOGICALLY SEVERE POLYNEUROPATHY

Laura Pinzón (Bogotá D.C, Colombia), Sergio Gaitán (Bogotá D.C, Colombia)

INTRODUCTION/BACKGROUND: EDX studies are critical in determining the underlying pathologic process of most peripheral nerve and motor neuron diseases. However, in patients with a loss of action potentials, borderline findings, or atypical symptoms, neuromuscular ultrasound is a complement to reach the diagnosis.

CASE REPORT: A 50-year-old woman presented with an 18-year history of weakness, atrophy, ascending weakness in the extremities, areflexia, and neuropathic pain. She had genetic studies reporting variants of uncertain significance of the KIF1B and PRX gene related to Charcot-Marie-Tooth disease and of the SETX gene related to ALS. In the NCS there was an absence of sensory and motor potentials. In the EMG there were signs of chronic denervation, especially in the lower limbs. Neuromuscular ultrasound revealed a homogeneous cross-sectional area (CSA) increase >150% of the upper limit in most of the peripheral nerves of the 4 extremities, including a sciatic nerve with a CSA of 81 mm2, suggestive of a severe demyelinating polyneuropathy.

SUMMARY/CONCLUSION: Neuromuscular ultrasound is an adjunct in the EDX laboratory. Its greatest utility lies in differentiating an increase in the size of the nerve associated with demyelination processes in patients with doubtful electrodiagnosis or clinical symptoms. There are different patterns of involvement (focal vs generalized or uniform vs non-uniform) that allow guiding the diagnosis. We suggest exploring sites of usual non-entrapment, especially in patients with multiple entrapments.

Laura Pinzón, MD

Resident and Fellow Member Award Recipient

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A CASE OF BULBAR-PREDOMINANT AXONAL POLYNEUROPATHY AND MYOPATHY WITH AN INFLAMMATORY COMPONENT ASSOCIATED WITH VACUOLE, E1 ENZYME, X-LINKED, AUTOINFLAMMATORY, SOMATIC SYNDROME

Taha Qarni (Philadelphia, PA), Elizabeth Isaacoff (Philadelphia, PA), Sara Stone (Philadelphia, PA), Michael Baer (Philadelphia, PA), Chafic Karam (Philadelphia, PA)

INTRODUCTION/BACKGROUND: Vacuole, E1 enzyme, X-linked, autoinflammatory, somatic syndrome (VEXAS) is a newly described multisystem inflammatory condition associated with somatic mutations in the UBA1 gene. Case reports have described demyelinating inflammatory polyneuropathies as a manifestation of VEXAS. We present a case of a patient with an axonal polyneuropathy and myopathy with an inflammatory component predominantly affecting the bulbar muscles.

CASE REPORT: A 61-year-old male with a history of prostate cancer (in remission) was admitted for work-up of 6 months of fevers of unknown origin and 3 months of progressive dysphagia, generalized weakness, and paresthesias. During his hospitalization, he developed a skin rash and orbital inflammation. His exam was notable for bulbar weakness and mild proximal weakness in his arms and legs. An EMG/NCS demonstrated a length-dependent, moderate, axonal sensorimotor polyneuropathy with mild myopathic changes. A bone marrow biopsy was notable for myeloid/erythroid vacuolation. A sural nerve biopsy demonstrated active and chronic axonal neuropathy and increased number of inflammatory cells, and a right biceps muscle biopsy demonstrated mild neurogenic and myopathic changes with increased inflammatory cells. Given the constellation of systemic symptoms, he underwent genetic testing which subsequently revealed a somatic mutation in the UBA1 gene, consistent with a diagnosis of VEXAS. He was started on prednisone 40 mg daily with a plan to consider JAK2 inhibitors.

SUMMARY/CONCLUSION: VEXAS is a rare cause of polyneuropathy that should be considered in patients with appropriate systemic symptoms and bone marrow findings. This is the first case describing a patient with bulbar-predominant axonal neuropathy and myopathy with an inflammatory component.

Taha Qarni, MD

Resident and Fellow Member Award Recipient

HIDING IN PLAIN SIGHT: A CASE OF MULTIFOCAL ACQUIRED DEMYELINATING SENSORY AND MOTOR NEUROPATHY MASKED BY MULTIPLE CONCOMITANT NEUROPATHIES

Julia Greenberg (New York, NY), Perrin Pleninger (New York, NY)

INTRODUCTION/BACKGROUND: Coexisting acute or chronic neuropathies of other etiologies can greatly complicate diagnosis of chronic acquired demyelinating neuropathies. We present a case of likely multifocal acquired demyelinating sensory and motor (MADSAM) neuropathy initially masked by superimposed compressive brachial plexopathy and co-existing chronic sensorimotor axonal polyneuropathy.

CASE REPORT: A 59-year-old man with a history of chronic kidney disease (CKD), hepatitis C infection, and polysubstance use presented with 2 months of painless left upper extremity weakness after syncope and prolonged left arm pressure in the setting of heavy alcohol use. He also endorsed paresthesias in his hands and feet and gait difficulty for >1 year. Initially his presentation was attributed to a combination of left arm compressive brachial plexopathy and chronic sensorimotor polyneuropathy in the setting of multiple medical comorbidities. Examination revealed severe proximal>distal weakness and absent reflexes in the left arm, weakness of the intrinsic right hand muscles, left foot drop, diminished sensation in a stocking distribution, and absent knee and ankle jerks bilaterally. EDX studies revealed a widespread, severe and asymmetric demyelinating sensorimotor polyneuropathy, as well as a more profound multifocal axonal motor process affecting the left arm with relative radial sparing. Cerebrospinal and serologic studies demonstrated albuminocytologic dissociation, low levels of anti-GM1 antibodies, and no evidence of neoplastic, rheumatologic, or other autoimmune conditions. He was treated with IVIg with improvement in his weakness.

SUMMARY/CONCLUSION: This case highlights the challenges of disentangling multiple concomitant polyneuropathies and the importance of combining a thorough history, exam, EDX studies, and serologic workup in diagnosis and management.

Julia Greenberg, MD

Resident and Fellow Member Award Recipient

MACROGLOSSIA AS A PRESENTING FEATURE OF THE ADULT ONSET POMPE DISEASE

Carlos Lara (Chicago, IL), Elizabeth Blair (Chicago, IL), Helene Rubeiz (Burr Ridge, IL), Kourosh Rezania (Chicago, IL), Betty Soliven (Chicago, IL)

INTRODUCTION/BACKGROUND: Late-onset Pompe disease (LOPD) is a rare autosomal recessive glycogen storage disease associated with decreased alpha-glucosidase enzyme activity. LOPD commonly presents with respiratory and limb-girdle muscle weakness, but there may be a long delay in making the appropriate diagnosis especially when LOPD presents with less frequent clinical phenotypes.

CASE REPORT: We present a 65-year-old African American female with tongue hypertrophy, dysarthria, and dysphagia who underwent a partial glossectomy, but had regrowth of lingual tissue and worsening of symptoms for a period of 4 years. She did not have limb muscle weakness or respiratory symptoms. CT scan of the head and neck demonstrated almost total fatty replacement of the tongue and a tongue biopsy also showed evidence for fibrous-adipose replacement. Laryngoscopy revealed normal laryngeal structures and video-swallow evaluation demonstrated normal oral and pharyngeal phases. There was no other abnormality on the neurologic examination. Initial laboratory investigations showed mild elevation of CK (266 U/L, normal 9-185 U/L) and aldolase elevation (9.8 U/L, normal 2-8 U/L). Nerve conduction study and electromyography (EMG) of the limb muscles were normal; EMG of genioglossus showed spontaneous activity (positive waves and fibrillation potentials) with full motor unit recruitment. Dried blood spot demonstrated low GAA enzyme activity levels (0.38 µmol/L/hr; normal 2.10-29 µmol/L/hr). Next-generation sequencing showed 2 pathogenic GAA mutations (c.-32-13T>G and c.258dup) confirming the diagnosis of LOPD.

SUMMARY/CONCLUSION: LOPD may present with isolated progressive macroglossia and bulbar symptomatology without limb or respiratory weakness.

Carlos Lara, MD

Resident and Fellow Member Award Recipient

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A MISTAKEN DIAGNOSIS OF AMYOTROPHIC LATERAL SCLEROSIS: A CASE OF MULTIPLE LUMBAR NERVE ROOT SCHWANNOMAS

Thomas Mehner (Madison, WI), Collin Kreple (Madison, WI)

INTRODUCTION/BACKGROUND: Each diagnosis of ALS must come with a careful consideration of mimicking conditions. This case presents a unique disease process which can present with similar clinical features and electrodiagnostic findings.

CASE REPORT: A 52-year-old man presented for EDX study to evaluate progressive left leg weakness over 11 years and widespread fasciculations. The patient saw a neurologist early in the disease course and was diagnosed with possible ALS based on exam and EDX testing at the time. During the next 8 years the weakness progressed to complete foot drop. Our exam revealed left knee flexion/extension 4/5, ankle plantarflexion 4+/5, and ankle dorsiflexion 0/5. On our NCS, the left peroneal motor study was absent and needle EMG showed widespread fibrillation potentials and sharp waves and fasciculations in the bilateral lower extremities. Recruitment was significantly decreased with long and large units in the tested lower extremity muscles. The EDX findings appeared consistent with bilateral L3-S1 radiculopathies or segmental anterior horn cell disease affecting the lumbosacral cord region. A lumbar MRI was then obtained and revealed multiple enhancing masses along the distal spinal cord with mass effect. The patient subsequently underwent a T11-L1 laminectomy and resection of 5 tumors in the L5 root, which pathology determined were schwannomas.

SUMMARY/CONCLUSION: Lumbar nerve root schwannomas exerting mass effect in the lower spinal cord and cauda equina area can lead to progressive weakness and diffuse denervation on EMG, which may provoke the thought of ALS. However, with close clinical examination and imaging studies, a unique and treatable condition was revealed.

Thomas Mehner, DO

Resident and Fellow Member Award Recipient

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MEDIAN AND RADIAL NEUROPATHY DUE TO BRACHIAL ARTERY ANEURYSM: CASE REPORT

Nathalia María Pérez Becerra (Bogotá, Colombia), Jully Carolina Gomez Gil (Bogotá, Colombia), Fernando Ortiz-Corredor (Bogotá, Colombia)

INTRODUCTION/BACKGROUND: Ischemic heart disease is common in the elderly population and one treatment option is cardiac catheterization through the femoral or brachial artery. Peripheral nerve injury is more common when using the brachial artery with an incidence of up to 1.4% in median nerve damage, although figures vary according to the cohort studied. The causes of median nerve palsy are associated with direct injury to the nerve by the access route or compression by hematoma or pseudoaneurysms.

CASE REPORT: A 70-year-old female patient presented with a history of cardiac catheterization by right radial puncture in June 2022. Subsequently, she presented with decreased strength of the first, second, and third fingers of the right hand associated with paresthesia. Electrodiagnostic studies showed a severe lesion with axonal damage of the right median nerve in the distal third of the arm as well as absence of sensory response of the ipsilateral radial and ulnar nerves. Musculoskeletal ultrasonography with Esaote equipment with linear transducer array SL2325 of 18 MHz shows pseudoaneurysm in the brachial artery of approximately 1.5 cm in diameter.

SUMMARY/CONCLUSION: Cardiac catheterization through the right brachial artery is a viable option when a femoral approach is not possible and its complications are usually related to hypersensitivity to the contrast medium or the formation of false aneurysms; however, neurological complications may occur. This case demonstrates the usefulness of the joint use of electrodiagnostics and ultrasound for the diagnosis of neuropathies following arterial catheterization.

Nathalia María Pérez Becerra, MD

Resident and Fellow Member Award Recipient

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NEUROMUSCULAR ULTRASOUND TO SUPPORT EARLY ELECTRODIAGNOSIS OF GUILLAIN-BARRE SYNDROME: A CASE REPORT

Nathalia María Pérez Becerra (Bogota, Colombia), Jorge Arturo Diaz Ruiz (Bogota, Colombia), Liliana Rodriguez (Bogota, Colombia), Jorge Munoz (Bogota, Colombia)

INTRODUCTION/BACKGROUND: Guillain-Barre syndrome (GBS) is a polyradiculoneuropathy affecting peripheral nerves and nerve roots by an immune-mediated mechanism, usually secondary to viral infection. It is characterized by ascending symmetric weakness associated with sensory disturbances and hypo/areflexia. Among the variants of GBS are acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), and acute motor and sensory axonal neuropathy (AMSAN). An increase in nerve diameter has been reported with the use of neuromuscular ultrasound, especially in proximal segments of the upper limbs in demyelinating polyneuropathies, but this is inconsistent in axonal involvement.

CASE REPORT: A 19-year-old female presented with upper respiratory symptoms and urinary tract infection progressing to symmetrical cephalocaudal weakness with progressive gait compromise and right face compromise. Additionally, she presented paresthesias in her hands and feet. The initial electrodiagnosis reported sensory-motor polyneuropathy in active phase, probably primary axonal, with ultrasound scan with increased cross-sectional area (CSA) in right cervical roots. A control study, performed 15 days later, showed demyelinating sensory-motor polyneuropathy, in subacute-chronic phase with persistent increase in the CSA of the right C5, C6, and C7 roots, measuring 8.4, 10.8, and 12.4 mm^2 respectively.

SUMMARY/CONCLUSION: In GBS, increased CSA has been reported in 47-83% of patients in early stages, being more predominant in the cervical roots. Taking this into account, this case report raises the usefulness of neuromuscular ultrasound in early stages of the disease that can guide the diagnosis and treatment when an AIDP type variant is suspected.

Nathalia María Pérez Becerra, MD

Resident and Fellow Member Award Recipient

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MAGNETIC RESONANCE NEUROGRAPHY AND QUANTITATIVE MUSCLE MRI OF PARSONAGE-TURNER SYNDROME INVOLVING THE LONG THORACIC NERVE

Jonathan Morena (New York, NY), Ek Tsoon Tan (New York, NY), Qian Li (New York, NY), Gracyn Campbell (New York, NY), Pravjit Bhatti (New York, NY), Darryl Sneag (Plainview, NY)

INTRODUCTION: Parsonage-Turner syndrome (PTS) is characterized by severe, acute upper extremity pain and subsequent paresis and most commonly involves the long thoracic nerve (LTN). Magnetic resonance neurography (MRN) can detect LTN hourglass-like constrictions (HGCs) and quantitative muscle MRI (qMRI) can quantify serratus anterior muscle (SAM) neurogenic changes.

OBJECTIVE: 1) To characterize MRN/qMRI findings in LTN-involved PTS. 2) To investigate associations between qMRI biomarkers and EMG motor unit recruitment (MUR) levels.

METHODS: We retrospectively investigated 30 PTS subjects (25M/5F, mean/range age=39/15-67 years) with scapular winging who underwent 3.0 Tesla bilateral chest wall qMRI and unilateral brachial plexus MRN. EMG was performed on average 185 days from symptom onset (all ≥ 2 weeks from symptom onset) and 5 days preceding MRI.

RESULTS: The LTN was identified on MRN in 23/30 patients and HGCs were seen in 91% of cases (21/23). All 30 subjects had diffuse SAM edema on the affected side compatible with active denervation. Additionally, qMRI was significantly different to the contralateral, uninvolved side: increased T2 ($p<0.001$) and fat fraction ($p=0.013$) and decreased muscle diameter ($p=0.003$) and cross-sectional area ($p<0.001$). There were no significant associations between individual qMRI biomarkers and EMG MUR levels.

SUMMARY/CONCLUSION: MRN can confirm PTS by identifying HGCs in most cases of LTN involvement. qMRI provides an objective measure of SAM changes. Lack of association between qMRI and EMG MUR levels for the SAM, as has been previously reported for other denervated muscles, could be related to MRI breathing artifacts and EMG sampling error. Further investigation and analysis are warranted.

Jonathan Morena, DO

Resident and Fellow Member Award Recipient

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A NOVEL INTRONIC ALPHA-TROPOMYOSIN 3 GENE MUTATION IN A PATIENT WITH NEMALINE MYOPATHY

Christopher Brewer (Chicago, IL), Mohammed Alhaidar (Chicago, IL), Betty Soliven (Chicago, IL), Kourosh Rezania (Chicago, IL)

INTRODUCTION/BACKGROUND: Nemaline myopathy presents with a symmetric proximal muscle weakness and is associated with normal or slightly elevated creatine kinase and presence of nemaline rods on muscle biopsy. Nemaline rods are intracytoplasmic inclusions formed by clusters of z-discs with variable aberrant actin crosslinking, usually associated with mutations in nebulin and actin, and rarely alpha-tropomyosin 3 (TPM3).

CASE REPORT: A 41-year-old female presented with 26 years of slowly progressive bilateral proximal limb weakness. Examination was significant for symmetric proximal weakness and hyporeflexia. She had normal tone, no fasciculations, no myotonia, and no muscle tenderness. The cranial nerves and sensation were intact. Creatine kinase was 99 U/L. EMG displayed increased insertional activity in the right deltoid and biceps, and early recruitment in the right deltoid, biceps, triceps, tibialis anterior, gastrocnemius, iliopsoas, and infraspinatus muscles. Gastrocnemius and deltoid muscle biopsy showed atrophy, nemaline rod inclusions, scattered ragged red fibers, and cytochrome oxidase negative fibers. Genetic testing revealed a novel homozygous TPM3 (c.855-1 G>A) mutation. This results in substitution in a consensus splice site just proximal to the beginning of the final exon, which may disrupt splicing at this site, resulting in a protein lacking the last amino acid residues critical for binding of alpha-tropomyosin-3 to actin.

SUMMARY/CONCLUSION: We identified a novel intronic mutation in the TPM3 gene in a patient with nemaline rod myopathy.

Christopher Brewer, MD, PhD

Resident and Fellow Member Award Recipient

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NODAL AND PARANODAL ANTIBODY MEDIATED DEMYELINATING NEUROPATHY

Akhil Shivaprasad (Houston, TX), Sheetal Shroff (Houston, TX), Sara Benitez (Houston, TX), Ashley Anderson (Pearland, TX), Melody Badii (Los Angeles, CA), Robert Smith (Houston, TX)

INTRODUCTION: Nodal and paranodal proteins like neurofascin (NF) 155 and 186/140 are required for clustering of voltage-gated sodium channels at nodes of Ranvier for rapid nerve conduction. IgG antibodies specifically IgG4 subtype against these proteins has been linked to combined central and peripheral demyelination.

OBJECTIVE: We report clinical characteristics, associated disorders, neuroimaging, and treatment response of patients with positive neurofascin antibodies.

METHODS: Nine patients with positive neurofascin antibodies were identified and their charts were reviewed for data collection.

RESULTS: Of the 9 patients, 2 were female. All except 1 were confirmed by Western blot method. Seven (77%) patients were positive for IgG NF155, 2 (22%) for IgG NF140, and 3 for contactin-1. Two patients had other autoimmune antibodies like MOG and SSA/SSB. Predominant phenotype on EMG/NCS was sensorimotor demyelinating polyradiculoneuropathy. Three patients had acute-subacute onset of symptoms that rapidly progressed to mimic Guillain-Barre syndrome (GBS). Other associated disorders included motor neuron disease, retroperitoneal liposarcoma, and malignant melanoma previously treated with ipilimumab and nivolumab. Three patients had significant T2 flair hyperintensities on MRI brain and 1 patient had enhancing cranial nerves at presentation. Four out of the 9 are on IVIg, 1 plasmapheresis, and 1 on rituximab. One of them was weaned off IVIg and 2 are in the process of deciding the treatment.

SUMMARY/CONCLUSION: The majority of our patients were NF155 positive, and none were of IgG4 subtype. Most were associated with chronic demyelinating form with only a minority presenting acutely and only 2 patients had changes on brain MRI. IVIg was the preferred treatment of choice.

Akhil Shivaprasad, MD

Resident and Fellow Member Award Recipient

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SUCCESSFUL MANAGEMENT OF PAINFUL LEGS-MOVING TOES SYNDROME WITH FUNCTIONAL ELECTRICAL STIMULATION

Alexis Kaiser (Indianapolis, IN), Loretta VanEvery (Indianapolis, IN)

INTRODUCTION/BACKGROUND: Painful legs-moving toes (PLMT) syndrome is a rare adult-onset disorder that includes neuropathic pain in the feet and legs with associated writhing movements of 1 or more toes. Typically, symptoms are not responsive to neuropathic medications.

CASE REPORT: A 73-year-old female presented to clinic with paresthesias in her right foot and continuous movements of all toes. Neurologic exam was significant for intermittent, involuntary right great toe and ankle dorsiflexion. Her EMG was significant for a bilateral multilevel radiculopathy involving L4/5 in the left lower extremity and L4-S1 on the right lower extremity. Over a 2-year period, she was trialed on low dose clonazepam followed by gabapentin (900 mg 3 times per day) combined with duloxetine (60 mg daily). She was then switched to pregabalin (50 mg 3 times per day). She had minimal improvement in neuropathic pain and her right-sided movements continued. Due to lack of response to neuropathic medications, a Bioness L300 Go Quick Fit electrode was trialed in her right lower extremity. As the functional electrical stimulation (FES) was increased, the patient's toe movements stopped and her gait stability improved.

SUMMARY/CONCLUSION: PLMT syndrome remains challenging to successfully manage. Many patients have limited response to gabapentin or pregabalin. There are case reports detailing improvement with epidural spinal cord simulation, lumbar epidural blocks, vibratory stimulation (VS), botulinum toxin injections, and transcutaneous electrical nerve stimulation (TENS). FES devices are non-invasive and low risk, and may represent an additional treatment option for these patients.

Alexis Kaiser, MD

Resident and Fellow Member Award Recipient

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ACUTE MOTOR AXONAL NEUROPATHY WITH LOWER LIMB INVOLVEMENT: ELECTRODIAGNOSTIC STUDY, ULTRASONOGRAPHY, AND MAGNETIC RESONANCE IMAGING

Luisa Castaño Herrera (Bogota, Colombia), Andrea Karina Peña Yara (Bogota, Colombia), Liliana Rodriguez (Bogota, Colombia), Jorge Arturo Diaz Ruiz (Bogota, Colombia), Jorge Nicolás Muñoz (Bogota, Colombia)

INTRODUCTION/BACKGROUND: Guillain-Barre syndrome (GBS) diagnosis is made mainly through clinical and electrophysiological evaluation, however ultrasonography (US) and magnetic resonance imaging (MRI) are essential in cases of atypical presentation.

CASE REPORT: A patient presented with a history of 2 days of flaccid paraparesis without sensory or autonomic alteration. The electrophysiological study shows an absence of F wave in the left peroneal nerve and low persistence in the right peroneal and tibial nerves; the sensory and motor neuroconductions are normal. In the electromyography there is decreased recruitment in the lower limbs. Evaluation with US reports an increase in the cross-sectional area (CSA), especially at the level of cervical roots and median nerve, without alteration in US of lower limbs. The MRI shows enhancement of anterior roots from T12 to L1.

DISCUSSION: Although there are no clinical and electrophysiological findings in the upper limbs, the median nerve had an increased CSA on US and is the most prone to enlargement compared to other nerves. It has recently been identified that the increase in the CSA of the vagus nerve is also related to the risk of autonomic dysfunction. GBS patients presenting with paraparesis, unlike those with quadriparesis, have been found to have milder forms and less cranial nerve involvement. The study with MRI and US turns out to be key for the adequate diagnosis in diseases such as spondylodiscitis with albuminocytological dissociation that can present as a flaccid paraparesis and confuse the diagnosis.

CONCLUSION: The support of images such as MRI and US is essential in cases of atypical presentation of GBS.

Luisa Castaño Herrera, MD

Resident and Fellow Member Award Recipient

CONTACTIN-1 ANTIBODY ASSOCIATED INFLAMMATORY POLYRADICULONEUROPATHY

Ashley Santilli (Rochester, MN), Nathan Staff (Rochester, MN), Divyanshu Dubey (Rochester, MN), Michelle Mauermann (Rochester, MN)

INTRODUCTION/BACKGROUND: Antibodies targeting paranodal antigens, including neurofascin-155 and contactin-1, have been infrequently identified in cases of chronic inflammatory demyelinating polyradiculoneuropathies (CIDP). We present a case of contactin-1 antibody positive inflammatory polyradiculoneuropathy, highlighting the clinical, electrodiagnostic, and imaging characteristics of this rare disorder.

CASE REPORT: A 75-year-old male developed subacute, asymmetric, painless distal lower limb weakness and numbness resulting in recurrent falls. Three months later, fingertip numbness and bilateral upper limb tremor developed. Evaluation revealed lumbar spinal stenosis. He underwent L2-S1 lumbar diskectomy and fusion without improvement and with subsequent acute symptomatic decline 2 weeks postoperatively, leaving him non-ambulatory. Associated symptoms included dysarthria, dysphagia, dyspnea, facial weakness, constipation, and labile blood pressure. Electrodiagnostic testing 6 months after symptomatic onset revealed a severe mixed axonal and demyelinating polyradiculoneuropathy, with significantly prolonged blink responses (R1 29.1). Laboratory evaluation revealed positive contactin-1 antibody. Cerebrospinal fluid testing showed cell count 6, 92% lymphocytes, and protein 246. MRI lumbar spine showed lumbosacral nerve root enhancement. CT chest, abdomen, pelvis was unremarkable. His symptoms were attributed to contactin-1 antibody positive inflammatory polyradiculoneuropathy. He received IVIg without response. He subsequently received plasma exchange (PLEX) and rituximab with clinical and electrodiagnostic stabilization.

SUMMARY/CONCLUSION: Contactin-1 antibody associated inflammatory polyradiculoneuropathy is a rare disorder characterized by a more aggressive clinical course, higher morbidity, and frequent IVIg treatment failure compared to idiopathic CIDP. As clinical outcomes are dependent on early recognition and initiation of appropriate treatment, often with rituximab, increasing recognition of the clinical and electrodiagnostic features which should prompt serologic evaluation for contactin-1 antibodies is imperative.

Ashley Santilli, MD

Resident and Fellow Member Award Recipient

NOVEL A302T VARIANT IN THE EXPANDING RETICULON-2 RELATED SPECTRUM IN SPASTIC PARAPLEGIA 12

Baljinder Singh (New York City, NY), Darine Kassar (Houston, TX)

INTRODUCTION/BACKGROUND: Reticulon-2 (RTN2) gene encodes a member of reticular family of prototypic endoplasmic reticulum (ER)-shaping proteins involved in ER morphogenesis. Spastic paraplegia 12 (SPG12) is a subtype of autosomal dominant pure hereditary spastic paraplegia, with onset of symptoms typically beginning in childhood. We described the clinical and genetic features of 2 SPG12 patients with novel A302T variant.

CASE REPORT: Two cases were a 61-year-old-man and a 64-year-old-woman respectively, with childhood onset of chronic progressive lower limb spasticity and difficulty walking. Physical examination showed increased muscle tone, hyperreflexia, and Babinski signs in the lower extremities in both patients. Patient 1 had ataxia and dysmetria. No visual symptoms, seizures, or dementia were reported in either patient. RTN2 gene mutation was identified by whole genome sequencing and both cases were heterozygous for the mutation in p.Ala302Thr (GCC>ACC) in exon 5 in the RTN2. Family history was remarkable for similar clinical phenotype with unknown genetic results.

SUMMARY/CONCLUSION: The A302T variant in the RTN2 gene has not been reported previously as a pathogenic variant, nor as a benign variant as well to our knowledge. The A302T variant was not observed in approximately 6500 individuals of European and African American ancestry in the NHLBI Exam Sequencing Project indicating it is not a common variant, revealing the RTN2 related spectrum is still expanding. The A302T variant is a non-conservative amino acid substitution, which is likely to impact secondary protein structure as these residues differ in polarity, charge, and size.

Baljinder Singh, MD

Resident and Fellow Member Award Recipient

A CASE OF POST-INFECTIOUS HERPES SIMPLEX VIRUS TYPE 1-RELATED BIBRACHIAL PAN-PLEXOPATHY

Adenike Adewuyi (Chicago, IL), Erik Pioro (Chicago, IL)

INTRODUCTION/BACKGROUND: Brachial plexitis typically presents with acute onset shoulder pain followed by weakness and sensory loss often following a viral illness. Here we present a case of severe bilateral pan-plexopathy after herpes simplex virus type 1 (HSV-1) infection.

CASE REPORT: A 53-year-old woman with longstanding peripheral artery disease and type 2 diabetes complicated by bilateral below-knee amputations presented with right leg pain and drainage requiring a through-knee amputation. She developed sepsis from HSV-1 viremia and was treated with acyclovir. She subsequently developed acute onset bilateral arm weakness. Exam showed flaccid right arm paralysis with absent reflexes. Neck and left arm weakness was present with pathologic hyperreflexia and positive Hoffmann sign. Sensation was absent on the right arm to all modalities but intact on the left. Cervical spine MRI showed severe C5-6 canal stenosis. NCS revealed absent sensory and motor responses and reduced amplitudes on the right and left arm, respectively. EMG showed marked ongoing denervation and no voluntarily activated motor units in all right arm muscles including the trapezius. Ongoing denervation was less prominent in the left arm with marked subacute to chronic motor axon loss. Brachial plexus MRI demonstrated edema throughout the plexus. She received 5 sessions of plasma exchange with minimal improvement of right arm strength and stable left arm strength.

SUMMARY/CONCLUSION: We present a rare, atypical case of severe bibrachial pan-plexopathy with bilateral spinal accessory neuropathy and superimposed left cervical myeloradiculopathy. The patient's surgery and medical complications likely played a role in the severity of her presentation. Prompt EMG/NCS provided key information that informed her treatment recommendations.

Adenike Adewuyi, MD, PhD

Resident and Fellow Member Award Recipient

OBINUTUZUMAB FOR THE TREATMENT OF REFRACTORY SYSTEMIC LUPUS ERYTHEMATOSUS ASSOCIATED CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY

Adenike Adewuyi (Chicago, IL), Shubadra Priyadarshini (Chicago, IL), Arjun Seth (Chicago, IL)

INTRODUCTION/BACKGROUND: Obinutuzumab is a CD20 monoclonal antibody with higher affinity than rituximab for the CD20 epitope. It has been studied in stage III/IV lupus, but not in patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). We describe a case of obinutuzumab use in treating lupus associated CIDP.

CASE REPORT: A 22-year-old with refractory lupus complicated by nephritis and pericarditis and treated with multiple rounds of cyclophosphamide, mycophenolate, and prednisone, presented with multiple recurrent episodes of ascending numbness and weakness beginning in 2019. Each episode coincided with a lupus flare. She was diagnosed with CIDP on electrodiagnostic studies. Cerebrospinal fluid (CSF) studies showed cytoalbuminologic dissociation. She failed IVIg but responded to plasma exchange (PLEX). She required tracheostomy twice. In 2021, she presented with quadriparesis and was treated with cyclophosphamide, rituximab every 3 months, PLEX, and steroids with remission of her lupus and CIDP for 10 months. In 2022, she presented with monthly CIDP/lupus flares and was treated with PLEX, steroids, and rituximab. Five days after her rituximab dose, her CD20 count was <1 mm^3 but re-constituted to 10 mm^3 2 weeks later. She was thought to be a rituximab non-responder and was started on obinutuzumab. After 2 months, her neurologic exam is normal, CIDP and lupus are in remission, and her CD20 count is <1 mm^3.

SUMMARY/CONCLUSION: This case highlights a rare case of treatment refractory lupus and CIDP that has responded to obinutuzumab after failing rituximab. Obinutuzumab appears safe and effective in patients with autoimmune-related CIDP who appear to be rituximab non-responders.

Adenike Adewuyi, MD, PhD

Resident and Fellow Member Award Recipient

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SAFETY AND EFFICACY OF ECULIZUMAB THROUGHOUT THREE PREGNANCIES IN A PATIENT WITH TREATMENT REFRACTORY GENERALIZED MYASTHENIA GRAVIS

Nadia Khalil (Tampa, FL), Jerrica Farias (Tampa, FL), Niraja Suresh (Tampa, FL), Claudia Guerra Hernandez (Tampa, FL), Clifton Gooch (Tampa, FL), Tuan Vu (Lutz, FL)

INTRODUCTION/BACKGROUND: Eculizumab is a humanized monoclonal antibody against complement protein C5, which is approved for the treatment of anti-acetylcholine receptor antibody positive, generalized myasthenia gravis (AChR Ab+ gMG). Safety data regarding the use of eculizumab during pregnancy in women with gMG are limited. We previously reported a patient with AchR Ab+ gMG who had favorable maternal and fetal outcomes while on eculizumab. This report provides follow-up on this patient, as she subsequently had 2 additional successful pregnancies.

CASE REPORT: This 27-year-old woman with treatment refractory gMG had 3 pregnancies (at ages 23, 24, and 25) while on eculizumab. She had a beta-hemolytic Streptococcus urinary tract infection during her first pregnancy, candida vulvovaginitis during the second and third pregnancies, and disseminated gonococcal infection during the third pregnancy. Due to hypertension during the first pregnancy, labor was induced at 38 weeks. For the other 2 pregnancies, labor and delivery were uncomplicated at 38w1d and 38w0d, respectively. Throughout all pregnancies, her gMG symptoms remained well-controlled, except for mild MG-related weakness 3 months post-partum and during the first trimester. Her 3 daughters had normal fetal development and no neonatal complications.

SUMMARY/CONCLUSION: This report provides additional data on the use of eculizumab during pregnancy. While efficacy and fetal outcomes were favorable, this report also highlights the potential for infectious adverse events. This report adds to the data on pregnancy outcomes in patients with gMG treated with eculizumab and may be helpful in determining risk-benefit stratification.

Nadia Khalil, MD

Resident and Fellow Member Award Recipient

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MONONEURITIS MULTIPLEX SECONDARY TO CRYOGLOBULINEMIA-MEDIATED VASCULITIS FROM SMOLDERING MYELOMA: A CASE REPORT

Shubadra Priyadarshini (Chicago, IL), Arjun Seth (Chicago, IL)

INTRODUCTION/BACKGROUND: Vasculitis is a well-recognized cause of mononeuritis multiplex. Among vasculitides, cryoglobulinemia is rare, but can herald underlying systemic disease.

CASE REPORT: A 69-year-old man developed numbness, burning pain, and a petechial rash in his feet and ankles. One month later, he developed right hand extension weakness and numbness over the dorsum of his hand, followed by bilateral foot weakness. Nerve conduction studies showed a right radial mononeuropathy and severe length-dependent sensorimotor axonal neuropathy. Needle electromyography showed denervation with subacute reinnervation in the right upper extremity and active denervation in the left lower extremity. Right sural nerve and gastrocnemius muscle biopsies showed a necrotizing vasculitis. Serum evaluation with protein electrophoresis showed an IgG monoclonal gammopathy. Bone marrow biopsy showed smoldering myeloma. Further testing showed positive cryoglobulins, with cryoglobulin immunofixation showing monoclonal IgG, the same gammopathy associated with his smoldering myeloma. He was diagnosed with mononeuritis multiplex secondary to cryoglobulinemia-mediated vasculitis from smoldering myeloma. He was treated with IV steroids and rituximab, with stabilization in exam. With weaning of steroids, his pain and weakness recurred. He was therefore treated with daratumumab, a CD38 monoclonal antibody, to definitively treat his myeloma with stabilization and improvement in exam.

SUMMARY/CONCLUSION: This case illustrates that mononeuritis multiplex can be the first sign of a primary systemic disorder. Prompt evaluation with labs, electrodiagnostic testing, and nerve/muscle biopsies is critical to identify the etiology and direct treatment. In this case, identifying cryoglobulinemia vasculitis secondary to smoldering myeloma prompted more definitive oncologic treatment for myeloma with clinical stabilization and improvement.

Shubadra Priyadarshini, MD

Resident and Fellow Member Award Recipient

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ONSET OF RADIATION-INDUCED BRACHIAL PLEXOPATHY 30+ YEARS AFTER INITIAL EXPOSURE: A CASE REPORT

Shaida Omid (San Diego, CA), Christina Chrisman (Phoenix, AZ)

INTRODUCTION/BACKGROUND: Delayed onset of radiation-induced peripheral nerve injury is a rare condition with well-described reports of symptoms presenting months following initial exposure. Here we present a case of electrodiagnostically confirmed radiation-induced brachial plexopathy (RIBP) in a 78-year-old woman who had received radiotherapy for breast cancer decades prior to the onset of symptoms.

CASE REPORT: Following a diagnosis of right sided breast cancer the patient was treated via resection, chemotherapy, and radiation to the right chest wall and axilla in 1985. Over 30 years later, she developed progressive paresthesia and weakness in her right arm. Prior to presentation in neuromuscular clinic, she had corrective carpal and cubital tunnel surgeries without improvement. Physical examination revealed weakness in the right upper extremity with elbow flexion and extension; shoulder abduction, external rotation and flexion; intrinsic hand muscles and finger flexion. There was atrophy of supraspinatus and infraspinatus with winged scapula. Reflexes were reduced in the right upper extremity. Sensation was reduced to pinprick on the dorsal hand and dorsolateral forearm. NCS/EMG was consistent with right brachial plexopathy localizing predominately to the upper trunk, with the presence of myokymia. MR brachial plexus was negative for malignancy. The patient was referred to occupational therapy.

SUMMARY/CONCLUSION: NCS/EMG play an essential role in confirming the diagnosis of delayed onset RIBP, with fasciculations or myokymia supporting radiation injury rather than malignancy. This case demonstrates that although RIBP is a rare complication of radiotherapy, it should be kept in the differential diagnosis in patients presenting with a history of radiation treatment, even decades after exposure.

Shaida Omid, MD

Resident and Fellow Member Award Recipient

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PITFALLS IN THE EVALUATION OF RESPIRATORY FAILURE IN MYASTHENIA GRAVIS PATIENTS: A CASE SERIES

Sanem Pinar Uysal (Cleveland, OH), Yuebing Li (Cleveland, OH)

INTRODUCTION/BACKGROUND: Respiratory failure in myasthenia gravis (MG) could be due to a variety of etiologies.

METHODS: We describe 3 MG patients with distinct presentations of respiratory failure.

CASE REPORT: Case 1: A 49-year-old female with longstanding MG presented with dry cough for 3 weeks. She denied dyspnea, dysphagia, and diplopia. She had slight lethargy, nasal speech, neck weakness, and tachycardia on exam. Blood gas revealed hypercarbic respiratory failure resulting in ICU admission. Symptoms improved with bilateral positive airway pressure (BiPAP) and plasmapheresis. Case 2: A 58-year-old female presented with ptosis, dysphagia, and dyspnea requiring intubation. She was diagnosed with MG and treated with IVIg and prednisone. Post-extubation, hoarseness was noted and attributed to posterior glottal swelling. Ptosis, dysphagia, and arm weakness gradually improved, but hoarseness worsened with subjective dyspnea. IVIg for possible myasthenic crisis did not lead to improvement. Ear, nose, and throat (ENT) exam revealed subglottic stenosis and she was diagnosed with antineutrophil cytoplasmic antibody (ANCA)-positive granulomatosis with polyangiitis. Case 3: An 85-year-old female with MG presented with mild limb weakness and lethargy, and was found to be persistently hypoxic despite successful treatment of pulmonary embolism. Her hypoxia did not improve with IVIg. A large interatrial septal aneurysm with patent foramen ovale (PFO) was revealed on echocardiogram and PFO closure eliminated hypoxia immediately.

SUMMARY/CONCLUSION: Respiratory failure in MG can present without clinically overt signs of respiratory distress due to the sedating effect of hypercapnia. When typical signs of MG are absent in MG patients presenting with respiratory failure, non-myasthenic etiologies of hypoxia should be considered.

Sanem Pinar Uysal, MD

Resident and Fellow Member Award Recipient

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A TONGUE TWISTER: TONGUE WEAKNESS DUE TO PARANEOPLASTIC SYNDROME IN MULTIPLE MYELOMA

Ian Ackers (Lansing, MI), Alexander Doubek (Lansing, MI), Ryan O'Shaughnessy (Lansing, MI), John Tegtmeier (Lansing, MI), Michael Andary (East Lansing, MI)

INTRODUCTION/BACKGROUND: Cranial mononeuropathies are a rare presenting symptom of multiple myeloma.

CASE REPORT: A previously healthy 47-year-old female with no medical history, except for multiple myeloma in her father, presented as a direct inpatient admission from her otolaryngologist office due to progressive dysphagia and dysarthria over 2-3 weeks. Over this time, she was unable to tolerate solid foods and only tolerated liquids in small amounts. Physical exam demonstrated slight left tongue atrophy, diminished protrusion, inability to laterally deviate, and inability to elevate her tongue. Remaining cranial nerves were intact. Strength testing was normal. Reflexes were 2+ and symmetric. Inpatient EMG was performed due to suspected Epstein-Barr virus (EBV)-induced cranial neuropathy. On NCS, sural, left and right facial compound muscle action potentials (CMAPs), and left ulnar F-waves were normal. Needle EMG demonstrated 1+ fibrillation potentials in left genioglossus muscle with full recruitment. Right genioglossus was normal. Right masseter, temporalis, frontalis, upper trapezius, cervical/thoracic paraspinals, left arm, right leg, and left leg were normal. Left extensor digitorum brevis (EDB) had 2+ fibrillations. No fasciculations were noted. The patient's electrodiagnostic impression was incomplete left hypoglossal neuropathy. She underwent a tongue biopsy which was normal and her EBV serology was negative. She was subsequently diagnosed with multiple myeloma by bone marrow biopsy and her symptoms attributed to paraneoplastic syndrome.

SUMMARY/CONCLUSION: Cranial neuropathies have been described in the setting of multiple myeloma. Presentation secondary to paraneoplastic syndrome is unusual as direct bony invasion or plasmacytoma are more common. Multiple myeloma should be considered in the differential diagnosis of dysarthria and bulbar paralysis.

Ian Ackers, DO, PhD

Resident and Fellow Member Award Recipient

DESCENDING MONONEUROPATHIES: AN UNUSUAL PRESENTATION OF AL AMYLOIDOSIS

Andre Granger (Rochester, MN), Sarah Berini (Northfield, MN)

INTRODUCTION/BACKGROUND: Commonly, AL amyloidosis affects small then large fibers in a length-dependent fashion. Prominent involvement of the cranial nerves and spread in a descending pattern is atypical. Herein, we describe the clinical and pathologic features of a case of AL amyloidosis causing descending mononeuropathies.

CASE REPORT: A 62-year-old female presented for evaluation of multiple painless mononeuropathies evolving over 5 years. Her symptoms began with a persistent cough and perioral numbness. She then developed left ptosis, facial droop, hoarseness, and left ulnar mononeuropathy. High-dose prednisone and antivirals were ineffective. Cerebrospinal fluid analysis was normal. She subsequently developed diplopia, dysphagia, left CTS, autonomic symptoms, weight loss, and right hand sensorimotor deficits. Her physical exam showed moderate to severe sensorimotor deficits in the left face and bilateral hands. Differentials included infiltrative processes, such as amyloidosis or immunoglobulin M (IgM) deposition, or vasculitis. Workup revealed an IgM lambda monoclonal protein and normal anti-neutrophil cytoplasmic antibodies. Electrodiagnostic testing showed multiple mononeuropathies, with a severe left facial neuropathy. MRI brain showed abnormal thickening and enhancement of the left facial nerve. PET scan showed no evidence of occult malignancy or sarcoidosis. Abdominal fat aspirate was positive for AL amyloidosis. She therefore received a diagnosis of multiple mononeuropathies secondary to AL amyloidosis. At the time of abstract submission, a left facial nerve biopsy for definitive diagnosis was pending.

SUMMARY/CONCLUSION: Descending mononeuropathies can be a presentation of AL amyloidosis. Systemic and autonomic symptoms can be a clue to diagnosis.

Andre Granger, MD, MBA

Resident and Fellow Member Award Recipient

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THE UTILITY OF WHOLE EXOME SEQUENCING FOR NEUROMUSCULAR CONDITIONS

Sukhraj Gill (Danville, PA), Madeline Williamson (Danville, PA), J. David Avila (Danville, PA), Scott Friedenberg (Danville, PA)

INTRODUCTION: Genetic testing is often used in neuromuscular medicine. Whole exome sequencing (WES) is a phenotype-driven genetic testing option that can be used in cases of previous nondiagnostic panel testing, complex presentations, or otherwise strong suspicion for a hereditary condition.

OBJECTIVE: We sought to demonstrate the utility of WES in patients with suspected hereditary neuromuscular conditions.

METHODS: This was a retrospective cross-sectional study of adult neuromuscular patients who underwent WES from November 2019 to January 2023 within the Geisinger Healthcare System.

RESULTS: Of 52 patients who underwent WES, 8 (15%) had positive results yielding a diagnosis, 3 (5%) were identified as carriers of a genetic condition, 14 (26%) had variants of uncertain significance (VUS), 1 had a nondiagnostic pathogenic variant, 1 had both a carrier result and a VUS, 25 (48%) had negative test results,18 (34%) had family history of similar symptoms, and 40 (72%) had genetic panel testing prior to WES. Of the 8 patients diagnosed using WES, 5 had myopathic disorders and 3 had neuropathic disorders.

SUMMARY/CONCLUSION: In our cohort of 52 patients who underwent WES, 15% had diagnostic results and most of these (6/8) had prior nondiagnostic panel genetic testing. Additionally, 37% of patients had a nondiagnostic abnormal result (VUS, carriers, and nondiagnostic pathogenic variants). We recommend offering WES to patients with unrevealing panel testing to aid the diagnosis of neuromuscular conditions where suspicion for a genetic etiology is high.

Sukhraj Gill, MD

Resident and Fellow Member Award Recipient

Disclosures:

J. David Avila - Speaker bureau and consulting for Alnylam Pharmaceuticals, argenx, and Alexion

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HOW TO DIAGNOSE AMYLOIDOSIS EARLY? THE ANSWER MAY BE IN YOUR HANDS

Sukhraj Gill (Danville, PA), Brandon Carry (Danville, PA), Syed Kazmi (Danville, PA), J. David Avila (Danville, PA)

INTRODUCTION: CTS is an early manifestation of amyloidosis. Previous evidence indicates that amyloid deposits are present in 10.2% of patients undergoing carpal tunnel release (CTR).

OBJECTIVE: We sought to identify the prevalence of amyloidosis in patients undergoing CTR, to outline their neuromuscular and cardiac evaluations and determine the manifestations of the disease.

METHODS: This was a retrospective cross-sectional study of patients who had CTR and tenosynovial biopsy from January 2021 to September 2022 at Geisinger Health System.

RESULTS: Of 183 patients who underwent 194 tenosynovial biopsies, 36 (20%) tested positive for amyloidosis. Twenty-four patients (67%) had genetic testing and 2 were diagnosed with hereditary transthyretin amyloidosis (hATTR). The remaining 22 patients (61%) had wild-type transthyretin amyloidosis (wtATTR). Nineteen patients (53%) had EDX studies, of which 9 (25%) demonstrated a large fiber polyneuropathy (LFPN). Two patients (6%) had skin biopsies and 1 (3%) demonstrated a small fiber neuropathy (SFN). Twenty-nine patients (81%) had technetium pyrophosphate scintigraphy, of which 1 (3%) showed grade 1 cardiac amyloidosis. Both patients with hATTR had polyneuropathy (1 LFPN and 1 SFN) and 1 had cardiac amyloidosis. Eighteen patients (50%) were started on green tea extract and 1 (3%) was started on patisiran for amyloid polyneuropathy.

SUMMARY/CONCLUSION: In our cohort of patients who underwent CTR, 20% had amyloidosis. The majority had wtATTR, no polyneuropathy and no cardiac amyloidosis. These findings support that CTS is an early manifestation of amyloidosis. We strongly recommend obtaining tenosynovial biopsies in patients undergoing CTR for early detection of amyloidosis.

Sukhraj Gill, MD

Resident and Fellow Member Award Recipient

Disclosures:

J. David Avila - Speaker bureau and consulting for Alnylam Pharmaceuticals, argenx, and Alexion

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TEACHING PERIPHERAL NEUROANATOMY IN A DIGITAL ERA: DESIGNING AND ASSESSING ONLINE MODULES

Deborah Setter (Rochester, MN), Ruple Laughlin (Rochester, MN)

INTRODUCTION: Peripheral neuroanatomy is a challenging subject but crucial to know in neurology. However, most currently available resources are not targeted towards neurologists. We developed a video series that breaks down peripheral neuroanatomy and its application to the neuromuscular examination into fundamental, intermediate, and advanced levels to target different knowledge levels and enhance examination skills. Visual, aural, reading, and kinetic learning styles are all accommodated, and material is strategically repeated to maximize retention.

OBJECTIVE: Create videos that teach peripheral neuroanatomy by drawing neuroanatomy diagrams, organizing information into a table, then demonstrating the neuromuscular exam to contextualize the material.

METHODS: Nineteen adult and child neurology residents and fellows were surveyed to assess their support for this proposal. Videos were then created with the Mayo Clinic Media Support Services and pre- and post-tests were administered to 12 residents and medical students to measure subjective and objective growth.

RESULTS: Seventy-six percent of respondents reported that more peripheral neuroanatomy teaching was desired and 67% reported that there were not enough resources available to successfully teach themselves. After watching the educational videos, 100% of respondents agreed that the videos helped them learn the subject and improved their neuromuscular exam. On an objective test of anatomical knowledge, scores improved by an average of 20% ± 18% points (range 4%-56% improvement).

SUMMARY: Asynchronous peripheral neuroanatomy teaching modules led to subjective and objective growth in knowledge and filled a critical gap in neurological education.

Deborah Setter, MD, PhD

Resident and Fellow Member Award Recipient

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MULTIFOCAL MONONEUROPATHY SECONDARY TO INFLAMMATORY PSEUDOTUMOR OF THE PERIPHERAL NERVE

Madeline Singer (Philadelphia, PA), Chafic Karam (Philadelphia, PA), Eric Zager (Philadelphia, PA)

INTRODUCTION/BACKGROUND: Mononeuropathies secondary to mass-like lesions have a broad differential diagnosis that includes malignant, inflammatory, and infectious etiologies. Diagnosis is often based on biopsy, but in certain cases the biopsy can be nonspecific. Here, we present a case of ulnar and sciatic mononeuropathies due to inflammatory pseudotumor of the nerve (IPN), which is a rare and overlooked cause of mononeuropathy.

CASE REPORT: A 60-year-old man presented for 3 years of progressive right foot numbness, pain, and weakness. He also reported a history of ulnar neuropathy secondary to a palpable mass at the elbow. The ulnar nerve biopsy showed foci of neurovascular tissue, fibrosis, and inflammation but was nondiagnostic. On exam, he had weakness of the right sciatic and ulnar innervated muscles. Electrodiagnostics showed a sciatic neuropathy with sparing of the short head of the biceps femoris. MRI of the thigh and knee showed an enlarged distal sciatic nerve with cystic enhancement and heterogeneous fusiform thickening. Sciatic nerve biopsy showed loose epineural granulomatous inflammation, perivascular lymphocytes, and moderate axonal degeneration. The differential diagnosis included sarcoidosis, IPN, and less likely leprosy. Additional work-up for sarcoidosis with lumbar puncture and positron emission tomography (PET) scan was unrevealing. He was treated with high dose steroids for IPN.

SUMMARY/CONCLUSION: This case describes a patient with 2 separate mononeuropathies caused by IPN. IPN has been reported in 15 cases in the literature, however multifocal mononeuropathy due to IPN has only been described once. This case also discusses the work-up and differential diagnosis for peripheral nerve lesions associated with granulomas.

Madeline Singer, MD

Resident and Fellow Member Award Recipient

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TRACK CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY PROGRESSION THROUGH APPLE WATCH

Akash Doshi (Tucson, AZ), Holli Horak (Tucson, AZ)

INTRODUCTION/BACKGROUND: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired autoimmune relapsing-remitting neuropathy that tends to cause significant morbidity in patients. CIDP relapses are challenging to diagnose and there is not a reliable tool available at present.

CASE REPORT: A 54-year-old man developed numbness in his toes, which gradually ascended to his thighs. He also developed weakness in his legs. Lumbar puncture came back negative for any infection, however, it was positive for mild inflammation in the form of positive oligoclonal bands. Other labs were negative including ANA, RF, HIV, hepatitis panel, ANCA, GM1 antibody, vitamin B12, and vitamin B6. Washington University neuromuscular panel was also negative for any specific antibody. EMG showed evidence of sensory demyelinating neuropathy. He was started on IVIg 2 gm/kg per month for 3 consecutive months which showed partial response. Then, he was started on mycophenolate which helped to keep CIDP in remission. Since November 2022, the patient noticed that CIDP flare-ups were associated with worsening walking asymmetry on his Apple device. When he doesn't have worsening CIDP flare-up, his walking symmetry stays about 4 to 5%. When he experienced flare-ups, his walking asymmetry increases up to 8 to 9%. He noticed this pattern each time when he experienced a flare-up of CIDP.

SUMMARY/CONCLUSION: The Apple Watch can be used as a reliable tool to monitor the progression of CIDP patients. Wearable devices have been used in other neurological conditions such as multiple sclerosis and Parkinson, however, this is the first case of wearable device use in CIDP patients.

Akash Doshi, MD

Resident and Fellow Member Award Recipient

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CLINICAL EXPERIENCE WITH RAVULIZUMAB FOR TREATMENT OF ACETYLCHOLINE RECEPTOR POSITIVE GENERALIZED MYASTHENIA GRAVIS

Nakul Katyal (Redwood City, CA), Neelam Goyal (Palo Alto, CA), Srikanth Muppidi (Palo Alto, CA)

INTRODUCTION: Ravulizumab is a long-acting C5 complement inhibitor approved for the treatment of acetylcholine receptor positive generalized myasthenia gravis (AChR+ve gMG).

OBJECTIVE: To describe real world experience with ravulizumab in patients with AChR+ve gMG.

METHODS: Retrospective chart review of patients with AChR +ve gMG treated with ravulizumab at a single academic center. Patients for whom Myasthenia Gravis Activity of Daily Living (MG-ADL) scores were available before and after completion of treatment cycle were included in the cohort. Outcome measures were MG-ADL scores, medication changes, and adverse events.

RESULTS: A total of 5 patients (M:F 4:1) with mean age of 50.8 (±12.30) years received ravulizumab. Four out of 5 patients had clinically significant reduction (>2 points) in their MG-ADL scores while it remained stable for 1 patient who was switched from eculizumab to ravulizumab. Clinically meaningful reduction in total MG-ADL score was noted (pre-ravulizumab mean MG-ADL; 5.4 [±2.93] vs post-ravulizumab MG-ADL; 1.6 [±1.95]). Out of 4 patients who were on prednisone pre-ravulizumab, 3 had reduction in their daily prednisone dose. Two patients were on azathioprine and 2 were on mycophenolate prior to ravulizumab and this was continued during infusions. All patients tolerated the infusions well without any side effects and there were no reported severe infections during the follow-up period.

SUMMARY/CONCLUSION: This real-world study of ravulizumab in patients with AChR+ve gMG demonstrated improvement in MG-ADL and allowed for further reduction of concomitant prednisone use.

Nakul Katyal, MD

Resident and Fellow Member Award Recipient

Disclosures:

Neelam Goyal - Serves on Advisory board meeting for Alexion, argenx, Ra/UCB, and Janssen pharma

Srikanth Muppidi - Serves on advisory board meeting for Alexion/AstraZeneca, argenx, Ra/UCB, Horizon Pharma

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PLASMAPHERESIS IN PATIENTS WITH IMMUNE CHECKPOINT INHIBITORS RELATED MYOSITIS WITHOUT MYASTHENIA GRAVIS

Nakul Katyal (Redwood City, CA), Yunce Muharrem (Stanford, CA), Tamiko Katsumoto (Stanford, CA), Srikanth Muppidi (Palo Alto, CA)

INTRODUCTION/BACKGROUND: Immune checkpoint inhibitors (ICIs) may lead to various immune-related adverse events (irAEs) including neuromuscular conditions such as ICI-myositis and ICI-myasthenia gravis (MG). Plasmapheresis is typically not used in patients with myositis without evidence of MG. Here we describe 2 cases of ICI-myositis treated effectively with plasmapheresis.

CASE REPORT: A 64-year-old man with thymic cancer developed progressive subacute myalgias, proximal lower extremity weakness, and dyspnea 1 month after the second dose of nivolumab. Examination was notable for moderate weakness in proximal and distal muscles, with elevated creatine phosphokinase (CPK) levels of 1800 IU. Electrodiagnostic testing (EDX) revealed irritative myopathy with no evidence of neuromuscular junction (NMJ) dysfunction, consistent with ICI myositis. Treatment with IV Solu-Medrol, 3 sessions of plasmapheresis, followed by IVIg and slow prolonged steroid taper resulted in a rapid and dramatic improvement in strength. The second case was a 77-year-old man with stage IIIB squamous cell carcinoma of the lung who developed progressive proximal muscle weakness and became non-ambulatory after cycle 2 of durvalumab. In spite of oral prednisone therapy, his CPK levels remained elevated at 1400 IU. EDX revealed irritative myopathy without evidence of NMJ dysfunction. Treatment with 4 sessions of plasmapheresis followed by prednisone taper improved strength. He was able to ambulate with a walker after the last session of plasmapheresis.

SUMMARY/CONCLUSION: Plasmapheresis in conjunction with other immunosuppressive agents can result in rapid improvement in ICI-related myositis even in patients without associated ICI-MG.

Nakul Katyal, MD

Resident and Fellow Member Award Recipient

Disclosures:

Srikanth Muppidi - Serves on advisory board meeting for Alexion/AstraZeneca, argenx, Ra/UCB, and Horizon Pharma

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A CASE OF FULMINANT CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

Chineze Nwebube (Atlanta, GA), Jonathan Glass (Atlanta, GA), Rocio Garcia Santibanez (Atlanta, GA), Eleanor Thomas (Atlanta, GA)

INTRODUCTION/BACKGROUND: Chronic inflammatory demyelinating polyneuropathy (CIDP) can be difficult to diagnose particularly in patients with severe atypical presentations.

CASE REPORT: We report a 32-year-old male who presented with 6 days of rapidly progressing ascending weakness and numbness in the setting of a viral infection. His lumbar puncture (LP) was unremarkable, however MRI showed cauda equina enhancement suggestive of Guillain-Barre syndrome (GBS). He received 5 days of IVIg and was discharged after improvement. He presented 2 weeks later with dyspnea, dysphagia, and worsened weakness. Examination was notable for 0-1 strength throughout, absent vibratory sensation and diffuse areflexia. Repeat LP revealed albuminocytologic dissociation, MRI brain showed cranial nerve enhancement, and NCS showed absent motor responses in the median and ulnar nerves. Despite an extended course of plasma exchange (PLEX) for probable acute motor sensory axonal neuropathy, he was minimally responsive to treatment and required multiple admissions to the ICU for respiratory compromise. A radial nerve biopsy revealed active demyelination and a preserved population of thinly myelinated fibers, supporting a diagnosis of CIDP. He re-initiated PLEX for 16 sessions and was started on rituximab and prednisone. His strength improved to 4 throughout excluding dorsiflexion (1) and plantarflexion (2). He was discharged to rehab with a modified Rankin Scale of 4 after a 5-month hospitalization.

SUMMARY/CONCLUSION: We describe a case of fulminant acute onset CIDP that was initially diagnosed as GBS. When the patient did not improve as expected, repeat clinical evaluation, including physical exam and nerve biopsy, allowed for the correct diagnosis of CIDP.

Chineze Nwebube, MD, MSc

Resident and Fellow Member Award Recipient

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ULTRASOUND DIAGNOSIS OF CARPAL TUNNEL SYNDROME IN CHARCOT-MARIE-TOOTH TYPE 2A

Saniya Pervin (Lexington, KY), Vishakhadatta Mathur Kumaraswamy (Lexington, KY)

INTRODUCTION/BACKGROUND: Electrophysiologic localization of entrapment neuropathies can be challenging in axonal Charcot-Marie-Tooth (CMT). We present a case of bilateral carpal tunnel syndrome (CTS) confirmed by ultrasonography, which to our knowledge is the first such published report in CMT 2A.

CASE REPORT: A 36-year-old right-handed man presented with slowly progressive bilateral foot drops and gait imbalance beginning at age 15 and neuropathic pain in the lower limbs. He reported similar symptoms in his son. Exam showed atrophy and weakness of the lower limbs below the knees and in the intrinsic hand muscles, cavovarus foot deformities, areflexia, and distal symmetric sensory loss below the knees and below the wrists. He had a postural and action tremor in the upper limbs and a wide-based steppage gait. Genetic testing revealed a pathogenic mutation in the MFN2 gene. At follow-up, he complained of 3 months of intermittent paresthesias and pain in digits 1-3, worse on the left. Electrodiagnostic testing showed absent median, ulnar, and radial sensory responses with decreased ulnar motor amplitudes bilaterally. The left median motor response was absent. On the right, amplitude was reduced with prolonged latency. Neuromuscular ultrasound confirmed bilateral CTS by revealing enlarged, hypoechoic, mildly flattened median nerves at the wrists. A mild notch sign was present on the left, with a possible persistent median artery. Conservative management for several months provided no relief. He was referred to hand surgery for decompression.

SUMMARY/CONCLUSION: Ultrasound is useful for diagnosis of entrapment neuropathies in CMT 2.

Saniya Pervin, MBBS

Resident and Fellow Member Award Recipient

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DIPLOPIA IN A 67-YEAR-OLD WOMAN: A CASE OF CAROTID CAVERNOUS FISTULA WITH POSITIVE ACETYLCHOLINE RECEPTOR BINDING ANTIBODY

John Bireley (Cleveland, OH), Joshua Santucci (Cleveland, OH), Yuebing Li (Cleveland, OH), Devon Cohen (Cleveland, OH)

INTRODUCTION/BACKGROUND: Diplopia is a common chief complaint encountered in an outpatient neurology clinic, and carries a broad differential diagnosis.

CASE REPORT: A 67-year-old woman presented with new horizontal, binocular diplopia and ptosis of 8 months' duration. Associated symptoms included right-sided ptosis, pressure sensation behind the right orbit, bilateral chemosis, and increased lacrimation. Examination showed mild, right-sided, non-fatigable ptosis and limited abduction of the left eye. The differential diagnosis at the time of initial evaluation included myasthenia gravis (MG) and thyroid eye disease. Serum testing revealed a positive acetylcholine receptor binding antibody at a titer of 0.63 nmol/L (normal <0.21 nmol/L) and normal thyroid function. MRI of the brain and orbits without contrast showed symmetric short T1 inversion recovery (STIR) hyperintensity in the bilateral lateral rectus muscles with myotendinous junction sparing and normal muscle bulk. Treatment with pyridostigmine failed to improve her symptoms. Neuro-ophthalmic assessment identified prominent corkscrew vessels bilaterally on slit lamp exam, suggestive of elevated episcleral venous pressure. Digital subtraction angiography was recommended and revealed a carotid cavernous fistula (Barrow type D). The patient underwent coiling and onyx-18 embolization of the fistula. Her symptoms slowly improved with some persistent diplopia at 4-month follow-up.

SUMMARY/CONCLUSION: This case highlights the need for a comprehensive list of differential diagnoses for patients with acquired ophthalmoplegia and ptosis. Key learning points include an illustration of the stepwise diagnostic approach to evaluate for common etiologies, the importance of interpreting test results in the appropriate clinical setting, and the significance of recognizing specific signs and symptoms in achieving the correct diagnosis.

John Bireley, MD

Resident and Fellow Member Award Recipient

Disclosures:
Yuebing Li - Consulted for argenx, Catalyst, Immunovant, and UCB Pharma; received grant support from argenx

ELECTRODIAGNOSTIC CHARACTERISTICS OF SENSORY GANGLIONOPATHIES

Nicolas Ruan dos Santos Cavalcante (São Paulo, Brazil), Antonio Filho (São Paulo, Brazil), Jose Pedro Soares Baima (São Paulo, Brazil), Halisson Flamini (Sao Paulo, Brazil), Lucas Marenga de Arruda Buarque (São Paulo, Brazil), Ian Felipe Barbosa Souza (São Paulo, Brazil), Alberto De Mello (São Paulo, Brazil), Carlos Heise (Sao Paulo, Brazil)

INTRODUCTION: The term sensory ganglionopathy refers to the process in which there is involvement of the body of the sensory neuron at the dorsal root ganglia, with both central and peripheral axonal degeneration.

OBJECTIVE: Describe EDX findings on a series of patient cases with ganglionopathy.

METHODS: Retrospective study based on EDX exams from the Hospital das Clínicas of the University of São Paulo in the last 8 years. EDX criteria similar to Camdessanche criteria were applied. Sensory changes were considered length-dependent if the sural/radial ratio was below 21%. Sensory asymmetry was considered if side-by-side difference was above 50% of potential amplitude.

RESULTS: Twenty-seven patients were identified between November 2014 and April 2022. There was a predominance of females 77% (20). The age of the patients ranged from 11 to 86 years (mean: 53.5). About 88% of the cases (26) met Candessanche criteria. We observed asymmetry in the action potentials in 53% (14) of the cases. Six cases (23%) had a length dependent distribution. There was a predominance of Sjögren syndrome in 34% (9), undetermined etiology in 34% (9), neoplasms in 27% (7), and celiac disease in 7% (2). The H reflex was not obtained in 88% (23) of the cases. The blink reflex was altered in 75% of the cases, but the test was done in only 8 cases.

SUMMARY/CONCLUSION: It was possible to observe non-length dependence, predominance of this pathology in females, and some motor involvement in paraneoplastic etiologies. An important finding is that sural/radial ratio may not differentiate sensory ganglionopathy from polyneuropathy in isolation.

Nicolas Ruan dos Santos Cavalcante, MD

Resident and Fellow Member Award Recipient

RELAPSING SEVERE IMMUNE-MEDIATED DEMYELINATING POLYNEUROPATHY AS A PRESENTING FEATURE OF SYSTEMIC LUPUS ERYTHEMATOSUS

Javed Khanni (Germantown, MD), Kent Werner (Bethesda, MD), Jonathan Bresner (Arlington, VA), Tiffany Pike-Lee (Derwood, MD)

INTRODUCTION/BACKGROUND: Acute inflammatory demyelinating polyneuropathy (AIDP) is a rare presenting manifestation of systemic lupus erythematosus (SLE). We present a case of a relapsing immune-mediated demyelinating polyneuropathy as the initial presenting feature of SLE, successfully treated with rituximab and hydroxychloroquine.

CASE REPORT: A 34-year-old female with no significant past medical history presented with acute descending flaccid paralysis, bilateral six nerve palsy, areflexia, dysautonomia, and bulbar weakness with respiratory failure following a diarrheal illness. She was initially diagnosed with a variant of Guillain-Barre syndrome and treated with IVIg without improvement. Laboratory workup revealed albuminocytologic dissociation on CSF and positive GM1 IgM (titer 169IV normal 0-50IV) on ganglioside panel, negative West Nile virus, paraneoplastic panel, unremarkable MRI brain C/T L spine. She was treated with plasmapheresis for 7 days with improvement and was able to be discharged ambulatory. Two months later, the patient re-presented with recurrent weakness. Interval electrodiagnostic testing showed mixed axonal and demyelinating features and active ongoing denervation. She was treated with 5 days of plasmapheresis. She was found to have positive RNP, anti-Smith, and double stranded DNA with proteinuria and underwent kidney biopsy which showed stage 3 lupus nephritis. She was started on rituximab and hydroxychloroquine and showed significant clinical improvement. The patient has remained stable for over 4 months.

SUMMARY/CONCLUSION: Clinicians should have a high suspicion for underlying autoimmune conditions such as SLE in patients who present with relapsing immune mediated demyelinating polyneuropathies or AIDP. Rituximab may be a treatment consideration in these patients.

Javed Khanni, MD

Resident and Fellow Member Award Recipient

INCIDENTAL ELECTRODIAGNOSTIC FINDINGS OF LEFT RICHE-CANNIEU AND RIGHT MARINACCI ANASTOMOSIS: A CASE REPORT

Miriam Bekhit (Brooklyn, NY), Anam Purewal (Brooklyn, NY), Simron Gill (Brooklyn, NY), Chow Ng (Queens, NY), Sanjeev Agarwal (Brooklyn, NY)

INTRODUCTION/BACKGROUND: Anomalous innervations of the upper limb peripheral nerves is not uncommon. It is important to be aware of them during routine NCS to avoid misdiagnosis and associated iatrogenic injury.

CASE REPORT: A 45-year-old female with a history of right hand crush injury requiring tendon repairs and open reduction and internal fixation in the first metacarpophalangeal (MCP) joint presented with left-sided thumb and wrist pain with no reported injury to this hand, which has been gradually worsening and impairing activities of daily living. Pain was reported to be up to 10/10 intensity, worse with activity, and unrelieved by conservative management. Patient was referred for EMG to evaluate for CTS. Examination was positive for tenderness to palpation and hyperesthesia of left first carpometacarpal (CMC) joint, decreased sensation to temperature and monofilament over first and second left digits. MRI was significant for mild intramuscular and soft tissue edema adjacent to the first CMC joint and opponens pollicis muscle, suggestive of complex regional pain syndrome. EDX study showed evidence of left Riche-Cannieu and right Marinacci anastomosis in the upper extremities and mild slowing of conduction velocity of the right radial and ulnar sensory fibers. This is 1 of the few cases to have different anomalous innervations in upper extremities, and with concomitant all-ulnar left hand.

SUMMARY/CONCLUSION: Identification of anomalous innervations should be part of routine NCS protocols wherever applicable. If these anomalies are not recognized, they may easily be mistaken for technical abnormalities or for actual pathology leading to inappropriate surgical intervention.

Miriam Bekhit, MD

Resident and Fellow Member Award Recipient

ACUTE-ONSET CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY ASSOCIATED WITH COMMON VARIABLE IMMUNODEFICIENCY: A CASE REPORT

Miriam Bekhit (Brooklyn, NY), Simron Gill (Brooklyn, NY), Anam Purewal (Brooklyn, NY), Getahun Kifle (Brooklyn, NY), Sanjeev Agarwal (Brooklyn, NY)

INTRODUCTION/BACKGROUND: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired immune-mediated neuropathy, characterized by a relapsing-remitting or progressive course of proximal and distal symmetric weakness. Some patients may present acutely with a Guillain-Barre syndrome (GBS)-like presentation.

CASE REPORT: A 52-year-old male with panhypopituitarism secondary to resected pineal germ cell tumor presented with 1 week of bilateral lower extremity weakness. He had a notable history of urinary tract infection prior to symptom onset. Lumbar puncture showed albuminocytologic dissociation. The patient received IVIg for presumably GBS and was admitted to acute rehabilitation. Physical exam was consistent for 2/5 lower extremity and 3/5 upper extremity strength bilaterally, areflexia, and profound sensory loss to fine touch and vibration in bilateral lower extremities. The patient showed worsening of motor strength over the next month with minimal functional improvement. He showed signs of respiratory distress requiring intubation and transfer to ICU. Hospital course was prolonged for 6 months, requiring 3 intubations and percutaneous endoscopic gastrostomy placement for dysphagia. Workup was significant for profound humoral deficiency suggestive of common variable immunodeficiency (CVID). Complete metabolic and infectious workup was negative. EDX testing showed severe demyelinating sensorimotor peripheral polyneuropathy with secondary axonal features. He received 2 rounds of IVIg, plasma exchange, corticosteroids, and azathioprine as maintenance therapy with much improvement.

SUMMARY/CONCLUSION: CIDP can have a variable presentation including bulbar weakness and respiratory dysfunction. It should be considered in patients initially diagnosed with acute inflammatory demyelinating polyneuropathy (AIDP) who show minimal to no improvement as they will more likely require long-term immune-modulating therapies.

Miriam Bekhit, MD

Resident and Fellow Member Award Recipient

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QUANTITATIVE ULTRASOUND OF THE RECTUS FEMORIS IN PATIENTS WITH INCLUSION BODY MYOSITIS

Joseph Ditrapani (Boston, MA), Hilda Gutierrez (Boston, MA), Soleil Samaan (Boston, MA), Courtney McIlduff (Boston, MA), Seward Rutkove (Boston, MA)

INTRODUCTION: New techniques are required to help identify optimal biopsy sites in myopathies such as inclusion body myositis (IBM). Quantitative ultrasound (QUS) is a painless, noninvasive technique that can be used to objectively measure muscle health. Diseased muscle is associated with increased gray scale level (GSL).

OBJECTIVE: The objective of this study was to compare GSL values of rectus femoris, a muscle that is commonly affected in IBM, in patients and gender-matched healthy controls.

METHODS: QUS was performed with a total of 4 IBM patients (4 males, mean age 71.3 years, SD 3.19) with clinical quadriceps weakness and 4 healthy volunteers (4 males, mean age 52.3 years, SD 12.8) without neuromuscular disease. Images were obtained with rectus femoris in a relaxed state using an FDA approved Terason t3000 ultrasound machine and a linear 5-12 MHZ transducer. GSL was obtained from a region of interest on each image using ImageJ software. An unpaired 2-sample t-test was completed comparing the mean GSL values of the rectus femoris amongst diseased versus healthy controls.

RESULTS: The mean GSL value of the rectus femoris for IBM patients was 45.7 versus 25.1 for healthy controls ($p=0.11$, 95% confidence interval of the difference -6.25 to 47.5).

SUMMARY/CONCLUSION: QUS showed higher mean GSL of the rectus femoris in IBM patients compared to healthy controls. As a more cost-efficient alternative to MRI, QUS could be used as a bedside tool to confirm involved muscle sites for biopsy in IBM and other muscle disorders.

Joseph Ditrapani, MD, MPH

Resident and Fellow Member Award Recipient

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CONUS MEDULLARIS SYNDROMES ARE A COMMON MIMIC OF DIVERSE NEUROMUSCULAR DISEASES

Michelle Glantz (Chicago, IL), Rabia Malik (Chicago, IL), Madhu Soni (Chicago, IL), Ricardo Fontes (Chicago, IL)

INTRODUCTION/BACKGROUND: Conus medullaris syndromes are characterized by either or both upper or lower motor neuron dysfunction secondary to structural injury to the most distal spinal cord. The clinical presentation is variable and can pose diagnostic challenges to neuromuscular clinicians.

OBJECTIVE: To describe a series of patients presenting to a tertiary care center neuromuscular clinic for a presumed neuromuscular disease and later found to be symptomatic of compression of the conus medullaris.

METHODS: We identified patients seen between 2021 and 2023 who underwent evaluation for neuromuscular disease and were later identified as having a conus medullaris syndrome.

RESULTS: We identified 5 cases who were referred for neuromuscular evaluation and subsequently diagnosed with conus medullaris compression. All had very motor-predominant symptoms and severe leg atrophy was common. One patient underwent extensive genetic evaluation for a presumed hereditary distal myopathy. One patient received immunotherapy for a suspected immune-mediated motor neuropathy. One patient underwent extensive evaluation for HIV-related motor neuron disease versus mononeuropathies. All patients were ultimately referred for surgical evaluation.

SUMMARY/CONCLUSION: Conus medullaris syndromes can present with a wide range of upper versus lower motor neuron signs, including prominent atrophy. The presentation can feature a paucity of sensory symptoms. As such, these patients may be referred to and undergo extensive evaluation with neuromuscular neurologists or physiatrists. Careful choice and review of neuro-imaging is essential in order to identify and manage this treatable presentation.

Michelle Glantz, DO

Resident and Fellow Member Award Recipient

BILATERAL PARSONAGE-TURNER SYNDROME WITH FLACCID PARALYTIC BICEPS BRACHII AND CLINICAL BRACHIALIS SPARING: A CASE REPORT

James Meiling (Rochester, MN), Marianne Luetmer (Rochester, MN), Marcus Vinicius Pinto (Rochester, MN), James Klaas (Rochester, MN), Lyell Jones (Rochester, MN)

INTRODUCTION/BACKGROUND: Parsonage-Turner syndrome (PTS) is an inflammatory neuromuscular syndrome that characteristically presents as acute-onset arm pain with subsequent disabling weakness. While commonly affecting motor-predominant peripheral nerves, like the musculocutaneous nerve, atrophy of 1 muscle with complete sparing of an identically innervated other is uncommon.

CASE REPORT: A 39-year-old male presented with bilateral biceps paralysis. Three months previously he received a tetanus immunization without any reactions. One month later he awoke to excruciating right shoulder pain with radiation into his anterolateral forearm. A few days later he noted poor activation of his right biceps with relatively preserved elbow flexion, prompting a 5-day trial of prednisone 40 mg without improvement. The following month the left biceps underwent a similar symptomatic progression. Both biceps exhibited flaccid paralysis yet clinically preserved sub-biceps brachialis activation. He also had decreased anterolateral forearm sensation. NCS showed absent lateral antebrachial cutaneous sensory nerve action potentials (SNAPs) and a low amplitude right radial SNAP. EMG demonstrated (2+) right biceps fibrillation potentials with no voluntary activation of bilateral biceps and diffuse reduced recruitment of mildly complex motor unit potentials throughout the right upper limb. He was diagnosed with asymmetric (right worse than left) PTS significantly affecting bilateral biceps and clinical brachialis sparing.

SUMMARY/CONCLUSION: While both biceps and brachialis share an identical innervation, PTS affects biceps in 61% of patients and appears to favor biceps over brachialis involvement. Preserved brachialis strength may provide functional elbow flexion despite presence of a flaccid biceps, necessitating a high index of suspicion for this disorder.

James Meiling, DO

Resident and Fellow Member Award Recipient

IATROGENIC BRACHIAL PLEXOPATHY FROM AN INTERSCALENE BRACHIAL PLEXUS NERVE BLOCK: A CASE REPORT

James Meiling (Rochester, MN), Christine Hunt (Jacksonville, FL)

INTRODUCTION/BACKGROUND: An interscalene brachial plexus nerve block (ISNB) is an effective option for regional anesthesia during shoulder surgery, with a major complication rate of 0.35%. Although rare, iatrogenic brachial plexus injuries can occur during shoulder surgery due to plexus traction, abnormal positioning, or ISNB.

CASE REPORT: A 68-year-old male presented with right upper limb pain. Three months previously he underwent a right arthroscopic rotator cuff repair and preoperative ISNB with immediate stabbing and sharp postoperative anterolateral shoulder pain upon awakening from anesthesia. He exhibited continued pain yet normal strength and sensation; there was no allodynia. He had atrophy throughout the right upper limb, particularly in the pectoral girdle and supraspinatus. His clinical picture was not consistent with complex regional pain syndrome (CRPS), nor with Parsonage-Turner syndrome (PTS). A brachial plexus MRI showed atrophy, edema, and enhancement within the right supraspinatus, infraspinatus, teres minor, and deltoid muscles, reflecting postoperative inflammation, PTS, or a possible underlying brachial plexopathy. NCS showed borderline low radial sensory amplitude. EMG was significant for triceps brachii fibrillations and long duration extensor digitorum communis motor unit potentials. He was diagnosed with an iatrogenic middle trunk or posterior cord brachial plexopathy from an ISNB.

SUMMARY/CONCLUSION: Brachial plexopathy is a difficult diagnosis and benefits from the use of multiple diagnostic examinations, including history, physical examination, brachial plexus MRI, and EDX. Having the correct diagnosis is key to an effective treatment plan, which is why it was important to clinically distinguish between CRPS, PTS, and iatrogenic brachial plexopathy.

James Meiling, DO

Resident and Fellow Member Award Recipient

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GUYON CANAL NEUROPATHY WITH PARESTHESIAS IN DIGITS 3-5: ELECTRODIAGNOSTIC EVIDENCE OF BERRETTINI ANASTOMOSIS MAY EXPLAIN SYMPTOM EXTENSION TO DIGIT 3

Amber Vocelle (Lansing, MI), Cheryl Craig (Berkley, MI), Colin Buday (Lansing, MI), Daniel Jimenez (Lansing, MI), Michael Andary (East Lansing, MI), Geoffrey Seidel (Troy, MI)

INTRODUCTION/BACKGROUND: Berrettini anastomosis (BA) is an anatomical sensory crossover in the palm that occurs between the ulnar and the third common median palmar sensory nerves. This common ulnar sensory crossover results in ulnar nerve derived sensory fibers supplying digit 3 (D3). Multiple EDX studies have documented ulnar nerve stimulation nerve conduction waveforms measurable on D3 in the presence of CTS. However, there have been no reported cases of Guyon canal neuropathy with EDX evidence of BA.

CASE REPORT: A 49-year-old male with no relevant past medical history presented to EMG clinic with complaints of right D3-5 paresthesias without weakness. Subsequent NCS elicited prolonged ulnar sensory nerve action potential (SNAP) peak latency recorded from D5 across the wrist, consistent with ulnar neuropathy of Guyon canal. The same prolonged ulnar SNAP peak latency was recorded from D3 when stimulating the ulnar nerve at the wrist consistent with BA. Motor and EMG data were normal.

SUMMARY/CONCLUSION: This is the first reported case of EDX evidence of BA in a patient with Guyon canal ulnar neuropathy. Together with the patient's sensory findings, this illustrates that ulnar distribution paresthesias extending to D3 in the setting of Guyon canal sensory ulnar neuropathy may be secondary to BA.

Amber Vocelle, DO, PhD

Resident and Fellow Member Award Recipient

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NEUROGENIC THORACIC OUTLET SYNDROME PRESENTING DECADES AFTER NEONATAL BRACHIAL PLEXUS PALSY: TWO RELATED LESIONS?

Kyle Medley (Ann Arbor, MI), Sandra Hearn (Ann Arbor, MI)

INTRODUCTION/BACKGROUND: Neurogenic thoracic outlet syndrome (nTOS), classically a lesion of the lower trunk or anterior primary rami of C8 and T1, arises in the setting of longstanding regional structural pathology. We present a case of nTOS in an adult with a prior history suspicious for neonatal brachial plexus palsy (NBPP).

CASE REPORT: A 30-year-old female with a history of clavicular fracture at birth and lifelong stable right medial upper limb numbness presented with (a) 1 year of progressive right thenar eminence atrophy/weakness and (b) progressive right neck/periscapular pain. Exam additionally revealed patchy sensory loss (largely medial) and asymmetrically diminished brachioradialis reflex. Findings: Right upper limb NCS: low ulnar sensory and median motor amplitudes. Median and medial antebrachial cutaneous (MABC) sensory and ulnar motor studies were largely normal. EMG: rare fibrillations in opponens pollicis and decreased recruitment of large motor unit action potentials through the T1 > C8 myotomes. MRI brachial plexus: prominent right C7 transverse process with possible fibrous band distorting the C8 root and lower trunk.

SUMMARY/CONCLUSION: 1. Co-occurrence of nTOS and NBPP raises question of whether regional congenital anomalies predispose to both conditions. Regional trauma associated with NBPP may also modify risk of nTOS years later. 2. This case, with relative sparing of MABC fascicles, exemplifies that nTOS may have heterogeneous EDX abnormalities beyond the classic T1 > C8 pattern. 3. Progressive and focal T1/C8 deficit, in the setting of presumed NBPP, may herald a second lesion at/about the thoracic outlet.

Kyle Medley, DO

Resident and Fellow Member Award Recipient

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A CASE OF ULNAR MONONEUROPATHY FROM HEREDITARY SENSORY AND AUTONOMIC NEUROPATHY TYPE IV RELATED CHARCOT JOINT

Nathaniel Wooten (Chapel Hill, NC), Kristopher Karvelas (Chapel Hill, NC), Rebecca Traub (Chapel Hill, NC)

INTRODUCTION/BACKGROUND: Hereditary sensory and autonomic neuropathy type IV (HSAN IV) is an autosomal recessive disorder in the NTRK1 gene resulting in sensory loss and anhidrosis. It is a disease of small fibers, sparing large sensory and motor function on NCS. Charcot joint, a change in the joint structure secondary to sensation loss, is a well-described complication of HSAN IV. However, entrapment neuropathies and accompanying EDX and NM US results secondary to Charcot joint have not been previously described.

CASE REPORT: A 13-year-old boy with HSAN IV presented with 3 months of right hand numbness and weakness in the setting of right elbow Charcot joint, previous fracture, and surgery. Electrodiagnostic testing showed an absent sensory evoked response in the right ulnar nerve. The right ulnar motor study showed low compound muscle action potential (CMAP) amplitudes, but focal slowing could not be localized. Studies of the left ulnar nerve and bilateral median nerves were normal. Needle EMG showed active denervation in the abductor digiti minimi (ADM) and first dorsal interosseous (FDI) muscles. Neuromuscular ultrasound showed no focal enlargement but there was an abnormal abrupt turn of the nerve over the anterior epicondyle, consistent with scar tissue.

SUMMARY/CONCLUSIONS: HSAN IV causes disease of small and autonomic nerve fibers with NCS typically being normal. This case describes the EDX and US findings of an entrapment neuropathy secondary to Charcot joint in this disease.

Nathaniel Wooten, MD

Resident and Fellow Member Award Recipient

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ATYPICAL PATHOLOGICAL FEATURES IN IDIOPATHIC INFLAMMATORY MYOPATHIES

Hassan Alhussein (Birmingham, AL), Usama Tariq (Birmingham, AL), Coreen Schwartzlow (Hoover, AL), Kenkichi Nozaki (Birmingham, AL)

INTRODUCTION: In idiopathic inflammatory myopathies (IIMs), myopathology of immune-mediated necrotizing myopathy (IMNM) is known for myofiber necrosis with minimum inflammation, while that of other IIMs is for various interstitial inflammation. In clinical practice of myopathology interpretation, however, both inflammation and myofiber necrosis are seen in the same patient frequently, and in such a case, it is difficult to classify IIM based on myopathological features.

OBJECTIVE: Investigate atypical myopathological features in IIMs.

METHODS: We retrospectively reviewed medical record and myopathology of IIM cases who were clinically evaluated and underwent muscle pathology interpretation at the University of Alabama at Birmingham from 2014 to 2022.

RESULTS: Seventy-eight IIM cases were classified into IMNM (29), sporadic inclusion body myositis (sIBM, 16), polymyositis with mitochondrial pathology (PM-mito, 10), dermatomyositis (5), antisynthetase syndrome (ASS, 6), and overlap myositis (OM, 12). Endomysial inflammation was seen in 9 IMNM cases (31%). In other IIMs, myofiber necrosis was most frequently seen in ASS (5/6, 83%), followed by dermatomyositis (4/5, 80%), sIBM (9/16, 56%), PM-mito (2/10, 20%), and overlap myositis (3/12, 20%).

SUMMARY/CONCLUSION: We identified myopathological features which were considered to be atypical in each IIM actually to be frequent. Clinical and serological information is important in IIM classification.

Hassan Alhussein, MD

Resident and Fellow Member Award Recipient

DIAGNOSING X-LINKED MYOPATHY WITH EXCESSIVE AUTOPHAGY AFTER 30 YEARS: GENETIC, ULTRASONOGRAPHIC, AND ELECTRODIAGNOSTIC FINDINGS

Vanessa Dwairi (Pittsburgh, PA), Alaina Giacobbe (Pittsburgh, PA), Sasha Zivkovic (Madison, CT), David Lacomis (Pittsburgh, PA)

INTRODUCTION/BACKGROUND: X-linked myopathy with excessive autophagy (XMEA) is a rare disorder caused by a mutation in the vacuolar ATPase assembly factor (VMA21) gene leading to dysregulation of organelle autophagy in the lysosomal pathway. Clinical features include slowly progressive proximal weakness with onset before the age of 20 years and loss of ambulation by the age of 50-70 years. EDX usually shows widespread complex repetitive and myotonic discharges, even in muscles unaffected clinically.

CASE REPORT: A 65-year-old male presented with slowly progressive, lower greater than upper extremity proximal weakness since his teenage years. A family history of unspecified weakness followed an X-linked pattern. Extensive workup over 30 years prior to presentation revealed mildly elevated serum creatine kinase and otherwise inconclusive EDX and muscle histopathology. He carried a diagnosis of suspected X-linked spinal motor atrophy that was rebuked by genetic testing which showed a pathogenic mutation in the c.*6A>G variant of the VMA21 gene. Neuromuscular ultrasound was more informative than repeat EDX which revealed some muscles with prominent hyperechogenicity and decreased bone echo. Directed muscle biopsy showed an autophagic vacuolar myopathy.

SUMMARY/CONCLUSION: XMEA is a rare disorder that can be easily misdiagnosed if not considered in the differential diagnosis. Our case demonstrates a diagnostic challenge as EDX did not show typical spontaneous discharges and it took over 30 years, multiple neurologic evaluations, and genetic screening to obtain a diagnosis. Especially in XMEA, neuromuscular ultrasound may aid in diagnosis even when EDX findings are inconclusive.

Vanessa Dwairi, MD

Resident and Fellow Member Award Recipient

A CASE OF PORPHYRIC NEUROPATHY MISDIAGNOSED AS MOTOR NEURON DISEASE

Morgan Heber (Cleveland, OH), Benjamin Claytor (Cleveland, OH)

INTRODUCTION/BACKGROUND: Acute intermittent porphyria (AIP) is an inherited, metabolic disorder characterized by discrete attacks of abdominal pain, psychiatric symptoms, and motor-predominant neuropathy. Diagnosing porphyric neuropathy poses many challenges, but it should be in the differential for young patients presenting with a motor-predominant neuropathy or neuronopathy.

CASE REPORT: A 37-year-old male presented with 9 months of rapidly-progressive weakness, muscle atrophy, and preserved reflexes. His electrodiagnostic testing demonstrated normal sensory responses along with active and chronic diffuse denervation leading to a diagnosis of ALS. On further history, he revealed significant abdominal pain about a year prior with extensive workup including exploratory laparotomy. Twenty-four-hour urine porphobilinogen was 463 µmol/L (normal <1.8 µmol/L) and genetic testing found a pathogenic mutation of hydroxymethylbilane synthase, consistent with autosomal dominant AIP. He was diagnosed with porphyric neuropathy secondary to AIP and treated with prophylactic givosiran and hematin for acute attacks.

SUMMARY/CONCLUSION: This case demonstrates the many potential pitfalls in the diagnosis of porphyric neuropathy. The clinical and electrodiagnostic findings may mimic ALS or other motor-predominant neuropathy/neuronopathy. Additionally, with the seemingly unrelated nature of AIP's visceral and psychiatric symptoms, patients may fail to mention them. Thus, screening for a history of AIP's symptoms should be pursued while evaluating any young person with a motor neuropathy. A history of abdominal pain of unclear etiology, transient psychiatric symptoms, or dark urine should prompt further investigation to avoid the implications of incorrectly delivering a devastating diagnosis while delaying treatment of a reversible neuropathy.

Morgan Heber, MD

Resident and Fellow Member Award Recipient

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IS REPETITIVE NERVE STIMULATION TESTING LESS INFORMATIVE IN VERY EARLY-STAGE MYASTHENIA GRAVIS?

Morgan Heber (Cleveland, OH), Jeremy Hill (Cleveland, OH), Yuebing Li (Cleveland, OH)

INTRODUCTION: Repetitive nerve stimulation (RNS) is an important tool in the diagnostic evaluation for myasthenia gravis (MG), especially in seronegative patients. The current literature demonstrates conflicting findings regarding the sensitivity of RNS for early-stage patients.

OBJECTIVE: To compare the sensitivities of RNS in early-stage (≤ 1 month from symptom onset) and late-stage (> 1 month from symptom onset) MG.

METHODS: Electronic medical records were retrospectively searched for MG patients who underwent RNS between the years of 2017-2021 at our institution. Additional data including patient demographics, Myasthenia Gravis Foundation of America (MGFA) classification, antibody results, and thymus status were collected.

RESULTS: The study identified 177 MG patients with a mean age of 60 years; 92 were male and 85 female. An average of 3 nerves were tested per patient per RNS session. Twenty patients had early-onset MG (median symptomatic duration of 3 weeks) and 157 were late-onset (median duration of 12 months). One hundred twenty-eight patients were acetylcholine antibody positive, 7 positive for muscle specific tyrosine kinase antibody, and 40 were seronegative. When including all MGFA classes, RNS was positive in 55.0% of cases in early-onset patients and 60.5% of those late-onset (p=0.64). While there was a trend towards increased RNS sensitivity in patients with more severe symptoms, no difference was observed within the same MGFA classification between early and late-onset subgroups.

SUMMARY/CONCLUSION: RNS sensitivity in early-stage myasthenic patients is similar to those with late-stage MG. These findings support the use of RNS in the diagnostic evaluation of MG in those presenting acutely.

Morgan Heber, MD

Resident and Fellow Member Award Recipient

Disclosures:

Yuebing Li - Consulted for argenx, Catalyst, Immunovant, and UCB Pharma; received grant support from argenx

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LONGITUDINAL MANAGEMENT OF SIALORRHEA IN VETERANS WITH AMYOTROPHIC LATERAL SCLEROSIS USING BOTULINUM TOXIN

Josh Wilson (Seattle, WA), Jared Neeley (Salt Lake City, UT), Ileana Howard (Woodinville, WA)

INTRODUCTION: Bulbar symptoms are common in ALS and contribute to an increased risk of aspiration-related morbidity and mortality. While formulations of botulinum toxin (BoNT) have been FDA-approved for sialorrhea management since 2018, there remains a paucity of investigations into its use in patients with ALS.

OBJECTIVE: To investigate the use of BoNT injections for sialorrhea over the course of disease in veterans with ALS.

METHODS: Treatment records from 2013-2023 for a single ALS center were reviewed to identify patients with ALS who underwent BoNT injection for sialorrhea (n=19). Records were reviewed for frequency and timing of injections, potential adverse events related to BoNT injections, concurrent antisialagogues, and surgical management.

RESULTS: Nineteen unique patients were identified for this review. Of these, 47.4% had more than 1 injection (range 1-7); 5 (26.3%) stopped injections due to secretion changes. No immediate post-procedural complications were noted. In 26% of patients, 1 or more antisialogogues were discontinued after injection. Two patients were admitted for aspiration pneumonia within 3 months after their injection; however, both went on to repeat injections. Following tracheostomy, 87.5% continued to receive BoNT injections post-procedurally.

SUMMARY/CONCLUSION: In this single-center retrospective review, BoNT injections appear to be safe and effective for managing ALS-related sialorrhea. The most common reason for discontinuation cited was a change in secretion quality. Following tracheostomy, a majority of patients continued injections.

Josh Wilson, MD

Resident and Fellow Member Award Recipient

Disclosures:

Jared Neeley - Serves as Medical Science Liaison for Merz Therapeutics

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ACUTE MOTOR AXONAL NEUROPATHY AS A COMPLICATION OF GRAFT VERSUS HOST DISEASE

Benjamin Rardin (Portland, OR), Stephan Castro (Portland, OR), Robert Fuino (Portland, OR), Justin Miller (Portland, OR), Amanda Keller (Portland, OR), Matthew G McCaskill (Portland, OR), Nizar Chahin (Portland, OR)

INTRODUCTION/BACKGROUND: Neuromuscular manifestations of graft versus host disease (GVHD) include myositis most commonly, followed by neuromuscular junction (NMJ) disease and acute inflammatory demyelinating polyradiculoneuropathy (AIDP). This case describes a rare example of acute motor axonal neuropathy (AMAN) occurring as a suspected manifestation of GVHD.

CASE REPORT: A 58-year-old man presented with 2 weeks of progressive muscle weakness. His history was notable for essential thrombocytosis requiring bone marrow transplant which was further complicated by GVHD with skin and gastrointestinal symptoms occurring several months preceding onset of weakness. On exam the patient was noted to have symmetric proximal more than distal upper extremity weakness as well as distal lower extremity weakness without sensory deficits. He did not have any symptoms or findings suggestive of porphyria. Given this exam, there was concern for a myopathic process. Serum workup was unremarkable and muscle biopsy showed neurogenic changes. Lumbar puncture showed cytoalbuminologic dissociation. NCS showed diffusely low compound motor action potential without exercise facilitation. Overall, combined needle EMG and NCS demonstrated a severe, subacute, motor axonal polyradiculoneuropathy consistent with AMAN. The patient was subsequently treated with plasma exchange and experienced gradual improvement in weakness.

SUMMARY/CONCLUSION: In this patient with subacute progressive weakness without sensory changes, there was a high suspicion for GVHD-related myositis. The AMAN variant of Guillain-Barre syndrome (GBS) is an uncommonly described manifestation of GVHD that presents without sensory deficits. This case illustrates the importance of considering AMAN in this patient population as there are key differences in acute management as well as in risk of recurrence and overall prognosis.

Benjamin Rardin, MD

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NEUROMUSCULAR ULTRASOUND FEATURES OF SARCOID TIBIAL MONONEUROPATHY

Hemani Ticku (Cleveland, OH), David Preston (Shaker Heights, OH)

INTRODUCTION/BACKGROUND: Sarcoidosis is a multisystem granulomatous disease characterized by non-caseating granulomas, frequently affecting the nervous system. Neurosarcoidosis commonly manifests as leptomeningeal involvement, cranial nerve palsies, myopathy, or polyneuropathy. Peripheral mononeuropathy has been reported but is rare. An increase in nerve cross-sectional area and fascicular size have been reported on neuromuscular ultrasound (NMUS) in sarcoid neuropathy.

CASE REPORT: A 35-year-old woman developed increased lacrimation and pain in the right eye, a lump on the back, and pain and weakness of left ankle and toe plantarflexion along with numbness of the sole and lateral foot over 3 months. MRI orbits showed a mass in the right lacrimal gland. Positron emission tomography scan showed hypermetabolic activity in the same area in addition to a subcutaneous mass in the back and in the left lower extremity in the posterior compartment. Biopsy of the subcutaneous mass showed non-caseating granulomatous inflammation consistent with sarcoidosis. EDX showed a non-localizable left tibial neuropathy. On NMUS, the tibial nerve cross-sectional area was normal. Multiple nodules along the tibial nerve and hypoechoic material encasing the tibial nerve were noted, representing sarcoid granulomas and granulomatous inflammation, respectively. There was denervation atrophy preferentially affecting the lateral head of the gastrocnemius muscle and more severely the flexor hallucis longus muscle.

SUMMARY/CONCLUSION: In addition to direct neural involvement, mononeuropathy in sarcoid can also occur from external compression and encasement of nerve by granulomatous inflammation which can be assessed by NMUS. This case also highlights the importance of NMUS in the ability to localize an electrically non-localizable mononeuropathy.

Hemani Ticku, MD

Resident and Fellow Member Award Recipient

NONLOCALIZABLE ULNAR NEUROPATHY DUE TO GANGLION CYST - ROLE OF NEUROMUSCULAR ULTRASOUND

Hemani Ticku (Cleveland, OH), Christopher Geiger (Cleveland, OH)

INTRODUCTION/BACKGROUND: EDX, being the mainstay of diagnosis of focal neuropathies, help localize and grade severity of mononeuropathies. However, the diagnosis of non-localizable neuropathies due to structural lesions can be challenging using EDX alone. Neuromuscular ultrasound (NMUS) provides dynamic and anatomical details and can aid in increasing diagnostic accuracy of such cases and lead to better patient outcomes.

CASE REPORT: A 68-year-old right-handed man presented with 1 month of left hand weakness, numbness, and paresthesia on the volar medial hand including digits 4 and 5, and a painful swelling at the left wrist. He had marked weakness of left first dorsal interosseous (FDI) muscle and minimal weakness in abductor digiti minimi (ADM) with preserved strength of long finger flexors and non-ulnar C8 innervated muscles. NCS/EMG showed a severe, chronic, non-localizable left ulnar neuropathy without active denervation. The FDI was disproportionally affected compared to hypothenar muscles. NMUS showed evidence of ulnar nerve compression just proximal to Guyon canal but distal to take off of the dorsal ulnar cutaneous branch. At this location, the nerve was being compressed by a large, well-circumscribed, hypoechoic mass which was seen to communicate with underlying carpal joint space, suggesting a ganglion cyst. The intrinsic hand muscle echotexture was preserved, suggesting the pathophysiology to be focal demyelination, favoring good prognosis following treatment.

SUMMARY/CONCLUSION: The case highlights the importance of NMUS in diagnosis and prognosis of a non-localizable mononeuropathy due to a structural lesion.

Hemani Ticku, MD

Resident and Fellow Member Award Recipient

LAMBERT-EATON MYASTHENIC SYNDROME PRESENTATION AS EVALUATION FOR CARPAL TUNNEL SYNDROME

Tyler Crissinger (Portland, ME), Michael Kleinman (Portland, ME)

INTRODUCTION/BACKGROUND: Lambert-Eaton myasthenic syndrome (LEMS) is a prototypical presynaptic neuromuscular junction disorder, and while it is often a manifestation of a paraneoplastic disease, it is underdiagnosed. This case report highlights an atypical clinical presentation which came to light through electrodiagnostic testing.

CASE REPORT: A 61-year-old man with a history of cigarette smoking presented for a nerve conduction study due to a complaint of hand weakness and suspicion for carpal tunnel syndrome. His nerve conduction study and electromyography were instead significant for findings consistent with LEMS, which then led to workup for malignancy. Small cell lung cancer was eventually discovered years later.

SUMMARY/CONCLUSION: LEMS can have variable presentation and neurologists should be aware of characteristics of neuromuscular junction disease. In performing electrodiagnostic studies, if there are diffusely low amplitude compound motor action potentials out of proportion to exam, one should consider expanding the test for signs of post-exercise facilitation and other testing if needed, such as repetitive stimulation or single fiber electromyography.

Tyler Crissinger, MD

Resident and Fellow Member Award Recipient

A CASE OF PRIMARY MEMBRANOUS NEPHROPATHY IN A PATIENT WITH MYASTHENIA GRAVIS

Sarah Smith (King, NC), Rachana Gandhi Mehta (Winston-Salem, NC)

INTRODUCTION/BACKGROUND: Ten to 20% of myasthenia gravis (MG) patients have other autoimmune diseases. Membranous nephropathy (MN) in the setting of MG has been reported infrequently in the literature. We present a case of nephrotic syndrome secondary to primary MN in a patient with nonthymomatous MG.

CASE REPORT: A 60-year-old male presented with diplopia and fatigue and was diagnosed with MG based on positive AChR antibody in 2016. CT chest did not show any evidence for thymoma. His ocular symptoms responded very well to pyridostigmine, but he continued to have severe fatigue despite adding prednisone and mycophenolate. In 2018, he began to have generalized edema with worsening of his fatigue and foamy urine. Further lab workup revealed severe proteinuria and positive anti-PLA2R antibodies indicating primary MN as an etiology for his nephrotic syndrome. The patient received rituximab infusion every 6 months for 2 years, oral cyclophosphamide 200 mg/day with a tapering course over 9 weeks and prednisone 60 mg/day with a tapering course over 7 weeks followed by tacrolimus for 1 year. Mycophenolate was discontinued in lieu of starting stronger immunosuppressants. His MG remained well controlled with switching immunotherapy and has been in remission since last rituximab infusion in October 2021.

SUMMARY/CONCLUSION: Our case illustrates rare co-existence of MG and MN. Presence of PLA2R antibodies suggests primary rather than secondary MN. In our case, MG preceded MN and the patient did not have evidence for thymoma. Substitution of mycophenolate with rituximab, cyclophosphamide, prednisone, and tacrolimus resulted in marked improvement in nephrotic syndrome and remission of MG.

Sarah Smith, MD

Resident and Fellow Member Award Recipient

EXPERIENCE WITH SUBCUTANEOUS IMMUNOGLOBULIN IN PATIENTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY AND OTHER ACQUIRED DEMYELINATING NEUROPATHIES

Mark Levine (Atlanta, GA), Vita Kesner (Atlanta, GA), Michael Khoury (Atlanta, GA), R. Carolina García-Santibáñez (Atlanta, GA), Andrés De León (Atlanta, GA)

INTRODUCTION: Subcutaneous immunoglobulin (SCIg) is newly approved by the FDA for maintenance treatment of chronic inflammatory demyelinating polyneuropathy (CIDP). There is sparse data on real-world experience with SCIg in CIDP or similar disorders.

OBJECTIVE: To describe the effectiveness and side effect profile of SCIg in CIDP and similar disorders and compare that to IVIg.

METHODS: A retrospective cohort analysis identified 12 patients with CIDP or similar disorders treated with SCIg. Charts were reviewed for patient and disease characteristics, and duration, effectiveness, and side effects of therapy.

RESULTS: Median age was 58 (IQR 15.5) and 83% were female. Fifty percent of patients had CIDP, 25% had multifocal motor neuropathy (MMN), and the remainder had other acquired demyelinating neuropathies. All but 1 had been on IVIg prior to starting SCIg. Eighty-two percent responded fully to IVIg and the remainder responded partially. Side effects were experienced by 45% on IVIg with the most common being headache and flu-like symptoms. The median time on IVIg before transition to SCIg was 14.5 months (IQR 70.0) and the median time on SCIg prior to data capture was 14.3 months (IQR 20.8). Only 1 patient discontinued SCIg and that patient had comorbid metastatic cancer. Nine of 11 (82%) had similarly effective response with SCIg as with IVIg. The only side effect experienced on SCIg was redness or discomfort at the injection site at a rate of 36%.

SUMMARY/CONCLUSION: In patients with CIDP or similar disorders, SCIg had a similar effectiveness and better side effect profile when compared to IVIg.

Mark Levine, MD, MA

Resident and Fellow Member Award Recipient

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A RARE, ATYPICAL CASE OF INCLUSION BODY MYOSITIS IN A PATIENT WITH DYSPNEA AS THE CHIEF AND PREDOMINANT COMPLAINT

Mark Levine (Atlanta, GA), Christina Fournier (Atlanta, GA), Jonathan Glass (Atlanta, GA), R. Carolina García-Santibáñez (Atlanta, GA), Eleanor Thomas (Atlanta, GA)

INTRODUCTION/BACKGROUND: Dyspnea due to diaphragm weakness in inclusion body myositis (IBM) is typically not a prominent feature and may occur in later stages of the disease. However, we describe a rare case of a patient found to have IBM with dyspnea as the presenting and chief complaint.

CASE REPORT: A 68-year-old man was referred to neurology clinic for 3 years of slowly progressive exertional dyspnea and orthopnea with restrictive pulmonary function tests. He denied focal muscle weakness, weight loss, increased falls, or sensory issues. On exam he had mild weakness in bilateral deltoids with otherwise full strength throughout. There was no atrophy, fasciculations, upper motor neuron signs, or fatigability. Motor neuron disease was suspected. Laboratory testing revealed normal creatine kinase (CK) and presence of anti-NT5C1a antibodies. Alpha-glucosidase activity was normal. CT chest showed bilateral diaphragm atrophy. EMG/NCS was nondiagnostic. There was no target muscle to biopsy. Over the next 2 years he developed only mild symmetric weakness of the iliopsoas and first dorsal interossei without finger flexor weakness. The dyspnea progressed minimally prompting consideration of an alternative diagnosis. A muscle biopsy of the right deltoid roughly 2½ years after initial presentation revealed grossly normal muscle architecture with several rimmed vacuoles and few ragged red fibers, confirming a diagnosis of IBM.

SUMMARY/CONCLUSION: In patients with isolated or prominent diaphragm weakness, the diagnosis of IBM should be considered in the right clinical context, especially if progression is slow and EDX testing is not consistent with a neurogenic etiology.

Mark Levine, MD, MA

Resident and Fellow Member Award Recipient

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PROGRESSIVE SENSORY NEURONOPATHY AS INITIAL PRESENTATION OF CEREBELLAR ATAXIA, NEUROPATHY, AND VESTIBULAR AREFLEXIA SYNDROME

Jenifer Moceri (Easton, PA), Kate Arner (Bethlehem, PA), Naaima Mufti (Easton, PA), Catherine Craven (Easton, PA), Divisha Raheja (Center Valley, PA)

INTRODUCTION/BACKGROUND: Cerebellar ataxia, neuropathy, and vestibular areflexia syndrome (CANVAS) is a recently defined genetic condition caused by biallelic AAGGG repeat expansions in the replication factor C subunit 1 (RFC1) gene and is characterized by varying degrees of late-onset progression ataxia, sensory neuronopathy, absent or reduced vestibulocochlear reflex, autonomic dysfunction, and chronic cough.

CASE REPORT: We present 1 case of confirmed CANVAS and a second case with CANVAS phenotype, but confirmation testing was negative. The first case is a 56-year-old female with progressive numbness and tingling in bilateral upper (BUE) and lower extremities (BLE), dysphagia, urinary retention, and cough. Additionally, she was found on exam to have profound sensory loss to all modalities, absent reflexes in the lower extremities, and mild weakness. She was initially treated with IVIg for 3 months with no improvement. NCS/EMG confirmed axonal sensory greater than motor neuropathy. Testing revealed TS-HGS and histone H3 IgM antibodies of unclear significance. Genetic testing confirmed RFC1 gene expansion consistent with CANVAS. The second case is a 48-year-old male with progressive weakness and numbness in BUE/BLE initially thought to be acute motor sensory axonal neuropathy (AMSAN). He was treated with IVIg for more than a year with minimal improvement. EMG/NCS was consistent with axonal sensory neuropathy. Genetic testing for CANVAS did not reveal RCF1 expansion.

SUMMARY/CONCLUSION: In patients presenting with progressive sensory neuronopathy, diagnosis of CANVAS should remain on the differential, particularly in those who have not responded to immunotherapy. While sensory neuronopathy is usually the first presenting symptom, other features tend to develop over the following decade.

Jenifer Moceri, DO

Resident and Fellow Member Award Recipient

NERVE CONDUCTION STUDIES OF SENSORY NERVES WITH PROVEN VASCULITIC NEUROPATHY OFTEN SHOW AN ABSENT ELECTRICAL RESPONSE

Benjamin Becker (Ann Arbor, MI), Long Davalos Loo (Cincinnati, OH), Zachary London (Ann Arbor, MI)

INTRODUCTION: Accurate nerve selection for nerve biopsy in vasculitic neuropathy (VN) is crucial. It is not known whether an absent or a low amplitude sensory nerve conduction response has a higher yield in detecting the appropriate nerves for pathological confirmation.

OBJECTIVE: To describe the NCS findings of nerves that were biopsied in patients with VN.

METHODS: Descriptive retrospective study of patients diagnosed with VN between January 2000 and April 2021 who had a nerve biopsy and prior NCS on the same nerve sampled.

RESULTS: We included 49 patients with VN (mean age: 56 ±14 years, 59% female, 69% systemic VN). There were 38 (77.5%) sural and 11 (22.5%) superficial radial nerve biopsies. The pathological findings showed 30 (61.2%) definite, 10 (20.4%) probable, and 2 (4%) possible VN; 7 (14.3%) samples did not meet pathological vasculitis criteria. In the definite group, 14 (46.8%) showed no response, 8 (26.6%) low amplitude and 8 (26.6%) normal NCS. In the probable group, 6 (60%) showed no response, 3 (30%) low amplitude, and 1 (10%) normal NCS. In the possible group, 1 (50%) showed no response and 1 (50%) normal NCS. In patients who did not meet pathological criteria, 2 (28.5%) showed no response, 2 (28.5%) low amplitude, and 3 (43%) normal NCS. Twenty-three nerves showed an absent electrical response: 14 (61%) definite and 6 (26%) probable pathological diagnosis.

SUMMARY/CONCLUSION: Most nerves with pathological VN findings showed no response on NCS. In patients with suspected VN, sural or superficial radial sensory nerves with absent response on NCS are good biopsy targets.

Benjamin Becker, MD

Resident and Fellow Member Award Recipient

PECULIAR CASE OF TRAUMATIC ULNAR NERVE INJURY RESULTING IN DENERVATION OF ABDUCTOR DIGITI MINIMI WHILE SPARING OTHER HAND INTRINSICS, GIVING INSIGHT INTO INTERFASCICULAR ANATOMY OF THE ULNAR NERVE

Aaron Charnay (Houston, TX), Yuting Jiao (Houston, TX)

INTRODUCTION/BACKGROUND: Traumatic peripheral nerve injury of the upper extremity most frequently involves the ulnar nerve, with laceration being the most common mechanism. The ulnar nerve at the wrist can be reliably divided into distinct volar sensory and dorsal motor components with bifurcation just distal to Guyon canal. The motor branch turns radially in the palm and gives off branches innervating the flexor pollicis brevis, first dorsal interosseous (FDI), and abductor digiti minimi (ADM). Injuries pre-bifurcation would seemingly affect all muscles beyond but when only certain muscles are affected while others are spared, the intricacies of fascicular nerve topography should be considered.

CASE REPORT: A 41-year-old man presented with left wrist laceration resulting in ulnar nerve injury just proximal to Guyon canal, 2 months prior, with severely reduced strength in ADM, decreased sensation focally over hypothenar eminence, and intact strength in FDI. Froment and Wartenberg signs were negative. NCS of the ulnar nerve to ADM showed markedly reduced compound motor action potential (CMAP) amplitude and prolonged latency compared to the unaffected hand while NCS of the same ulnar nerve to FDI was normal. All sensory studies were normal. EMG showed denervation potentials in ADM but no abnormal findings in FDI.

SUMMARY/CONCLUSION: While injury to the ulnar nerve distal to Guyon canal could potentially explain these findings, this patient's injury was well proximal to the wrist making a partial injury to the lateral aspect of the ulnar nerve pre-bifurcation more likely and worth further consideration of the detailed fascicular anatomy of the ulnar nerve.

Aaron Charnay, MD

Resident and Fellow Member Award Recipient

FACIAL DIPLEGIA IN A PATIENT WITH HEMOLYSIS, ELEVATED LIVER ENZYMES, AND LOW PLATELETS SYNDROME: A RARE MANIFESTATION OF MILLER FISHER SYNDROME

Ketevan Amirkhanashvili (Bronx, NY), Kelvin Kai Yin Chang (Providence, RI), Runjhun Bhatia (Bronx, NY), Sneha Bagchi (Bronx, NY), Fabreena Napier (Bronx, NY)

INTRODUCTION/BACKGROUND: Guillain-Barre syndrome (GBS) is a rare immune-mediated peripheral neuropathy that can manifest with weakness, areflexia, and paresthesias. Miller Fisher syndrome (MFS) is a variant of GBS that traditionally presents as ataxia, ophthalmoplegia, and areflexia. Prompt diagnosis and treatment improves outcomes, however diagnosis during pregnancy is commonly delayed since initial nonspecific symptoms are often attributed to changes in pregnancy and postpartum period. We describe a case of MFS, manifesting as facial diplegia, in a postpartum patient with hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome.

CASE REPORT: A 54-year-old woman with a recent diagnosis of HELLP syndrome presented on postpartum day 6 with acute onset of perioral numbness, dysphagia, and bilateral facial paresis. MRI of the brain showed enhancement of cranial nerve VII bilaterally, and lumbar puncture was notable for albuminocytologic dissociation. Her serum was positive for GQ1B IgM antibodies and she completed 5 days of IVIg for treatment of MFS with clinical improvement.

SUMMARY/CONCLUSION: While unilateral facial nerve palsy is a known complication in pregnancy, bilateral facial diplegia in pregnancy is rarer. It should prompt further investigation as it can be the presenting symptom of treatable but disabling MFS. GBS and MFS are often triggered by an inflammatory or infectious process. While the exact pathophysiology of HELLP syndrome is unknown, it is thought to be an inflammatory complement mediated disorder and may have triggered the onset of MFS in this patient.

Ketevan Amirkhanashvili, MD

Resident and Fellow Member Award Recipient

NATURAL HISTORY OF CONDUCTION SLOWING IN DIABETIC DISTAL SYMMETRIC POLYNEUROPATHY

Roopa Sharma (Harrison, NJ), Iqra Faiz (Newark, NJ), Kazim Jaffry (Newark, NJ), Nizar Souayah (Westfield, NJ)

INTRODUCTION: Conduction slowing beyond what is expected from a pure axonal loss was reported in diabetic distal symmetrical polyneuropathy (DSP).

OBJECTIVE: To characterize the natural history of conduction slowing in diabetic DSP.

METHODS: We retrospectively reviewed the changes in motor nerve conduction velocity (CV) of 71 patients with diabetic DSP who underwent at least 2 electrodiagnostic tests.

RESULTS: Thirty men and 41 women were included in the study. The mean age, HbA1C, and time between the first and subsequent studies were 55.91±10.44 years, 7.7±2.3, and 25±28 months respectively. Among 428 motor nerves, new CV slowing occurred in 13.5% with preservation of corresponding compound muscle action potential (CMAP) amplitudes in 84.4% of them. Out of 58 nerves with new conduction slowing, 15.5% had conduction slowing in demyelinating range per AAN criteria with preservation of corresponding CMAP amplitude in two-thirds of them. 53.5 % and 19.7% of DSP patients developed new conduction slowing in at least 2 motor nerves respectively. New worsening of CV in the demyelinating range was observed in 11.2% of diabetic DSP patients. Among the group of patients with at least 1 motor nerve with CV slowing in the demyelination range, there was a significantly higher number of patients who have more than 2 nerves with abnormal CV compared to the group who have no motor nerve with CV in the demyelinating range (87.5% vs 26.3%, $p<0.001$).

SUMMARY/CONCLUSION: In a subgroup of diabetic DSP patients, an evolving CMAP-independent motor nerve CV slowing may occur and may suggest a superimposed acquired demyelination.

Roopa Sharma, MD

Resident and Fellow Member Award Recipient

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MARKEDLY ABNORMAL LIPID ACCUMULATION IN RRM2B-RELATED PROGRESSIVE EXTERNAL OPHTHALMOPLEGIA: A CASE REPORT

Thapat Wannarong (Durham, NC), Karra Jones (Durham, NC), Natalia Gonzalez (Hillsborough, NC)

INTRODUCTION/BACKGROUND: The ribonucleotide reductase regulatory subunit M2B (RRM2B) is a nuclear-encoded mitochondrial maintenance gene with pathogenic variants linked to mitochondrial disease. We describe a case of RRM2B-related chronic progressive external ophthalmoplegia (PEO) and proximal limb and bulbar weakness with muscle biopsy demonstrating marked lipid accumulation without obvious mitochondrial abnormalities.

CASE REPORT: A 60-year-old woman presented with 6 months of rapidly progressive, symmetric proximal limb weakness progressing to wheelchair dependency, 100 lb weight loss, weakness of voice and cough, and exertional dyspnea. She noted long-standing restriction of eye movements that recently worsened. Physical examination demonstrated bilateral ophthalmoparesis, diffuse muscle atrophy, and weakness of craniobulbar, neck, and proximal>distal limb muscles. Electrophysiologic studies demonstrated a severe proximal myopathy without abnormal spontaneous activity to suggest active inflammation or myonecrosis. Muscle biopsy from the biceps brachii revealed a significant increase in lipid accumulation within myofibers, along with an increased number of mitochondria. While lipid droplets showed a significant increase in size and number overall, type 1 fibers were more affected than type 2 fibers. No ragged red fibers, COX-negative fibers, or paracrystalline inclusions were observed. Comprehensive genetic testing identified a heterozygous pathogenic variant (c.979 C>T) in the RRM2B gene.

SUMMARY/CONCLUSION: In this presentation of autosomal dominant RRM2B-related PEO, characterized clinically by severe, subacute progressive proximal muscle and bulbar weakness, the muscle biopsy revealed a marked accumulation of abnormal lipid droplets without obvious mitochondrial abnormalities. While consideration was given to a primary lipid storage disease, mitochondrial myopathies can also present with a significant increase in lipid as seen here.

Thapat Wannarong, MD

Resident and Fellow Member Award Recipient

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ACQUIRED RIPPLING MUSCLE DISEASE WITH ACETYLCHOLINE RECEPTOR ANTIBODIES

Thapat Wannarong (Durham, NC), Karissa Gable (Hillsborough, NC), Vern Juel (Durham, NC)

INTRODUCTION/BACKGROUND: Acquired rippling muscle disease (RMD) is associated with autoimmune disorders, or less commonly with cancer. Acetylcholine receptor (AChR) antibodies are most commonly observed in RMD in parallel with the presumed immune-mediated etiology of acquired RMD. We report a case series of acquired RMD with AChR antibodies.

CASE REPORT: Three patients with acquired RMD seen at our institution were identified from the electronic medical record. These patients were men with classic RMD symptoms beginning in their fourth to sixth decade. Two developed ocular myasthenia gravis (MG) after the onset of RMD, while the third had no MG symptoms. None had other autoimmune disorders or malignancies. AChR-binding antibodies were detected in all 3 patients and 2 had positive striational antibodies. None had thymoma. Creatine kinase was mildly elevated and caveolin-3 genetic testing was all negative. EMG showed electrical silence during spontaneous muscle contractions in 2 of 3 patients. One patient had a muscle biopsy which exhibited decreased caveolin-3 sarcolemmal immunoreactivity. All patients received at least 1 immunosuppressive (IS) therapy. While MG symptoms responded to IS treatment, RMD symptoms were more refractory. Only 1 individual who received IVIg experienced significant improvement in RMD symptoms. Symptomatic treatment for RMD yielded only minimal benefit.

SUMMARY/CONCLUSION: Acquired RMD is a rare disorder of muscular hyperexcitability, presumably related to an underlying immune-mediated phenomenon. Most cases of RMD/MG were heralded by RMD and may only exhibit minimal or no manifestations of MG despite AChR antibody positivity. IS therapies appear to be ineffective for RMD symptoms, although 1 patient had significant symptomatic benefit with IVIg.

Thapat Wannarong, MD

Resident and Fellow Member Award Recipient

ACUTE FLACCID PARALYSIS AMONG ADULT ADMISSIONS TO THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA: ETIOLOGIES AND CLINICAL CHARACTERISTICS

Michelle Kvalsund (Rochester, NY), Melody Asukile (Lusaka, Zambia), Lottie Hachaambwa (Baltimore, MD), Musambo Kapapa (Lusaka, Zambia), Frighton Mutete (Lusaka, Zambia), Stanley Zimba (Lusaka, Zambia), Mwaka Monze (Lusaka, Zambia), Michael Andary (East Lansing, MI), Gretchen Birbeck (Rochester, NY), David Herrmann (Rochester, NY)

INTRODUCTION: Acute flaccid paralyses (AFP) are common sequelae of recent emerging diseases, but there are substantial knowledge gaps about AFP in sub-Saharan Africa with consequence to regional and global health security.

OBJECTIVE: Describe the etiologic spectrum and characteristics of adults presenting with AFP to the University Teaching Hospital in Lusaka.

METHODS: Admission logs were prospectively screened to identify eligible cases (age ≥18 years, flaccid paralysis with predominant lower motor neuron signs, and symptom onset ≤4 weeks).

RESULTS: Sixty-six (0.13%) AFP admissions were identified during 17 months of surveillance. Twenty-two (33%) had symptom duration >4 weeks, 1 (2%) was <18 years, 1 (2%) declined, and 2 (4%) died before enrolment. Among 40 enrolled, 25 (63%) were female with mean age 37.2 (SD 13.0). Most (n=29; 73%) were from Lusaka province and spoke English (n=26; 65%). Mean education was 12 (8.5-12) years. HIV burden was high (n=19; 48%). Guillain-Barre syndrome (GBS) (n=20; 50%) subtypes included acute inflammatory demyelinating polyneuropathy (n=6; 30%), acute motor axonal neuropathy (n=6; 30%), and acute motor sensory axonal neuropathy (n=2; 10%). Six (30%) had indeterminate EDX. Myeloradiculitis (n=7; 18%), channelopathies (n=3; 8%), nutritional neuropathies (n=2; 5%), cauda equina syndrome (n=2; 5%), myasthenia gravis (n=1; 3%), myelopathies (n=3; 8%), lumbosacral plexopathy (n=1; 3%), and organophosphate-induced delayed polyneuropathy (n=1; 3%) were also included.

SUMMARY/CONCLUSIONS: GBS is the most common AFP etiology at a national referral center in Zambia. Our findings suggest resource constraints prevent/delay presentation for neurological care. Improved referral networks are needed for research and surveillance in this setting.

Disclosures:

Michelle Kvalsund - Receives research funding from the American Neuromuscular Foundation Development Award, National Institutes of Health, MRC strategic award to establish an International Centre for Genomic Medicine in Neuromuscular Diseases, and Allen Foundation

Musambo Kapapa - Receives funding from a MRC strategic award to establish an International Centre for Genomic Medicine in Neuromuscular Diseases

Gretchen Birbeck - Received NIH research grants; serves on the Editorial Board for Neurology and Lancet Neurology; Ambassador to Zambia for the Royal Society of Tropical Medicine & Hygiene

PATIENT-REPORTED SEVERITY OF PAIN INTERFERENCE IN CHARCOT-MARIE-TOOTH DISEASE TYPE 1A: FINDINGS FROM A DIGITAL REAL-WORLD STUDY

Florian Thomas (Hackensack, NJ), Shahram Attarian (Marseille, France), Teresa Sevilla (Valencia, Spain), Filippo Genovese (Bologna, Italy), Amy Gray (Glenolden, PA), Simon Bull (Christchurch, United Kingdom), Daniel Tanesse (Saint-Alban, France), Allison Moore (New York, NY), Courtney Hollett (New York, NY), Xavier Paoli (Paris, France), Laura Day (Oxford, United Kingdom), Johnny King Lam Lau (Oxford, United Kingdom), Samuel Llewellyn (Oxford, United Kingdom), Mark Larkin (Oxford, United Kingdom), Youcef Boutalbi (Paris, France)

INTRODUCTION/OBJECTIVE: This analysis explores the relationship between pain interference in Charcot-Marie-Tooth disease 1A (CMT1A) and multiple clinical variables.

METHODS: Adults with CMT1A in the EU5 or USA were recruited to an ongoing, international, digital study exploring the real-world impact of CMT. Patient-reported outcome (PRO) data on pain interference were collected via the PROMIS® Pain Interference Short Form 6a, administered on the study app, CMT&Me. Linear regression was used to evaluate relationships between PRO responses and a series of explanatory clinical variables.

RESULTS: Residency in Germany (ß=0.078, p<0.001) or the UK (ß=0.059, p=0.003) were associated with greater severity of pain interference vs the USA (reference). Beta represents the coefficient in the model, showing the direction and magnitude of the effect on the PRO outcome variable. Diagnosis age of 0-10 years (ß=-0.041, p=0.049) was associated with lesser severity of pain interference vs diagnosis age of 31-40 (reference). Reporting of weakness in the feet (ß=0.081, p<0.001), balance problems (ß=0.068, p=0.003), hearing loss (ß=0.076, p<0.001), hammer toes (ß=0.03, p=0.037), aching (ß=0.035, p=0.035), burning (ß=0.042, p=0.01), severe fatigue (ß=0.208, p<0.001), and use of analgesics (ß=0.031, p=0.028), opioids (ß=0.094, p<0.001), CBD oil (ß=0.088, p<0.001), or neuroleptics (ß=0.067, p=0.002) were associated with greater severity of pain interference. Reporting of numbness (ß=-0.059, p=0.001), high arches (ß=-0.074, p<0.001), flat arches (ß=-0.088, p<0.001), and use of antidepressants (ß=-0.051, p=0.004) or walking aids (ß=-0.027, p=0.037) were associated with lesser severity of pain interference.

SUMMARY/CONCLUSION: This study evidences a range of clinical variables predicting the impact on severity of pain interference of CMT1A.

PATIENT-REPORTED SYMPTOM SEVERITY OF CHARCOT-MARIE-TOOTH DISEASE TYPE 1A: FINDINGS FROM A DIGITAL REAL-WORLD STUDY

Florian Thomas (Hackensack, NJ), Shahram Attarian (Marseille, France), Teresa Sevilla (Valencia, Spain), Filippo Genovese (Bologna, Italy), Amy Gray (Glenolden, PA), Simon Bull (Christchurch, United Kingdom), Daniel Tanesse (Saint-Alban, France), Allison Moore (New York, NY), Courtney Hollett (New York, NY), Xavier Paoli (Paris, France), Laura Day (Oxford, United Kingdom), Johnny King Lam Lau (Oxford, United Kingdom), Samuel Llewellyn (Oxford, United Kingdom), Mark Larkin (Oxford, United Kingdom), Youcef Boutalbi (Paris, France)

INTRODUCTION/OBJECTIVE: This analysis explores the relationship between disease severity in Charcot-Marie-Tooth disease type 1A (CMT1A) and a range of clinical variables.

METHODS: Adults with CMT1A in the EU5 or USA were recruited to an ongoing, international, digital study exploring the real-world impact of CMT. Data on symptom severity were collected via a bespoke single-question patient-reported outcome (PRO) instrument, administered on the study app, CMT&Me. Participants evaluated the current severity of their symptoms using 4 response options: none, mild, moderate, and severe. Linear regression was used to evaluate relationships between the PRO responses and a series of explanatory clinical variables.

RESULTS: Residency in France (ß=0.2, p=0.003), Germany (ß=0.428, p<0.001), Italy (ß=0.209, p=0.012), Spain (ß=0.246, p=0.001), and the UK (ß=0.131, p=0.019) were associated with greater symptom severity when compared with the USA (reference). Beta represents the coefficient in the model, showing the direction and magnitude of the effect on the PRO outcome variable. Diagnosis at 0-10 years (ß=0.166, p=0.005) or 11-20 years (ß=0.132, pp=0.016) was associated with greater symptom severity when compared with 31-40 years (reference). Reporting of a greater time in years from symptom onset to diagnosis (ß=0.004, p=0.006), weakness in the arms (ß=0.168, p<0.001), hearing loss (ß=0.116, p=0.013), difficulty breathing (ß=0.15, p=0.005), burning sensation (ß=0.165, p=0.001), and/or severe fatigue (ß=0.202, p<0.001) at study baseline was associated with greater subsequent symptom severity.

SUMMARY/CONCLUSION: This study evidences a range of clinical variables impacting on symptom severity of CMT1A disease. Further exploration could increase understanding of disease burden and elucidate therapeutic targets.

VIDEO-BASED GAIT ANALYSIS OF SPASTIC HEMIPARETIC GAIT

Ronald Cotton (Chicago, IL), Anna Tessiatore (Chicago, IL), Allison DeLillo (Chicago, IL)

INTRODUCTION: Despite the prevalence of clinical interventions for spasticity in hemiparetic gait after stroke or traumatic brain injury, there are no clinically accessible tools for routinely characterizing these gait impairments. If such tools were available, they would allow objective and quantitative analysis of these gait impairments to better assess the efficacy of our interventions.

OBJECTIVE: To develop tools that can easily be used in the clinic and community to monitor gait impairments, particularly spastic hemiparetic gait, leveraging recent artificial intelligence (AI) techniques.

METHOD: To address this gap, we have developed 2 complementary approaches using computer vision and human pose estimation. One approach uses markerless motion capture to track movements and performs inverse kinematic fits with biomechanical models to track joint movements. Our second approach performs video-based gait analysis from smartphone videos and can measure more kinematics and muscle activations with wearable sensors.

RESULTS: We found both systems enable gait analysis with minimal setup time, making them appropriate for integration into clinical workflows. The markerless motion capture system captures kinematic features of hemiparetic gait including insufficient dorsiflexion for toe clearance with compensatory hip hiking or circumduction. It also detects changes in kinematics in response to interventions such as functional electrical stimulation of the peroneal nerve or using an ankle foot orthosis. The smartphone-based system also captures the gait asymmetries of hemiparetic gait and impaired muscle activation patterns.

SUMMARY/CONCLUSION: Using advances in AI for movement analysis has great potential to enable more quantitative biomarkers of spastic hemiplegic gait and for monitoring responses to interventions.

RECURRENCE OF ACUTE MOTOR AND SENSORY AXONAL NEUROPATHY IN FORTY MONTHS IN ONE ADULT PATIENT WITH EXCELLENT RECOVERY

Ali Al-Samak (Leeds, United Kingdom), Shwe Tun (Huddersfield, United Kingdom), Khine Khine Lwin (Huddersfield, United Kingdom), Myat Thura (Huddersfield, United Kingdom), Aye Aye Thet (Wakefield, United Kingdom)

INTRODUCTION/BACKGROUND: We report a case of acute motor and sensory axonal neuropathy (AMSAN) recurrence in a patient in 40 months. The Guillain-Barre syndrome (GBS) incidence in the UK is 2 per 100,000 per year. Acute inflammatory demyelinating polyneuropathy (AIDP) is the most common form of GBS. Axonal motor and sensorimotor variants (AMSAN) incidence was reported as 15%. Recurrence rate of GBS is 3-6% of cases. In a large cohort of adult GBS patients, the most common GBS subtype was AIDP (77%) and around 23% of patients presented with a GBS variant.

CASE REPORT: A 60-year-old man presented in 2019 with an acute, ascending weakness becoming quadriparetic in 5 days. He had flu-like illness followed by diarrhoea 3 weeks earlier. Flaccid quadriparesis and generalized areflexia led to GBS diagnosis and treated with IVIg. A complete recovery ensued after IVIg. He was hospitalized again in 2023 with acute onset proximal legs weakness 2 weeks after gastroenteritis. In 5 days, he couldn't stand. Exam revealed lower limbs weakness more than upper limbs with areflexia. He never had sensory symptoms. High cerebrospinal fluid (CSF) protein and NCS revealed AMSAN (despite lack of sensory symptoms) with positive anti-GQ1b antibody. He regained full strength in 5 days without any residual weakness after IVIg.

SUMMARY/CONCLUSION: GBS is uncommon and recurrent GBS is rare, variant type even rarer. Recurrent Miller Fisher syndrome had been reported before. Our anti-GQ1b antibody positive AMSAN recurrence case achieved a great outcome after IVIg.

IMPROVING MILD CARPAL TUNNEL SYNDROME DETECTION WITH AN ADDITIONAL (MEDIAN - ULNAR) LATENCY COMPARISON

Elliot Bodofsky (Camden, NJ), Stephen Cohen (Camden, NJ), Adam Schindelheim (Camden, NJ)

INTRODUCTION: Carpal tunnel syndrome (CTS) is by far the most common focal nerve compression and one of the most common reasons for referral for NCS. But mild, easily treatable cases are often missed on NCS. Previous studies have shown the (median sensory – ulnar motor) latency difference (MSUMLD) is a sensitive and specific measure for CTS.

OBJECTIVE: To determine if the addition of the MSUMLD to the standard (median – ulnar) motor and sensory latency differences can significantly improve detection of mild CTS cases.

METHODS: Review of an academic PM&R NCS database (2013-2019) to identify all upper extremity tests with normal Median motor and sensory latencies, as well as those reported normal. Upper limits of normal for (median – ulnar) motor latency difference was 1.1 msecs, 0.4 msecs for (med – uln) sensory, and 0.8 msecs for MSUMLD.

RESULTS: There were a total of 798 upper extremities tested, and 156 with normal median and ulnar latencies. Of these, 22 met diagnostic criteria for CTS by either the (median – ulnar) motor or sensory latency difference, or both. An additional 11 upper extremities exceeded the established difference for MSUMLD (otherwise normal), for a total of 33 using the 3 criteria. One upper extremity out of 39 reported normal showed a minimally increased MSUMLD. The 3 criteria were highly correlated.

SUMMARY/CONCLUSION: The MSUMLD greatly increases the detection of mild CTS, with few false positive tests. Since it is a single simple calculation, MSUMLD should be strongly considered for mild CTS NCS.

LONG-TERM HEALTHCARE RESOURCE UTILIZATION AND COSTS AMONG PATIENTS WITH NEWLY DIAGNOSED MYASTHENIA GRAVIS: A SWEDISH NATIONWIDE POPULATION-BASED STUDY

Qian Cai (Titusville, NJ), Alberto Batista (Titusville, NJ), Qiaoyi Zhang (Titusville, NJ), Jakob Börsum (Stockholm, Sweden), Kavita Gandhi (Titusville, NJ), Gabriel Isheden (Stockholm, Sweden), Peter Kunovszki (Budapest, Hungary), Kristin Heerlein (Neuss, Germany)

INTRODUCTION: Myasthenia gravis (MG) is a rare autoimmune disorder characterized by muscle weakness and fatigue. Little is known about long-term healthcare resource utilization and associated costs in patients with newly diagnosed MG in Sweden.

OBJECTIVE: To compare all-cause and MG-related inpatient admissions, outpatient specialist visits, and associated costs during the first year (Y1) and the second year (Y2) after initial MG diagnosis.

METHODS: Data were linked from 4 Swedish nationwide population-based registries. Adults with ≥ 2 primary diagnosis of MG (ICD-10-SE: G70.0) in inpatient or outpatient specialist visits (≥ 12 months apart, ≥ 1 MG diagnosis recorded by a neurologist) during 1/1/2010-12/31/2017; who had a pharmacological treatment for MG were selected. Index date was the date of first primary MG diagnosis. Patients were also required to have ≥ 24 months post-index follow-up and should not have a MG diagnosis before index date (back until 2001).

RESULTS: A total of 554 patients were included [mean (±SD) age: 62 (±18.2) years; female: 45.7%]. Post-index, Y1 had significantly higher rates of corticosteroid use (60% vs 48%) and rate of thymectomies (12.1% vs 2.7%); higher all-cause (70.9% vs 34.7%) and MG-related (62.5% vs 15.9%) hospitalization rates; and higher all-cause (difference= €7294) and MG-related (difference= €6629) costs, than Y2 (all $p<0.01$).

SUMMARY: More treatments and/or surgeries are performed in the first year after diagnosis than later in the disease course, leading to higher costs immediately after diagnosis. Findings highlight the need for use of more efficacious treatments early in the disease course.

Disclosures:

Qian Cai - Employee of Janssen Pharmaceuticals and may hold stock in Johnson & Johnson

Alberto Batista - Employee of Janssen Pharmaceuticals and may hold stock in Johnson & Johnson

Qiaoyi Zhang - Employee of Janssen Pharmaceuticals and may hold stock in Johnson & Johnson

Jakob Börsum - Employee of SDS Life Science

Kavita Gandhi - Employee of Janssen Pharmaceuticals and may hold stock in Johnson & Johnson

Gabriel Isheden - Employee of SDS Life Science

Peter Kunovszki - Employee of Janssen Pharmaceuticals and may hold stock in Johnson & Johnson

Kristin Heerlein - Employee of Janssen Pharmaceuticals and may hold stock in Johnson & Johnson

A COMPUTER-DRIVEN MODEL TO IDENTIFY CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY: A PLANNED ANALYSIS IN THE PHASE 2B TRIAL OF THE FCRN INHIBITOR, BATOCLIMAB

Todd Levine (Paradise Valley, AZ), Jonathan Katz (San Francisco, CA), Glenn Zenner (Temecula, CA), Karissa Sanabria (New York, NY), Shuang He (New York, NY), Ian Gourley (Wayne, PA)

INTRODUCTION: Published reports concerning diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) in clinical practice suggest up to a 70% rate of overdiagnosis. Thus, clinical trials in CIDP utilize consensus guidelines and expert adjudication committees to ensure appropriate enrollment; however, diagnostic discordance, even among experts, still exists, potentially due to heterogeneity of clinical presentation and complexity of guidelines.

OBJECTIVE: To assess retrospectively whether a computer-driven algorithm may improve upon expert, guideline-driven adjudication in identifying patients with CIDP.

METHODS: The FcRn inhibitor, batoclimab, is being investigated in a phase 2b, randomized, placebo-controlled clinical trial in adult patients with active CIDP. CIDP diagnosis and eligibility decisions will be confirmed by a central adjudication committee. Data will also be uploaded into a computerized diagnostic platform, developed by InCircle Review©, that analyzes clinical history, exam features, and laboratory and electrodiagnostic values against set criteria. The application has been developed to reduce subjectivity, thereby increasing consistency in the diagnosis of study participants. Following trial completion, statistical analyses will be conducted to correlate between the 2 approaches.

RESULTS: Details of the phase 2b trial design and planned analysis will be presented.

SUMMARY/CONCLUSION: This retrospective analysis could help to establish a standardized, automated approach to patient enrollment in CIDP trials, potentially reducing discordance among adjudicators who currently use guideline-centric methods.

Disclosures:

Todd Levine - Consultant for Immunovant, Inc and InCircle Review

Jonathan Katz - Consultant for Immunovant, Inc and InCircle Review

Glenn Zenner - Consultant for InCircle Review

Karissa Sanabria - Employee of Immunovant, Inc

Shuang He - Employee of Immunovant, Inc

Ian Gourley - Employee of Immunovant, Inc

THE SYNUCLEIN-ONE STUDY: DETECTION OF CUTANEOUS PHOSPHORYLATED ALPHA-SYNUCLEIN FOR THE DIAGNOSIS OF PURE AUTONOMIC FAILURE

Todd Levine (Paradise Valley, AZ), Christopher Gibbons (Boston, MA), Bailey Bellaire (Scottsdale, AZ), Jade Stohl (Scottsdale, AZ), Roy Freeman (Boston, MA)

INTRODUCTION: An important unmet need exists for a validated, well-characterized, simple, reproducible marker of synuclein pathology.

OBJECTIVE: The Synuclein-One study is an NIH-funded 30-site, multicenter trial of 427 subjects with Parkinson disease (PD), dementia with Lewy bodies (DLB), multiple system atrophy (MSA), pure autonomic failure (PAF), and healthy controls. The study was designed to describe the sensitivity, specificity, accuracy, and precision of the Syn-One Test in patients with synucleinopathies. Enrollment closed in January 2023, with final data analysis by April 2023.

METHODS: After signing informed consent, all participants completed detailed neurologic examinations, medical and neurological history review, cognitive evaluation, orthostatic vital signs, RBD questionnaire, MSA red flags, and Parkinson Disease Questionnaire-39. Skin biopsies at the distal leg, distal thigh, and posterior cervical sites were performed. All clinical data were reviewed by a blinded expert consensus panel to confirm the referring diagnosis. The Syn-One Test was performed at CND Life Sciences and the Neurocutaneous Laboratory at Beth Israel Deaconess Medical Center. Phosphorylated alpha-synuclein deposition was quantified by 2 readers, blinded to referring diagnosis and results of the other reader.

RESULTS: Final unblinded results will be presented at the AANEM 2023 annual meeting with a focus on test sensitivity, specificity, accuracy, and precision as it relates to the diagnosis of pure autonomic failure and the utility of the Syn-One Test in the diagnostic paradigm of patients with dysautonomia.

SUMMARY/CONCLUSION: The Synuclein-One study is the largest investigation of cutaneous phosphorylated alpha-synuclein detection across all 4 synucleinopathies and will advance the field of neurodiagnostic testing in neurodegenerative disease.

Disclosures:

Todd Levine - CMO with financial interest in CND Life Sciences

Christopher Gibbons - Financial interest in CND Life Sciences

Bailey Bellaire - Employee of CND Life Sciences

Jade Stohl - Employee of CND Life Sciences

Roy Freeman - Financial interest in CND Life Sciences

CLINICAL, NEUROPHYSIOLOGICAL, AND ULTRASONIC CHANGES IN A CASE OF PERIPHERAL NERVE DAMAGE IN LEPROSY

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INTRODUCTION/BACKGROUND: Leprosy is a chronic infectious disease caused by Mycobacterium leprae, which is transmitted by respiratory secretions and mainly affects the skin and peripheral nerves. Nerve damage in leprosy is mostly manifested as polyneuritis moniliformis, leading to sensory, motor, and autonomic neuropathy. In recent years, there are fewer patients with typical neuropathy in leprosy.

CASE REPORT: We report a case of leprosy peripheral neuropathy as the first manifestation in a middle-aged male with progressively increasing numbness, weakness, and pain in the extremities; sensory loss in the extremities with rash formation as the main clinical manifestation; a history of previous contact with leprosy patients; a deformity of the hands in the form of claw-shaped hands on examination; and decreased sensation in the extremities and trunk. Ultrasound examination of peripheral nerve of extremities found significant thickening of upper arm of bilateral ulnar nerve; hypoechoic peripheral ulnar nodules; significant thickening of the sciatic, tibial, and common peroneal nerves; increased thickened intraneural blood flow; multiple nodular hypoechoics around the popliteal nerve; enlarged hyperdolicular lymph nodes of bilateral elbow; and multiple subcutaneous hypoechoic nodules.

SUMMARY/CONCLUSION: Ultrasound and electrophysiology are helpful in the diagnosis of leprosy neuropathy. Significant nerve thickening is the most important manifestation of ultrasound, but it is not specific. Concurrent peripheral and subcutaneous nodular hyperplasia and lymph node enlargement are more helpful for diagnosis.

IMMUNOGLOBULIN G REDUCTION EXPLAINS A LARGE PROPORTION OF CLINICAL EFFICACY IN GENERALIZED MYASTHENIA GRAVIS – A MODEL-BASED META-ANALYSIS OF FCRN INHIBITORS

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INTRODUCTION: Generalized myasthenia gravis (gMG) is a rare chronic autoimmune neuromuscular disease. Anti-FcRn antibodies (e.g., nipocalimab [in evaluation], efgartigimod [approved]) inhibit FcRn-mediated IgG recycling thus lower circulating serum IgG, including anti-AChR pathogenic autoantibodies, in the treatment of gMG.

OBJECTIVE: Model-based meta-analysis of clinical data from 4 anti-FcRn treatments were used to explore IgG as a potential biomarker for the clinical endpoint, MG-ADL score.

METHODS: The proportion of treatment effect (PTE) method was used, wherein the contribution of a biomarker (e.g., IgG) to the overall treatment-related change in clinical endpoint is calculated as the ratio of an estimated surrogate-contribution (if statistically significant) versus an estimated treatment-effect. Clinical data for nipocalimab (NCT03772587), efgartigimod (NCT02965573, NCT03669588, NCT04735432), rozanolixizumab (NCT03052751, NCT03971422), and batoclimab (NCT03863080, NCT04346888) were combined from 8 studies. PTE was calculated using weighted regression on steady-state, aggregate values of placebo-corrected change from baseline MG-ADL (ΔΔMG-ADL) and percent change of IgG from baseline (ΔIgG) from all studies. No covariates or random effects were included due to limited data (18 datapoints).

RESULTS: The estimated IgG coefficient was statistically significant (0.03±0.005 [SE]), suggesting 10% ΔIgG translates to ΔΔMG-ADL of ~0.3. The PTE (%CV) from all aggregate-level FcRn data was 0.82 (15%) indicating that a majority of the anti-FcRn effect on ΔΔMG-ADL could be explained by ΔIgG.

SUMMARY/CONCLUSION: Since ΔIgG explains a large proportion of anti-FcRn effect on ΔΔMG-ADL, IgG could be used as a potential biomarker for clinical efficacy. This would increase the efficiency of clinical trials (size and duration) to reduce burden for patients with gMG.

Disclosures:

Mehrdad Javidi - Johnson & Johnson employee; might hold Johnson & Johnson stock

Anne-Gaëlle Dosne - Johnson & Johnson employee; might hold Johnson & Johnson stock

Mahesh N. Samtani - Johnson & Johnson employee; might hold Johnson & Johnson stock

Jocelyn Leu - Johnson & Johnson employee; might hold Johnson & Johnson stock

Yaowei Zhu - Johnson & Johnson employee; might hold Johnson & Johnson stock

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Juan-José Pérez-Ruixo - Johnson & Johnson employee; might hold Johnson & Johnson stock

Chandni Valiathan - Johnson & Johnson employee; might hold Johnson & Johnson stock

EVALUATION OF COMPLEMENT BIOMARKERS AFTER TREATMENT WITH NIPOCALIMAB IN GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: Anti-AChR autoantibodies activate the classical complement pathway, causing postsynaptic membrane damage at the neuromuscular junction (NMJ). Nipocalimab can lower anti-AChR autoantibody titers, which may impact complement activation in gMG patients.

OBJECTIVE: To explore whether nipocalimab treatment reduces complement activation in the Vivacity MG phase 2 study.

METHODS: Serum samples were collected at baseline and longitudinally. C3, C4, CH50, and C3D were measured. The median percent change (MPC) from baseline was used to evaluate changes in complement biomarkers over time. Changes on Day 57 in the treatment arms were compared to placebo using the Mann-Whitney U test.

RESULTS: In the lower dose group (5 mpk q4w), the MPC in C3, C4, and CH50 were similar to placebo. However, in the higher dosing groups (30 mpk q4w and 60 mpk q2w), the MPC in C3 increased 4.1% and 10.4%, respectively, at Day 57. Increases of 4.4% (30 mpk q4w) and 17.9% (60 mpk q2w) in C4 were observed. The MPC in CH50 increased 2.5% with 30 mpk q4w, but decreased 17.9% with 60 mpk q2w. Changes in C3 and C4 with 60 mpk q2w showed statistically significant differences ($p<0.05$) compared to placebo. Treatment with nipocalimab resulted in decreasing MPC in C3D but this finding was based on limited data (2-7 per treatment arm).

SUMMARY/CONCLUSION: Nipocalimab appears to have an effect on lowering but not completely suppressing complement activation, and may thus potentially reduce NMJ damage, while still allowing the complement pathway to be functional. Further evaluation in the ongoing phase 3 gMG trial with higher sample size is needed to test this finding.

MOTOR UNIT NUMBER INDEX IN IDIOPATHIC FACIAL PALSY

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INTRODUCTION: Idiopathic facial nerve palsy is a common clinical condition, usually with a unilateral onset. Some patients cannot be diagnosed early and the complications cause great physical and psychological pain to the patients. Motor unit number index (MUNIX) is a new EMG technique.

OBJECTIVE: We hypothesize that MUNIX is meaningful for early assessment of idiopathic facial nerve palsy and can reflect the severity of the disease.

METHODS: We completed a reproducibility trial in 20 healthy controls demonstrating good reproducibility of MUNIX facial muscles (orbicularis oculi muscle, zygomatic muscle, orbicularis oris muscle). We collected 43 patients with idiopathic facial nerve palsy with onset within 7 days and performed MUNIX testing on both facial muscles (healthy side as control), while completing clinical scale assessments.

RESULTS: The MUNIX values of the main affected muscles on the affected side were lower than on the healthy side in patients with idiopathic facial nerve palsy ($p<0.05$). The proportional decrease in sum MUNIX values (sum of 3 muscle MUNIX values) is positively correlated with House-Brackmann Grading System scores ($r=0.845$, $p<0.05$). The proportional decrease in sum MUNIX values was negatively correlated with Sunnybrook Facial Grading System scores ($r= -0.830$, $p<0.05$).

SUMMARY/CONCLUSION: The results confirm that our hypothesis is valid and MUNIX as a new EMG technique is effective for early assessment of idiopathic facial nerve palsy and correlates with disease severity. We suggest that MUNIX can be used as a clinical complement to EMG, which can help in the early diagnosis and quantitative assessment of idiopathic facial nerve palsy and guide clinical diagnosis and treatment.

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CASE REPORT: ACUTE ONSET OF RESPIRATORY DISTRESS CAUSED BY IDIOPATHIC BRACHIAL PLEXOPATHY

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INTRODUCTION/BACKGROUND: Idiopathic brachial plexopathy is a peripheral neuropathy of acute or subacute onset with significant pain that causes muscle weakness and atrophy of upper extremities. Unilateral or bilateral phrenic nerve involvement is seen in 7% of patients with idiopathic brachial plexopathy. Isolated idiopathic phrenic neuropathy is considered to be a variant of idiopathic brachial plexopathy. Cases of acute respiratory distress caused by idiopathic brachial plexopathy are rarely reported in the literature and are easily misdiagnosed in clinical practice.

CASE REPORT: A 63-year-old female patient presented with shoulder pain and breathing difficulty that progressed over 2 months. Arterial blood gas analysis suggested type 1 respiratory failure and clinical tests were performed to exclude organic cardiopulmonary abnormalities. Electromyography indicated bilateral phrenic neuropathy combined with left anterior interosseous neuropathy and partial involvement of the right superior brachial plexus trunk. The diaphragm ultrasound suggested no significant changes in the bilateral diaphragm during end-inspiration and end-expiration. We diagnosed the patient's acute dyspnea as being caused by idiopathic brachial plexopathy. The patient was treated with pulse steroid therapy, nerve nutrition, and rehabilitation exercises. Finally, the patient’s symptoms are relieved and a good prognosis was obtained.

SUMMARY/CONCLUSION: When encountering the acute onset of dyspnea in clinical practice, especially difficulty breathing in the prone position with neck and shoulder pain, it is important to consider the specific type of idiopathic brachial plexopathy after the exclusion of cardiopulmonary abnormalities. Early diaphragmatic ultrasound and neurophysiological examination can help diagnose. Early and clear diagnosis guides timely treatment, which can promote functional rehabilitation and improve the quality of life of patients.

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CARPAL TUNNEL SYNDROME RELATED TO LYMPHEDEMA IN WOMEN WITH BREAST CANCER

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INTRODUCTION: Lymphedema in breast cancer patients has been related to lymph node emptying, radiotherapy, and obesity. Other treatments used such as conventional chemotherapy, aromatase inhibitors (AI), monoclonal agents (MA), and radiotherapy may have effects on specific peripheral nerves. Studies are regarding the relationship between the severity of lymphedema and the presence of carpal tunnel syndrome (CTS).

OBJECTIVE: This study aims to review their association and their relationship with other treatments used.

METHODS: Cross-sectional study, descriptive analysis, and bivariate analysis with the chi-square test were performed to determine possible associations between CTS and factors such as lymphedema, exposure to conventional chemotherapy, AI, MA, and antiestrogens; additionally, a linear regression model was applied. SPSS v16 statistical software was used.

RESULTS: A total of 172 extremities of 86 women diagnosed with breast cancer were analyzed. The average age was 60.51 years (±10.88). Twenty-nine extremities (17%) showed lymphedema. The severity of CTS was classified with Padua, 2.9% corresponded to incipient, 24.4% mild, 38.9% moderate, 15.1% severe, 2.3% extreme, and 16.4% without CTS. In the bivariate analysis, an association was found between the presence of lymphedema and the development of CTS (OR 6.51; 95%CI 0.849 - 50.03; p=0.05), however, in the multivariate analysis this association was not as strong (OR: 6.14, p=0.082), without finding a statistical difference.

SUMMARY/CONCLUSION: More studies are needed to evaluate the risk factors associated with the development of CTS in cancer patients.

UNILATERAL SPINAL ACCESSORY NERVE INJURY ASSOCIATED WITH PLEXOPATHY SECONDARY TO RESECTION OF PAPILLARY THYROID CARCINOMA

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INTRODUCTION/BACKGROUND: In injuries associated with the spinal nerve, the main characteristics are associated with the impossibility of raising the shoulder and difficulties with neck rotation. The main causes for generating spinal accessory nerve injuries are mostly associated with trauma. We will observe the particular case of an injury associated with a surgical procedure.

CASE REPORT: We present the case of a 42-year-old patient who underwent surgical interventions twice for papillary thyroid carcinoma with tumor recurrence. After the second intervention, he presented a plexopathy due to the impossibility of movement and decreased sensitivity. Subsequently, he performed physical therapy intervention and improved his mobility and sensitivity. However, he presented difficulty in raising the shoulder, with electromyographic evidence of a right unilateral lesion of the accessory spinal nerve.

SUMMARY/CONCLUSION: In the presence of difficulty for shoulder elevation associated with the surgical history, electromyography and diagnostic images are important to determine the origin of the lesion.

FIBROMYALGIA SYNDROME: IS THERE A CORRELATION BETWEEN ELECTRODIAGNOSTIC FINDINGS AND MUSCLE HISTOPATHLOGY?

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INTRODUCTION: Individuals with fibromyalgia syndrome (FMS) complain of pain exacerbation, numbness, weakness, and fatigue even on light exertion, suggesting either a possible underlying neurological deficit or pre-existing structural muscle abnormalities.

OBJECTIVE: To assess peripheral neuromuscular dysfunction among FMS patients by interrelating different electrophysiologic and histopathologic studies, for further understanding of its pathophysiology.

METHODS: This case-control study included 30 FMS patients and 10 healthy matched volunteers. They all underwent basic motor and sensory nerve conduction studies, conventional needle EMG for proximal and distal limb muscles, sympathetic skin response (SSR) for median nerves, muscle fiber conduction velocity (MFCV) for biceps muscles, quantitative analysis of the interference pattern (before and after sustained contraction for 1 minute), and muscle biopsy from dominant limb quadriceps which was examined by light and electron microscopes.

RESULTS: Patients showed a higher incidence of entrapment neuropathy (46.7%) than controls, with no evidence of degeneration or regeneration in the muscles and significant delay in SSR latencies ($p<0.05$) than the controls suggesting dysautonomia. Patients showed significantly lower MFCV and higher drop percent in MFCV following sustained contraction ($p<0.001$), indicating pathological fatigue response. Light microscopy revealed a significantly higher percentage of fiber size variability, central nucleation, and predominance of fiber type I ($p\leq0.001$) among the patients. Electron microscopy revealed aggregation of bizarrely shaped mitochondria in all patients, but in none of the controls.

SUMMARY/CONCLUSION: A definite, but nonspecific, neurologic pathogenesis is involved in FMS and is correlated with muscle structure changes that may explain the widespread neurological manifestations they suffer.

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DISSOCIATION BETWEEN CREATINE KINASE LEVELS AND MYOPATHIC SYMPTOMS IN IMMUNE-MEDIATED NECROTIZING MYOPATHY: A CASE REPORT

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INTRODUCTION/BACKGROUND: Immune-mediated necrotizing myopathy (IMNM) is characterized by severe proximal weakness and extremely high muscle enzyme serum levels. Patients usually have auto-antibodies that recognize either 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase or the signal recognition particle (SRP).

CASE REPORT: A 54-year-old woman with a past medical history of dyslipidemia, arterial hypertension, and hypothyroidism presented with an 8-day history of progressive lower limb weakness leading to falls. Her pharmacological history included rosuvastatin for 4 months and previously atorvastatin for more than 2 years. Clinical examination showed mild weakness of the proximal lower limbs without other findings. On admission, serum creatine kinase (CK) levels were up to 339.000 U/L with hepatic and renal involvement requiring urgent hemodialysis. With levels 100 times above the upper normal limit, a diagnosis of IMNM was considered and immunosuppressive management with corticotherapy pulses and azathioprine was administered, with clinical and paraclinical improvement. Serologic and autoimmune profile, anti-SRP, and anti-Jo1 levels were negative and anti-HMGCR levels were indeterminate, however these were taken 10 days after the start of immunosuppressive therapy. The diagnosis was made based on a potential trigger of the immune response, CK levels, and anti-HMGCR indeterminate, possibly biased by the treatment administered.

SUMMARY/CONCLUSION: Although IMNM is characterized by extremely elevated CK levels, we did not find a case with such high (confirmed) levels and with such mild symptoms as our patient presented. It also suggests that in the study of idiopathic inflammatory myopathies, the specific autoimmune profile at admission should be taken to avoid biases such as those described.

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ENCEPHALOMYELITIS LONGITUDINALLY EXTENSIVE WITH POLYRADICULITIS AS A DEBUT OF NEUROPSYCHIATRIC LUPUS: A CASE REPORT

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INTRODUCTION/BACKGROUND: Neurological manifestations of systemic lupus erythematosus (SLE) are always a diagnostic challenge, especially those involving the central and peripheral nervous system due to their low prevalence. The association of neuromyelitis optic spectrum diseases (NMOSD) or myelin oligodendrocyte glycoprotein (MOG) antibodies are differential diagnoses that should always be investigated.

CASE REPORT: A 20-year-old man without personal and familial medical history was admitted to a local hospital after a nonspecific headache and intermittent fever of 3 months of evolution, without other symptoms (including behavioral changes). 3 days after admission, he presented sudden alteration of consciousness requiring orotracheal intubation. Clinical examination showed a comatose state, with normal reflexes and nuchal rigidity. Lumbar puncture reports albuminocytological dissociation, with negative reports to infection. Initial cerebral and cervical spine MRI showed multiple hyperintense lesions in T2-weighted in posterior thalamocapsular regions, splenium and brainstem with a longitudinally extensive lesion with demyelinating characteristics up to T2 segment. He progressed to symmetrical weakness with generalized areflexia despite myelopathy; autoimmune profile was compatible with EULAR criteria for SLE. Follow-up MRI showed cervical and thoracolumbar polyradiculitis confirmed by NCS. Immunosuppressive management was initiated with immunoglobulin and subsequent corticosteroid therapy with improvement of consciousness but persistence of motor and sensitive deficit. Autoantibodies related to NMODS and anti-MOG remain pending to define an overlap syndrome with SLE.

SUMMARY/CONCLUSION: Neurological manifestations of SLE are varied. Nevertheless this case shows a catastrophic debut with central and peripheral manifestations, a rare clinical presentation. The coexistence of systemic autoimmune diseases with demyelinating nervous diseases is still plausible.

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THE STUDY OF MUSCLE ELASTICITY USING SHEAR WAVE ELASTOGRAPHY

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INTRODUCTION: Ultrasound (US) elastography has been used for studying muscle disorders. Using shear wave elastography (SWE), muscle dynamics during contraction and relaxation can be obtained. Shear waves are generated by primary pulse waves created by the US transducer. These pulses create secondary lower frequency radiation acoustic forces which are perpendicular to the initial signal. The displacement and shear-wave velocity (SWV) in the tissue of interest, expressed as meters per second, is obtained through speckle tracking algorithms.

OBJECTIVE: To acquire normative elastography values of muscles in healthy volunteers.

METHODS: Muscle US studies were performed on 14 healthy volunteers. An 18 MHz probe was placed on the muscle bellies to measure muscle elastography from a longitudinal axis. The sites of testing were recorded using a bony landmark or elbow/knee crease and standardized positioning to maintain consistency. SWV values were obtained from 4 arm and 6 leg muscles. The mean SWV and standard deviations (STD) were calculated for each muscle group, in addition to the median and range values.

RESULTS: The healthy volunteers in this study have a median age of 42 (range 21-75). They include 8 females and 6 males. The median SWV for all the muscles was 2.69 (range 2.07-3.63). Results for individual muscles will also be presented.

SUMMARY/CONCLUSION: We obtained normative elastography values for 10 muscle groups and plan to expand our dataset as more healthy volunteers are recruited. We also will be evaluating inter-rater and intra-rater reliability.

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PROXIMAL CONDUCTION BLOCK MASQUERADING AS AXONOTMETIC TRAUMATIC BRACHIAL PLEXOPATHY

Niki Grzywnowicz (London, Canada), Thomas Miller (London, Canada), E. Ali Bateman (London, Canada)

INTRODUCTION/BACKGROUND: Traumatic brachial plexus injury (tBPI) is often axonotmetic with prolonged recovery that may be incomplete. In a suspected case of axonotmetic pan-plexus tBPI, EDX identified conduction block (CB) in the proximal arm which changed the patient's prognosis and management.

CASE REPORT: An 18-year-old man presented with left tBPI from a tractor crush injury. Immediate weakness of the shoulder, arm, and hand were associated with pain and numbness in the medial arm and forearm, with no recovery 4 months post-injury. MRI demonstrated enhancement of the upper trunk and no nerve root avulsions. Wasting and weakness were most pronounced distally in the hand intrinsic and forearm flexor muscles. Sensation was reduced in the medial arm, forearm, and hand with a positive Tinel sign at the medial mid-humerus. NCSs showed absent medial antebrachial cutaneous and reduced median and ulnar sensory amplitudes and normal distal median and ulnar motor amplitudes, not commensurate with his weakness: abductor pollicis brevis 10.9 mV, MRC 2/5; abductor digiti minimi 10.8 mV, MRC 1/5; and first dorsal interosseous 14.4 mV, MRC 1/5. EMG showed markedly reduced recruitment in all median and ulnar muscles in the forearm/hand with little denervation. CB was suspected for the median and ulnar nerves proximal to the elbow and confirmed on NCSs. Ultrasound demonstrated focal compression of these nerves at the mid-humerus.

SUMMARY/CONCLUSION: This case illustrates the importance of proximal NCSs to reconcile clinical and EDX findings and to provide accurate prognosis and treatment. The discovery of CB (in contrast to axonotmesis) has a more positive prognosis post-tBPI.

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IATROGENIC RADIAL NERVE PALSY FROM INTRAMUSCULAR INJECTION

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INTRODUCTION/BACKGROUND: Iatrogenic nerve injuries from intramuscular injections (IMI) are rare but serious. Fewer than 300 radial nerve injuries have been described; most required surgical intervention. This report describes a case of radial nerve axonotmesis from a single IMI, EDX evaluation, and recovery.

CASE REPORT: A 56-year-old man received a left upper limb IMI of ketorolac/morphine in an ER for acute lower back pain. He felt immediate pain in his posterior arm, forearm, and hand, followed by dense dysesthesias and wrist/finger drop. Examination 2 months post-IMI revealed weakness in wrist extension (MRC 3/5) and finger/thumb extension (MRC 0/5), with relative sparing of brachioradialis (MRC 4/5). There was a 50% reduction in sensory perception in the superficial radial sensory territory. EDX testing confirmed a left radial nerve axonotmesis. NCS demonstrated a significantly reduced radial motor compound muscle action potential (CMAP) for extensor indicis (EI) (0.2mV) and a reduced superficial radial sensory nerve action potential (SNAP) (8uV). EMG showed denervation and no volitional motor units in radially-innervated muscles distal to brachioradialis. A watch/wait approach including serial follow-up EDX testing every 2-3 months was favoured over surgery in part due to the presence of a CMAP in EI. Clinical improvement was mirrored in subsequent EDX testing; by 15 months post-IMI, EI had nascent motor units.

SUMMARY/CONCLUSION: The positive prognostic value of a CMAP in EI in this case of radial nerve injury from an IMI highlights the importance of EDX evaluation in the management of traumatic radial neuropathy.

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MONONEURITIS MULTIPLEX: A CASE SERIES

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INTRODUCTION: Mononeuropathy multiplex is a group of uncommon disorders. Definition is involvement of 2 or more noncontiguous peripheral nerves.

METHODS: We retrospectively reviewed data of patients with EDX of mononeuropathy multiplex. Etiology was divided as systemic vasculitis, isolated peripheral nerve vasculitis, chronic inflammatory neuropathy, infection (including leprosy), genetic, neoplastic disorders, and undetermined. EDX was classified as axonal, demyelinating, mixed, and associated pattern. When available, tissue biopsy was also reviewed.

RESULTS: A total of 100 patients were included. The most frequent etiology was systemic vasculitis with 51 patients. Among these, lupus was the most common diagnosis, but rarer vasculitis that are seldom associated with mononeuritis multiplex were also found. Isolated peripheral vasculitis was seen in 3 patients. Leprosy was the most frequent infection with 28 patients, only 2 presenting with pure neural leprosy. Chronic inflammatory neuropathy was represented by 3 cases of multifocal CIDP and 3 cases of multifocal motor neuropathy. Genetic was represented by 2 cases of hereditary neuropathy with pressure palsies. EDX was consistent with an axonal pattern in 70 cases, demyelinating in 12, mixed in 13, associated in 5. A total of 17 nerve biopsies, 44 skin biopsies, 3 salivary gland biopsies, and 7 renal biopsies were available for evaluation. Histology strongly suggested vasculitis in 33 biopsies, and 19 biopsies were diagnostic of leprosy.

CONCLUSION: Systemic vasculitis is the most frequent diagnosis. In our population, leprosy should be a concern in asymmetric neuropathy. Although a diagnostic challenge, an etiology can be clearly identified in the majority of patients. Non-neural tissue biopsies can be helpful with much less distress.

CHARACTERISTICS OF AUTOIMMUNE NODO-PARANODOPATHIES IN CHINA

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INTRODUCTION: Lack of definite biomarkers in chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) often causes misdiagnosis and non-response to treatment. Identification of antibodies to nodal proteins have categorized different subtypes of CIDP with specific clinical features and classified as autoimmune nodo-paranodopathies.

OBJECTIVE: We reported the collected clinical and treatment response profiles of 10 CIDP patients and 30 autoimmune nodo-paranodopathies.

METHODS: Forty patients in department of neurology, XuanWu Hospital, Capital Medical University were included. Existence of serum antibodies to neurofascin155 (NF155), neurofascin186 (NF186), contactin-associated protein 1 & 2 (CASPR1, CASPR2), contactin-1 (CNTN1), and myelin-associated glycoprotein (MAG) were detected. Patients underwent detailed evaluation of symptoms, brain MRI, and electromyography. In addition, demographic characteristics, disease history, and treatment responses were recorded (ONLS). Differences among patients with various serum antibody types were compared.

RESULTS: A total of 40 patients, including 22 with serum anti-NF155 antibody, 4 with anti-CASPR1, and 1 each for NF186, CNTN1, CASPR2, and MAG were included. The results showed 75% of the patients tested positive for serum antibodies, with 55% positive for anti-NF155. Compared to seronegative ones, patients with serum anti-NF155 exhibited younger ages, tremor, and more sensory dysfunction symptoms, as well as longer distal latency time. In addition, the anti-NF155 patients showed lower response to steroid and IVIg, compared to seronegative patients. The response to rituximab treatment was high for anti-NF155 positive patients.

SUMMARY/CONCLUSION: The patients with serum anti-NF155 antibody positive exhibited younger ages, more sensory dysfunction symptoms, longer distal latency time, and lower response to steroid and IVIg but good response to rituximab.

A RARE CASE OF HERPES ZOSTER LUMBOSACRAL PLEXOPATHY CAUSING LIMB PARESIS, PELVIC INSTABILITY, AND VESICULAR RASH

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INTRODUCTION/BACKGROUND: Herpes zoster rash (shingles) is caused by painful reactivation of varicella zoster virus (VZV) eliciting pain in a dermatomal distribution. Presentation occurs typically in adults over age 60. VZV lies dormant in the nervous system in patients previously infected with chickenpox. Zoster-associated neuropathy more commonly has sensory involvement. In this case, the patient had a rare presentation of zoster-associated lumbosacral plexopathy causing right hip and right lower extremity paresis.

CASE REPORT: A 77-year-old male presented for new onset right buttock and hip pain that radiated down his right lower extremity followed several days later by vesicular rash of right buttocks extending down to right foot. He was started on valacyclovir and gabapentin and his rash cleared. He developed right pelvic and right leg weakness making it difficult to walk. Lumbar spine MRI without contrast revealed multilevel degenerative changes and he was evaluated by neurosurgery who referred for EMG. Electrodiagnostic testing revealed a right subacute lumbosacral plexopathy. On neurological assessment he displayed right pelvic girdle and right lower extremity weakness, absent reflexes with marked Trendelenburg gait owing to right pelvic instability. He was started on IV methylprednisolone, IVIg treatment, and physical therapy regimen.

SUMMARY/CONCLUSION: Zoster-associated neuropathy typically affects sensory nerves causing neuralgia but may also present causing severe weakness. Our patient developed zoster-associated lumbosacral plexopathy causing limb paresis. Interestingly, our patient had difficulty walking predominantly due to pelvic instability. This unique case of zoster-induced weakness highlights lumbosacral plexopathy as an atypical neurologic complication.

Disclosures:

Derrick Fox - Served on advisory board for argenx, efgartigimod

OUTCOME OF MYOSITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

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INTRODUCTION: Idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of autoimmune disorders that affect muscle and potentially the lungs, skin, and joints. In addition to diaphragmatic muscle weakness, pulmonary involvement can manifest as interstitial lung disease (ILD), which can lead to mortality.

OBJECTIVE: To describe outcomes of patients with IIMs and ILD at the University of Kansas Medical Center (KUMC).

METHODS: After IRB approval, we searched the KUMC database for patients with IIM and ILD from ILD GAP list. We abstracted data from 19 patients with inflammatory myopathy and ILD.

RESULTS: Of 19 patients, there were 14 females and 5 males, with an average age of (64.36+/- 14.33). Ten patients were White. Average follow-up period was (5.9 +/- 6.12). The most common extrapulmonary manifestations were arthritis and muscle weakness (n=17). Fourteen patients required home oxygen and hospitalizations due to lung disease, 2 required lung transplant. Six patients died, average age was (60 +/- 14), with 4:2 female: male ratio, 4 were White. The number of therapies ranged from 1 (prednisone alone) to 5. Two patients had concurrent cancer and 5 required oxygen therapy. Out of the 13 patients who are still alive, 6 were African American. The number of treatments received ranged between 2 to 9 treatments. Only 3 had concurrent solid tumors and 9 patients required oxygen therapy.

SUMMARY/CONCLUSION: IIM with ILD is associated with high mortality. Factors predisposing to higher mortality include White race, younger median age, and lower median number of treatments received.

MILLS SYNDROME VARIANT

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INTRODUCTION: Mills syndrome is a rare condition characterized by slowly progressive spastic hemiparesis. Typically, there are no prominent lower motor neuron signs, but the disease may still be part of the ALS spectrum.

OBJECTIVE: To describe clinical characteristics, findings, and progression among patients with Mills syndrome.

METHODS: This is a retrospective chart review study of 12 patients with Mills syndrome who met criteria of gradual unilateral ascending/descending spastic hemiparesis. Symptoms, signs, pulmonary function tests (PFTs), and ALS Functional Rating Scale-Revised (ALSFRS-R) score were monitored. Diagnostic workup and death prevalence were collected.

RESULTS: Eleven patients with Mills syndrome had ultimately primary lateral sclerosis (PLS) and 1 patient had ALS diagnosis. All PLS patients had non-dominant side as initial symptom, and none progressed to involve contralateral side. Of PLS patients, 36%, 46%, and 18% had left arm, leg, and hemi-side involvement at onset respectively. If symptoms started in the arm, an average of 3 years elapsed before weakness occurred in the leg. If onset was in the leg, an average of 1 year until weakness occurred in the arm. Twenty-seven percent and 18% of PLS patients developed dysarthria and choking within an average of 2 and 7 years of onset respectively. Fifty percent of PLS patients had worsening PFTs but none required bilevel positive airway pressure (BiPAP). In PLS patients, ALSFRS-R score worsened by 0.5 points/year. None died over the 10-year follow-up period.

SUMMARY/CONCLUSION: ALS Mills syndrome is rare. PLS Mills variant has slower progression. More commonly, it starts in the nondominant lower extremity with mild bulbar and respiratory symptoms.

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INDIVIDUALIZING THERAPY FOR GENERALIZED MYASTHENIA GRAVIS: CAN CONTINUING MEDICAL EDUCATION HELP GUIDE TREATING CLINICIANS?

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INTRODUCTION: With the recent approvals of efgartigimod and C5 inhibitors, and the development of other pipeline agents, the treatment landscape for generalized myasthenia gravis (gMG) is helping clinicians (HCPs) more effectively individualize therapy.

OBJECTIVE: To assess the impact of continuing medical education (CME) on the ability of treating HCPs [T-HCPs] who manage gMG to account for comorbidities, disease presentation, and patient preferences when making individualized treatment recommendations.

METHODS: A 60-minute activity and four 15-minute case discussions were launched live-online on 09/09/22 and will remain on-demand for 1 year. Test questions were administered before and immediately after each activity. A follow-up survey on behavior change was sent to post-test respondents 2 months after activity completion. Chi-square tests compared paired responses ($p<0.05$; pre/post).

RESULTS: As of 3/08/23, 538 HCPs had engaged in the education (59% T-HCPs). Baseline performance showed most T-HCPs were comfortable recommending rituximab for a patient with MuSK+ MG (92%) and recognized bulbar involvement justified an aggressive therapeutic approach (89%). In contrast, many undervalued the importance of patients' ability to attend appointments (30%) or for comorbidities (52%) or acute infection (11%) in treatment decisions. After the education, T-HCPs' performance in each area ranged from 88% to 92%. Cost-related issues were the greatest barrier to initiating novel therapies.

SUMMARY/CONCLUSION: Live and on-demand education positively impacted T-HCPs' ability to personalize therapy for gMG. Overall low baseline performance related to newer concepts in therapy selection emphasizes that future education should continue to enhance T-HCPs' ability to identify patient and disease factors that drive therapy selection.

Disclosures:

James Howard - Received research support from Alexion Pharmaceuticals, argenx BVBA, Cartesian Therapeutics, Centers for Disease Control and Prevention, Myasthenia Gravis Foundation of America, Muscular Dystrophy Association, National Institutes of Health, PCORI, UCB Biosciences, and Takeda Pharmaceuticals; honoraria from F. Hoffmann-La Roche, Immunovant Inc, Merck EMD Serono, Regeneron Pharmaceuticals, Sanofi US, Horizon Therapeutics

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PEDIATRIC HMGCR-ASSOCIATED NECROTIZING MYOPATHY IN THE SETTING OF AN RYR1 VARIANT

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INTRODUCTION/BACKGROUND: Immune-mediated necrotizing myopathy (IMNM) is a rare form of inflammatory myopathy, characterized clinically by subacute proximal muscle weakness and pathologically by prominent myofiber necrosis with little or no inflammation. We present a pediatric case of anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (anti-HMGCR) IMNM in the setting of a likely pathogenic RYR1 variant.

CASE REPORT: A 12-year-old female presented for acute on chronic proximal muscle weakness. A comprehensive neuromuscular panel genetic test showed a likely pathogenic variant in RYR1 associated with malignant hyperthermia. Creatine kinase was elevated to greater than 20,000 U/L and she had positive antinuclear antibody. MRI of the pelvis and bilateral thighs was consistent with panmyositis. Biopsy of the right vastus lateralis muscle revealed scattered myofiber necrosis with associated myophagocytosis. She received IV methylprednisolone (IVMP) and IVIg which resulted in laboratory but not clinical improvement. HMGCR IgG subsequently resulted floridly positive >200. Clinical improvement was achieved with repeat courses of IVMP and IVIg and initiation of rituximab.

SUMMARY/CONCLUSION: Pediatric IMNM associated with anti-HMGCR antibodies is rare. There is no known association between ryanodine receptor 1 related myopathies and HMGCR IMNM. While the RYR1 variant in this case is not felt to be causative of presentation, it is possible abnormal ryanodine receptor channel increases IMNM disease severity. Steroids and IVIg are first line treatments for HMGCR-associated IMNM, with rituximab reserved for refractory cases. Due to the rarity of this condition, ongoing study of the pathophysiology, symptomatology, and management of pediatric cases of IMNM is needed.

SHORT-TERM PROGNOSTIC VALUE OF BLINK REFLEX AND FACIAL NERVE CONDUCTION STUDY ON BELL PALSY

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INTRODUCTION: Recovery from Bell palsy (BP) often needs substantial time and prolonged facial palsy is associated with synkinesis.

OBJECTIVE: This study is designed to identify the components of facial nerve study for the short-term prognostic factor.

METHODS: From 2016 to 2018, we recruited patients with BP. Facial function was assessed with House-Brackman scale (HBS) and electrophysiologic study for facial nerve was conducted (i.e., facial nerve conduction study, blink reflex) at each visit. The ratio of compound muscle action potential (CMAP) was defined that the value of the abnormal side is divided by that of the normal one. Visit 1 was within 10 days from onset and visit 2 was around 10 days from visit 1; visit-3 was around 1 month from visit 2. Prognosis 1 was checked at visit 2 (good prognosis: HBS ≤ 2) and prognosis 2 was at visit 3 (good prognosis: HBS = 1).

RESULTS: We included 83 (56.0±14.5, female 39). Visit 1 revealed HBS 2 for 27, 3(34), 4(15), 5(7). At visit 1, blink reflex was abnormal in all patients with at least 1 component and 59 studies showed no response. No response on visit 1 was associated with poor prognosis at prognosis 1 and prognosis 2 ($p=0.008$, OR 6.7 and $p<0.001$, respectively) and no response on visit 2 was also associated with poor prognosis 2 ($p<0.001$, OR 8.3). Facial nerve CMAP ratio was statistically different according to prognosis (prognosis 1: good 0.67±0.25 vs not good 0.44±0.22. $p=0.001$, prognosis 2: 0.73±0.23 vs 0.42±0.24. $p<0.001$).

SUMMARY/CONCLUSION: Blink reflex is a good tool for diagnosis of BP and no response at early stage applicable to short-term prognostic evaluation. Ratio of facial nerve CMAP within 20 days from onset also has short-term prognostic value.

IMMUNOGLOBULIN-G4 RELATED HYPERTROPHIC PACHYMENINGITIS PRESENTING AS MULTIPLE LOWER CRANIAL NERVE PALSIES

Bum Chun Suh (Seoul, Korea, South), Sang Beom Kim (Seoul, Korea, South)

INTRODUCTION/BACKGROUND: Immunoglobulin G4-related disease (IgG4RD) is a disease involving multiple organs such as the pancreas and biliary tract. Neurologic manifestation is associated with either direct or mass effect. We report a case of IgG4-related hypertrophic pachymeningitis presenting with multiple lower cranial nerve palsies.

CASE REPORT: A 65-year-old man presented with hoarseness and dysphagia for 5 months. Neurologic examination showed multiple lower cranial nerve (IX, X, XI, XII) palsies. Brain MRI showed diffuse dural thickening and enhancement along left posterior fossa, tentorium, and temporal fossa. We considered tumorous condition and also IgG4-related disease. Serum IgG was increased to 2183 mg/dL (700-1600) and serum IgG4 to 218 mg/dL (3-135). In cerebrospinal fluid (CSF) study, white blood cell (WBC) count was 9/mm^3, protein was 80.2 mg/dL, and glucose was 59 mg/dL. Biopsy specimen of ethmoid polyp showed chronic inflammation with moderate lymphoplasmacytic infiltration and some eosinophils. IgG4 was up to 60/HPF and IgG4/IgG ratio was about 10-20%. Fluorodeoxyglucose-positron emission tomography (FDG-PET) CT showed abnormally increased FDG uptake in left posterior fossa, tentorium, and left temporal fossa with some involvement of lung and iliac/renal artery. We diagnosed IgG4-related hypertrophic pachymeningitis with involvement of multiple organs. Steroid pulse therapy with 60 mg prednisolone maintenance. The patient improved clinically and radiologically. Serum IgG4 was normalized (50.3).

SUMMARY/CONCLUSION: IgG4RD can simultaneously involve various organs in addition to the pancreas and biliary tract. PET-CT is a very useful modality for multiple organ involvement. In patients with multiple cranial nerve palsies with mass-like lesions, IgG4RD should be differentiated and serum IgG4 and IgG level measurement and IgG4-specific histology are recommended.

IMPROVING SEROLOGICAL DIAGNOSIS OF MYASTHENIA GRAVIS BY A COMPREHENSIVE REFLEX TESTING ALGORITHM: A REAL WORLD EXPERIENCE WITH MORE THAN TWELVE THOUSAND PATIENT SAMPLES

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INTRODUCTION: Serological testing plays an essential role in the diagnosis of myasthenia gravis (MG) and with the development of novel methods, their algorithms have changed. We, at BC Neuroimmunology Lab, in a full reflex testing algorithm first assay acetylcholine receptor (AChR) Abs by Radio Immuno Precipitation of Antibodies (RIPA), if AChR Ab is absent, then reflex to muscle-specific tyrosine kinase (MuSK) Abs by RIPA. If samples are double seronegative, they are tested with clustered AChR Abs live cell-based assay (L-CBA). Further negative samples are tested for low-density lipoprotein receptor-related protein 4 (LRP4) Ab by CBA.

OBJECTIVE: This study reports the results of the improvement of the serological diagnosis of MG by a reflex testing algorithm.

METHODS: Between August 2021 and February 2023, we assayed 7,418 samples for AChR Ab and 3,640 samples for MuSK Ab by RIPA, and 744 for AChR Ab and 379 for LRP4 by CBA.

RESULTS: We found 681 AChR Ab-positive samples by RIPA. Among the 3,640 AChR Ab negative samples we found 57 positives for MuSK Ab by RIPA. Among double seronegative samples, L-CBA found 47 positive AChR Ab. Among seronegative samples for AChR Ab by both RIPA and CBA and MuSK by RIPA, we found 6 positive LRP4 Ab.

SUMMARY/CONCLUSION: While we found 9% AChR Ab positive by RIPA, we added another 10% to the seropositivity of clinically suspected MG by proposing a full reflex testing algorithm. This increment includes 2% MuSK Ab by RIPA, 6% AChR Ab, and about 2% LRP4 Ab seropositivity by CBA.

FORTY YEARS OF IMPROVING DIAGNOSTIC TESTING FOR MYASTHENIA GRAVIS

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INTRODUCTION: Antibodies to the acetylcholine receptor (AChR Abs) in myasthenia gravis (MG) have been recognized for over 40 years. BC Neuroimmunology has provided specialized clinical diagnostic services detecting these antibodies since 1984.

OBJECTIVE: We present clinical validation studies confirming the improvement of the serological diagnosis of MG through the years.

METHODS: The sensitivity of AChR Ab in definite MG patients (n=135) was compared with EDX (n=93). The accuracy of the RIPA and ELISA methods was compared by testing the serum of 90 definite MG patients and 40 controls. Live-Cell Based Assay (L-CBA) and the commercial Radioreceptor Assay (RRA) were compared against our RIPA assay, by assaying the serum of 38 MG patients and 50 controls.

RESULTS: AChR Ab positivity by RIPA in ocular (63%) and generalized MG (80%) was more sensitive than SFEMG or RNS, in ocular (42% and 18%) and generalized MG (78% and 63%). Our RIPA detected all samples of controls as negative and 85 serum of MG patients as positive for AChR Ab, while ELISA had 3 false positives and 19 false negatives. The specificity and sensitivity of RIPA were 100% and 94% vs 92.5% and 79% for ELISA. The specificity of RRA was the same as L-CBA (100%), but it had low sensitivity (100% vs 92%).

SUMMARY/CONCLUSION: L-CBA and RIPA were more sensitive and specific in detecting AChR Ab than ELISA. The sensitivity of L-CBA was higher than RRA. To avoid false negative results and to improve sensitivity, we perform L-CBA as complementary testing for RIPA in reflex testing.

CONTRASTING CLINICAL AND LABORATORY FEATURES ARE HELPFUL IN DIAGNOSING MCARDLE DISEASE

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INTRODUCTION: McArdle disease is a rare autosomal recessive myopathy due to myophosphorylase deficiency. Symptoms usually start in childhood or adolescence, but diagnosis is often delayed until adulthood.

OBJECTIVE: To identify key clinical and laboratory features facilitating early diagnosis of McArdle disease.

METHODS: A retrospective review was performed on 15 patients with McArdle disease. Diagnosis was made via genetic testing and/or enzymatic analysis of biopsied muscle. Collected variables include demographics, symptoms, physical exam findings, creatine kinase (CK) values; EMG, genetic testing, and muscle biopsy results; duration of diagnostic delay; and misdiagnoses.

RESULTS: Fifteen (9 males and 6 females) patients were included, with onset age from 6 months to 69 years (median 16 -18 years). Common symptoms included exercise intolerance (n = 15), rhabdomyolysis (n = 14), myoglobinuria (n = 9), and second wind phenomenon (n = 8). Muscle strength examination and EMG were typically normal or showed only mild abnormalities. In contrast, CK values were elevated in 930/931 measurements (range 273 to 75,510 IU/L) and exceeded 3,000 IU/L in 14/15 patients. Significant fluctuations of CK (defined as maximum/minimum ratio >5) were observed in all patients (ratio range 5.4 to 276.6, median 20.4). Duration of diagnostic delay ranged from 1 to 30 years (median 11 years). Ten patients were misdiagnosed, the most common misdiagnosis being myositis (n = 4).

SUMMARY/CONCLUSION: In McArdle disease, muscle strength exam and EMG findings are typically uninformative. However, persistently abnormal and significantly fluctuating CK values without associated changes in muscle strength can suggest the diagnosis.

DIAGNOSIS INEQUITIES IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS FACING SOCIAL DETERMINANTS OF HEALTH CHALLENGES: A SURVEY OF NEUROLOGISTS IN THE UNITED STATES

Nicole Wright (Birmingham, AL), Deborah Gelinas (Durham, NC), Paul Nisbet (Mt Pleasant, SC), Tom Hughes (Phoenix, AZ), Elizabeth Ashcraft (Pfafftown, NC), A. Gordon Smith (Richmond, VA)

INTRODUCTION: Social determinants of health (SDOH) challenges may contribute to care inequities in generalized myasthenia gravis (gMG).

OBJECTIVE: We surveyed US neurologists to better understand the impact of SDOH on patients receiving a diagnosis of gMG.

METHODS: The 42-item online healthcare access survey was deployed using email. Questions addressed demographics, diagnosis, treatment, and continuity of care for patients with gMG whom respondents considered to be facing SDOH challenges (racial/ethnic minority or financial limitations).

RESULTS: The survey, launched in October 2022, was completed by 150 neurologists. The majority (84% [126/150]) are board certified in neurology; the remainder, in neuromuscular or electrodiagnostic medicine. Roughly half of respondents are university affiliated. Respondents reported that 33% of their patients with gMG face inequities in healthcare access. More than half of respondents (55% [82/150]) indicated these patients experience longer duration between symptom onset and gMG diagnosis and a higher likelihood of diagnosis in an inpatient setting (56% [84/150]). Similarly, 55.3% (83/150) reported these patients have more difficulty scheduling appointments; 76.7% (115/150) reported these patients have more difficulty attending appointments; and 72.7% (109/150) reported these patients miss more appointments. Respondents suggested these disparities stem from cost, challenges with appointments, transportation difficulties, being less likely to seek care, and being more likely to visit an emergency room as disease progresses.

SUMMARY/CONCLUSION: Patients with gMG facing SDOH challenges are more likely to experience healthcare inequities when receiving diagnosis. Flexible scheduling, improved transportation options, and increased primary care education could shorten time between symptom onset and diagnosis.

Disclosures:

Nicole Wright - Consultant for argenx and Radius Pharmaceuticals

Deborah Gelinas - Employee of argenx

Paul Nisbet - Employee of One Research

Tom Hughes - Employee of argenx

Elizabeth Ashcraft - Employee of argenx

A. Gordon Smith - Consultant to Alexion, argenx, Eidos, Lexicon, Merz, and Sangamo

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TREATMENT-RELATED INEQUITIES IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS FACING SOCIAL DETERMINANTS OF HEALTH CHALLENGES: A SURVEY OF NEUROLOGISTS IN THE UNITED STATES

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INTRODUCTION: Social determinants of health (SDOH) contribute to inequities in outcomes for patients with generalized myasthenia gravis (gMG).

OBJECTIVE: US neurologists were surveyed to better understand the impact of SDOH on treatment access and utilization.

METHODS: The 42-item online survey on healthcare access was deployed using email. Questions focused on demographics, diagnosis, treatment, and continuity of care in patients with gMG they considered to be facing SDOH challenges (racial/ethnic minority or financial limitations).

RESULTS: The survey was completed by 150 neurologists in October 2022. Respondents estimated that 33% of their patients with gMG face care inequities. 74.7% (112/150) reported it is more difficult for these patients to afford prescribed gMG therapies. Compared to other patients with gMG, they view patients facing inequities as less receptive to infusion therapies and thymectomy; less likely to be presented with newer therapies; less likely to receive payor approval for antibody-based biologics, IVIg, and plasmapheresis; and more likely to experience difficulty traveling to infusion centers. 67.3% (101/150) of respondents reported these patients experience greater difficulty in continuing gMG treatment and 60.0% (90/150) said these patients have a greater likelihood of experiencing exacerbation or crisis-related hospitalization. Respondents identified cost of treatment/insurance and transportation issues as the biggest contributors to difficulties in obtaining and continuing gMG treatment.

SUMMARY/CONCLUSION: Patients with gMG facing SDOH challenges experience health care access inequities when initiating and continuing treatment. Assistance with drug costs, transportation, and in-home infusions, as well as increased awareness and patient advocacy, could mitigate treatment-related disparities in gMG treatment.

Disclosures:

Nicole Wright - Consultant for argenx and Radius Pharmaceuticals

Deborah Gelinas - Employee of argenx

Paul Nisbet - Employee of One Research

Tom Hughes - Employee of argenx

Elizabeth Ashcraft - Employee of argenx

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CARPAL TUNNEL SYNDROME IN AMYLOIDOSIS: AN EARLY MARKER OF THE DISEASE

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INTRODUCTION: Amyloidosis is a systemic condition and carpal tunnel syndrome (CTS) could precede the involvement of other organs.

OBJECTIVE: To evaluate the prevalence of amyloid in patients with CTS and its systemic involvement.

METHODS: We prospectively studied patients with CTS clinical and electromyographic criteria (March 2022-January 2023) in whom we analyzed samples of their anterior carpal ligaments and synovial tissue. Anatomopathologically, Congo Red staining and polarized light microscopy were obtained. In patients with positive amyloid, we performed genetic tests for transthyretin (TTR), immunoelectrophoresis with immunofixation in blood and urine, scintigraphy with pyrophosphate (PYP) uptake, and multidisciplinary evaluation.

RESULTS: Twenty-nine patients were included (20 women, mean age: 66 years, range 41-88). Five patients had amyloid (3 men). Four had bilateral CTS, 5 were of Anglo-Saxon origin and had no family history of CTS. One patient had biceps tendon rupture and another idiopathic heart failure. One patient was diabetic. One patient presented vitreous compromise and left ventricular hypertrophy by echocardiography. Outside of median nerve involvement, peripheral neuropathy was not demonstrated by nerve conduction studies. A patient with diabetes had small fiber involvement by quantitative sensory testing (QST). Immunoelectrophoresis study with immunofixation in blood and urine was normal in all cases. Genetic testing is pending in all cases. Three patients had negative PYP uptake scintigraphy.

SUMMARY/CONCLUSION: In our prospective study 17.2% of patients had amyloid.

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ANTIGEN-SPECIFIC IMMUNE THERAPY (CNP-106) FOR TREATMENT OF GENERALIZED MYASTHENIA GRAVIS: RATIONALE AND DESIGN OF FIRST IN-HUMAN RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION: Myasthenia gravis (MG) is a T-cell dependent B-cell mediated autoimmune disease with pathogenic antibodies directed against the acetylcholine receptor (AChR). Current therapies do not completely address autoimmune recognition of AChR, the root cause of disease, and are associated with possible serious side effects. New therapeutics targeting antigen specific autoimmunity are needed for this significant unmet medical need.

OBJECTIVE: A phase 1/2a celiac disease clinical trial demonstrated that CNPs encapsulating gliadin is safe and effective at inducing antigen-specific tolerance. This trial will investigate antigen-specific tolerance induced by CNPs encapsulating multiple AChR epitopes (CNP-106) in MG patients.

METHODS: The study is a multi-center phase 1b/2a double blind, placebo-controlled trial with enrollment target of 40 AChR antibody positive generalized MG participants. The aim of this study is to determine safety, evaluate antigen-specific T cells and other immunologic markers, and assess preliminary efficacy of CNP-106.

RESULTS: Data from pre-clinical models demonstrated that CNP-106 reprogrammed antigen specific T cells and reduced myasthenia clinical symptoms, highlighting the potential benefit of CNP-106 to stop progression of disease in MG patients.

SUMMARY/CONCLUSION: This study is the first to explore novel antigen specific therapy in MG. CNP-106 has the potential to induce tolerance to AChR and improve myasthenia clinical symptoms without the need for broad immunosuppression or chronic dosing. Results of this study will pave the way for a new class of therapeutics targeting antigen specific autoimmunity, leading to improvement in clinical disease and immune tolerance. The study rationale, design, and study status update will be presented.

Disclosures:

Richard Nowak - Clinical consultant for COUR Pharmaceuticals

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THE EFFECTS OF EARLY INITIATION OF IVIG IN THE TREATMENT OF ANTI-HMGCR IMMUNE-MEDIATED NECROTIZING MYOPATHY

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INTRODUCTION: Immune-mediated necrotizing myopathies (IMNMs) are a collection of rare systemic autoimmune conditions which damage muscle. One subtype of IMNM involves the production of anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) antibodies, referred to as anti-HMGCR IMNM. Recent evidence shows IVIg is a safe and effective treatment for this rare condition, however the importance of its use in early treatment is poorly characterized.

OBJECTIVE: To retrospectively examine and compare the clinical response in anti-HMGCR IMNM patients who received IVIg early in their treatment versus late.

METHODS: Retrospective chart review was performed on 31 anti-HMGCR IMNM patients who receive care at the OHSU Myositis Center, with clinical and serologic monitoring at a 3-month and 6-month time period. Twelve of these patients received IVIg "delayed", defined as 6 months after onset of symptoms, while 19 received it "non-delayed", i.e., prior to or at 6 months from onset. Treatments among these patients generally included steroids, a steroid-sparing immunosuppressant, and IVIg and were not standardized. Their clinical response was determined based on a total improvement score (TIS) as per 2016 ACR/EULAR myositis response criteria, which utilizes a combination of clinical and serologic markers.

RESULTS: At the 6-month evaluation, TIS response within the “delayed” and "non-delayed” groups were: 25%/5% no response, 42%/11% mild response, 25%/42% moderate response, and 8%/42% major response. TIS response was significantly statistically different as tested by Fisher's exact test at both 3 and 6 months.

SUMMARY/CONCLUSION: This limited retrospective chart review may suggest anti-HMGCR IMNM patients benefit from early aggressive treatment with IVIg.

EFFICACY, SAFETY, AND TOLERABILITY OF EFGARTIGIMOD IN PATIENTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY: RESULTS FROM THE ADHERE TRIAL

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INTRODUCTION: Efgartigimod is a human IgG1 antibody Fc fragment that blocks the neonatal Fc receptor (FcRn), which decreases recycling of immunoglobulin G (IgG) and reduces pathogenic IgG autoantibody levels that may play a role in pathogenesis of chronic inflammatory demyelinating polyneuropathy (CIDP). Currently, not all patients with CIDP achieve clinically meaningful benefits from available treatments, which can carry long-term safety risks, high costs, and burdensome administration. The ongoing global ADHERE trial (NCT04281472) investigates efficacy, safety, and tolerability of subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20).

METHODS: ADHERE enrolls adult patients with CIDP who are treatment naive or receiving standard treatments (i.e., corticosteroids, intravenous or subcutaneous immunoglobulin), which were withdrawn prior to day 1 of a ≤12-week run-in period. Following a ≤12-week open-label phase of 1000 mg efgartigimod PH20 SC weekly (stage A), treatment responders enter a 48-week randomized phase of weekly treatment versus placebo (stage B). ADHERE will recruit up to 360 patients in stage A until 88 events of clinical deterioration have been observed in stage B. Primary objectives include assessing evidence of clinical improvement (stage A) and efficacy of efgartigimod PH20 SC versus placebo based on time to occurrence of clinical deterioration (stage B) (both measured using adjusted Inflammatory Neuropathy Cause and Treatment [INCAT] score). Safety, tolerability, and immunogenicity will also be assessed.

RESULTS: ADHERE results will be presented at AANEM 2023.

SUMMARY/CONCLUSION: ADHERE is evaluating efficacy, safety, and tolerability of efgartigimod PH20 SC in CIDP patients and will conclude in the first half of 2023.

Disclosures:

Richard Lewis - Akcea, Alexion, Alnylam, Annexon, argenx, Boehringer Ingleheim, CSL Behring, Grifols, J&J, Novartis, Pfizer, Roche, Sanofi, Takeda, GBS-CIDP FI, MGFA, Peripheral Nerve Society- President, Medscape

Jeffrey Allen - Akcea tTerapeutics, argenx SE, Alexion, Alnylym, Annexon, CSL Behring, Grifols, Immuovant, Immupharma, Johnson & Johnson, Pfizer, Takeda

Ingemar Merkies - Talecris, CSL Behring, Octapharma, LFB, Novartis, UCB, J&J, argenx, GBS/CIDP Foundation International, and FP7 EU

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Erik Hofman - Employee of argenx

Chongbo Zhao - Zailab, Roche, Sanofi, Harbour Biomed

Pieter van Doorn - argenx, Hansa Biopharma, Immunic, Octapharma, Roche, Sanofi, Prinses Beatrix Spierfonds, Sanquin, and Grifols

PHASE 2 PROOF-OF-CONCEPT TRIAL EVALUATING SAR445088, A MONOCLONAL ANTIBODY TARGETING COMPLEMENT C1S, IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

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INTRODUCTION: Autoantibodies and complement activation may play a role in chronic inflammatory demyelinating polyneuropathy (CIDP). SAR445088, a humanized second-generation IgG4 monoclonal antibody, selectively targets active C1s within the classical complement pathway.

OBJECTIVE: Evaluate efficacy, safety, and tolerability of SAR445088 in adult CIDP patients.

METHODS: Global multi-center, phase 2, open-label study (NCT04658472) includes up to 110 CIDP participants across 3 groups: standard-of-care (SOC)-treated (immunoglobulin/corticosteroids) (n= up to 50); SOC-refractory (n= up to 40) and SOC-naïve (n= up to 20). Participants undergo initial 24-week treatment (Part A), followed by optional treatment extension for 52 weeks (Part B); those completing Part B can continue treatment until end-of-study (Part C). In Part A, primary endpoint is (i) SOC-treated group: percentage of participants with relapse, defined as ≥1-point increase in adjusted Inflammatory Neuropathy Cause and Treatment (INCAT) disability score from baseline up to 24 weeks after switching from SOC to SAR445088; (ii) SOC-refractory and SOC-naïve groups: percentage of participants with response, defined as ≥1-point decrease in adjusted INCAT score from baseline up to 24 weeks. Secondary and exploratory endpoints include safety, additional efficacy measures, and pharmacokinetics/pharmacodynamics. Part B and Part C examine long-term safety and efficacy durability. Data analysis uses Bayesian statistics with predefined efficacy criteria and placebo assumptions based on historical data. Each study group is assessed separately. Planned interim analysis with defined criteria will be conducted when 50% of each cohort completes 24 weeks.

RESULTS: Innovative study design and preliminary results (if available) will be presented.

SUMMARY/CONCLUSION: The study will establish proof-of-concept and inform design of a future phase 3 trial. This innovative trial design, based on different groups and Bayesian statistics, provides an efficient way of evaluating treatments in CIDP.

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MULTIFOCAL MOTOR NEUROPATHY WITH CONCURRENT SMALL FIBER AUTONOMIC NEUROPATHY

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INTRODUCTION/BACKGROUND: Multifocal motor neuropathy (MMN) is an acquired, immune-mediated neuropathy that is typically associated with GM1 antibodies and characterized by lower motor neuron predominant asymmetric pure motor weakness in the extremities. Small fiber neuropathy (SFN) is a disorder of peripheral nerves affecting the small myelinated (Aδ) fibers or unmyelinated C fibers that are involved in thermal perception, nociception, and autonomic functions. We report 2 cases of MMN with concurrent autonomic SFN.

CASE REPORT: Case 1 is a 53-year-old woman who presented with gradually progressive asymmetric proximal and distal extremity weakness of 5 years' duration. Subsequently, she developed symmetric pins and needles sensation in a length dependent pattern involving bilateral legs and hands of 4 years' duration. This was associated with lightheadedness, palpitations, dry eyes, dry mouth, bloating, constipation, abnormal sweating, and weight loss. Case 2 is a 36-year-old woman with history of Bell palsy, Meniere disease status post cochlear implants, who presented with gradually progressive asymmetric distal greater than proximal limb weakness of 5 years' duration. She had associated distal limb paresthesia, dry eyes, dry mouth, lightheadedness, palpitations, constipation, bloating, rash, delayed skin blanching, and hair loss. MRI brain was unremarkable in both. Serological testing revealed elevated GM-1 IgM antibody titers 1:3200 and 1:1600 (normal 1:800) respectively. Skin biopsy confirmed a length dependent and non-length dependent SFN respectively. They were started on intravenous immunoglobulins with significant improvement of symptoms.

SUMMARY/CONCLUSION: MMN is a pure motor syndrome and SFN is restricted to sensory and autonomic fibers. We report the first known occurrence of these 2 conditions combined.

CHARACTERISTICS AND TREATMENT PATTERNS AMONG PATIENTS WITH MULTIFOCAL MOTOR NEUROPATHY AND MIMIC DISORDERS: RETROSPECTIVE COHORT STUDY OF A UNITED STATES CLAIMS DATABASE

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INTRODUCTION: Diagnosis of multifocal motor neuropathy (MMN) is challenging. Real-world evidence describing patients is needed.

OBJECTIVE: To summarize the characteristics and treatment patterns of patients with MMN and distinguish MMN from MMN-mimics using claims data.

METHODS: De-identified patients (all ages) from the Optum Research Database (October 1, 2015–December 31, 2021) with ≥1 claim, an MMN ICD-10-CM code (first diagnosis date=index), and continuous enrollment in medical/pharmacy benefits 12 months pre- and post-index were included. Patients were stratified into MMN (≥2 claims with MMN ICD-10-CM codes ≥30 days apart; no ALS diagnosis during the minimum follow-up period) and MMN-mimic (excluded from MMN) cohorts. Results were described pre- and post-index.

RESULTS: Of 904 patients diagnosed with MMN, 336 (37.2%) remained diagnosed post-index. These patients were younger (mean: 64.9 vs 66.8 years; p=0.047) with longer follow-up (mean: 31.8 vs 27.2 months; p<0.001) than the MMN-mimic cohort. At pre-index, a higher proportion of patients with MMN (vs MMN-mimic cohort) received MMN-related medications (20.5% vs 9.0%; p<0.001) and corticosteroids (50.3% vs 43.3%; p=0.042); IVIg was the most common MMN-related medication (16.4% vs 4.9%; p<0.001). Subcutaneous immunoglobulin was not prescribed. At post-index, IVIg use increased in patients with MMN (28.0%); chronic inflammatory demyelinating polyneuritis prevalence increased across cohorts (MMN: 8.3% to 15.2%; MMN-mimic: 5.3% to 7.4%).

CONCLUSION: This study showed that MMN remains difficult to diagnose and that most participants had alternate diagnoses. Only 28.0% of patients with MMN received IVIg. Further education and improved diagnostics for MMN are needed.

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REDUCED IMMUNOGLOBULIN G AND ANTI-ACETYLCHOLINE RECEPTOR ANTIBODIES EXPLAIN NIPOCALIMAB EFFECT ON IMPROVED MYASTHENIA GRAVIS ACTIVITIES OF DAILY LIVING SCORE IN GENERALIZED MYASTHENIA GRAVIS PATIENTS

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INTRODUCTION: Nipocalimab is an anti-FcRn monoclonal antibody that lowers immunoglobulin G (IgG), including anti-acetylcholine receptor (AChR) antibodies.

OBJECTIVE: This analysis was conducted to quantify the relationship between IgG, anti-AChR antibodies and the clinical efficacy endpoint (Myasthenia Gravis Activities of Daily Living [MG-ADL] score) to understand if IgG or anti-AChR antibodies reduction could account for nipocalimab effect on MG-ADL.

METHODS: Data from 68 patients with generalized myasthenia gravis (gMG) from a phase 2 study (NCT03772587) were utilized for statistical and population modeling and simulation analyses to quantify the relationship between IgG, anti-AChR antibody and MG-ADL reduction.

RESULTS: IgG and anti-AChR antibody reduction expressed as percent change from baseline were highly correlated ($R^2=0.75$) and correlated similarly to MG-ADL improvement. IgG was selected to quantify the relationship to MG-ADL to allow inclusion of all patients (AChR+ and AChR-). Placebo-corrected change from baseline MG-ADL (ΔΔMG-ADL) was proportional to IgG reduction. A 50% IgG reduction was estimated to lead to a median ΔΔMG-ADL reduction of 1.07 points. Patients with higher individual baseline MG-ADL exhibited higher ΔΔMG-ADL reductions (e.g., a 2-fold baseline increase resulted in a 1.9-fold higher reduction). Simulations showed that a large proportion (>80%) of the nipocalimab-induced MG-ADL improvement could be explained by IgG reduction.

SUMMARY/CONCLUSION: Serum IgG reduction explains most of the ΔΔMG-ADL change following nipocalimab treatment. Thus, IgG reduction may qualify as a biomarker for efficacy if confirmed by data from the ongoing phase 3 study. The quantitative relationship between IgG, anti-AChR antibody, and MG-ADL is critical for model-informed decisions on nipocalimab development.

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QIGONG FOR PAINFUL DIABETIC POLYNEUROPATHY

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INTRODUCTION: Diabetic polyneuropathy (DPN) is the most common cause of neuropathy worldwide. Symptoms of pain and paresthesias markedly impair quality of life (QOL) and result in sleep disturbances, disability, and costly health care utilization. Pharmacologic therapies provide little if any relief. In small studies, Qigong, a mind-body practice that integrates body awareness, focused attention, and balance training, has shown to be helpful in the treatment of chronic pain.

OBJECTIVE: We studied the feasibility of utilizing Qigong to improve pain and QOL in patients with painful DPN.

METHODS: This was a non-randomized pilot study that included 10 patients with DPN. Subjects completed 9 weekly online group sessions of Qigong with trained instructors. Adherence rates, acceptability of the intervention, and technical issues were recorded as feasibility outcomes. Secondary outcomes of pain and QOL were measured by the visual analogue scale, Patient Reported Outcome Measurement Information System Neuropathic Pain Quality scale (PROMIS-PQ-Neuro) and Neuropathy-Specific QOL (Neuro-QoL) questionnaire.

RESULTS: Of 10 patients who entered the study, 9 (5 women, 4 men) completed the active intervention. The practice was well-tolerated with no adverse effects and was rated favorably by participants. Although the study was not powered for efficacy, a trend toward improved pain and QOL was observed in the secondary outcome measures pre- and post-treatment.

SUMMARY/CONCLUSION: Qigong is a feasible practice for patients with painful DPN with high adherence rates and acceptability ratings. While the underlying pathophysiology of mind-body practice-related pain modulation is unknown, functional changes in neural structures involved with cognitive pain processing may play a role.

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AMYLOID MYOPATHY WITH PATHOLOGICAL RESEMBLANCE TO DERMATOMYOSITIS

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INTRODUCTION/BACKGROUND: Amyloid myopathy is a rare manifestation of systemic amyloidosis. Typically, amyloid deposits in skeletal muscle are present in endomysial, perimysial, or perivascular distribution. Perifascicular atrophy and increased MHC1 expression are hallmarks of dermatomyositis and have not been reported with amyloid myopathy.

CASE REPORT: A 65-year-old African American male with hypertension, type 2 diabetes, and heart failure presented with 4 months of progressive dysphagia, dysarthria, shortness of breath, and difficulty raising his arms and ambulating. Examination revealed proximal upper and lower extremity weakness, hyporeflexia in the upper extremities, areflexia in the lower extremities, and hyperesthesia at the toes. Laboratory studies were notable for CK 125 (normal 50-185 U/L), SPEP with monoclonal free IgA (0.1g/dL) and monoclonal free lambda band (0.8 g/dL), elevated lambda free light chain (109 mg/dL, normal: 0.57-2.63 mg/dL), and low kappa/lambda ratio (0.017, normal 0.26-1.65). Myomarker panel showed anti-PM/Scl antibody of 38, normal <20. EMG showed a distal axonal sensorimotor polyneuropathy as well as an irritable myopathy. Cardiac amyloid scan with SPECT was negative for transthyretin (TTR) amyloidosis. Left deltoid biopsy showed perifascicular atrophy and increase in sarcolemmal MHC1 expression in a perifascicular distribution but no inflammatory infiltrates or blood vessel changes. Congo red-positive amyloid deposits were also present in a perifascicular distribution. Laser microdissection and mass spectroscopy confirmed the diagnosis of AL amyloidosis. Despite starting chemotherapy, the patient expired 4 months after his initial presentation.

SUMMARY/CONCLUSION: We present a case of amyloid myopathy with unusual histological features that resembled dermatomyositis.

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NERVE ALPHA-SYNUCLEIN IN SMALL-FIBER NEUROPATHY

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INTRODUCTION: Small-fiber neuropathy (SFN) is a common form of peripheral neuropathy affecting primarily unmyelinated or thinly-myelinated C and A-delta nerve fibers. Patients with SFN present with neuropathic pain, loss of sensation to temperature and pain, and autonomic symptoms, with sparing of motor function, proprioception, and tendon reflexes. While diagnostic testing can often reveal an underlying cause (particularly diabetes, autoimmune disorders, monoclonal gammopathies, and Fabry disease), around 50% of SFN remains idiopathic after extensive investigation. Recently, an additional etiology of small-fiber pathology has been described in patients with Parkinson disease and dementia with Lewy bodies: degeneration of small nerve fibers from deposits of alpha-synuclein in intra-epidermal nerve terminals. These deposits have been hypothesized to cause the mild neuropathic, autonomic, and gastrointestinal symptoms that can occur as prodromal features in these disorders. However, to date there have been no studies of the presence of synuclein deposits in patients with idiopathic SFN.

OBJECTIVE: To assess the presence of phosphorylated alpha-synuclein deposits in skin biopsy specimens from patients with idiopathic SFN.

METHODS: We co-stained skin biopsy specimens from patients with anti-PGP 9.5 antibodies (a marker of intraepidermal nerve fibers) and anti-phospho-alpha-synuclein antibodies and then viewed the specimens under a fluorescent light microscope.

RESULTS: We found no evidence of alpha-synuclein deposition in either idiopathic or symptomatic SFN.

SUMMARY/CONCLUSION: Alpha-synuclein deposition is not a common underlying cause of idiopathic SFN nor a pathologic accompaniment of symptomatic SFN.

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LONG-TERM EFFICACY AND SAFETY OF EFGARTIGIMOD PH20 SC IN ANTI-ACETYLCHOLINE RECEPTOR AUTOANTIBODY SERONEGATIVE PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: INTERIM ANALYSIS OF THE ADAPT-SC+ STUDY

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INTRODUCTION: Efgartigimod is a human immunoglobulin G (IgG)1 antibody Fc-fragment that reduces IgG levels (including pathogenic autoantibodies) through neonatal Fc receptor blockade. Patients with anti-acetylcholine receptor antibody-negative (AChR-Ab-) generalized myasthenia gravis (gMG), comprising 15%-20% of the gMG population, were included in the ADAPT-SC+ open-label study to receive subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20).

OBJECTIVE: To evaluate efficacy and safety of efgartigimod in AChR-Ab- patients with gMG enrolled in ADAPT-SC+.

METHODS: One hundred seventy-eight participants rolled over from ADAPT-SC (n=105) and ADAPT+ (n=73). Of the 164 receiving ≥1 dose of efgartigimod PH20 SC in ADAPT-SC+ through March 2022, 30 were AChR-Ab- (median[range] follow-up in AChR-Ab-: 204[84-311] days).

RESULTS: AChR-Ab- patients demonstrated improvements in mean (SE) change from study baseline in Myasthenia Gravis Activities of Daily Living (MG-ADL; -3.6 [0.53]) and Myasthenia Gravis Quality of Life 15-item Questionnaire, Revised (MG-QoL 15r; -3.3 [0.80]) scores at week 4 of cycle 1. Both results were consistent with those observed in AChR-Ab+ patients (MG-ADL, -4.1 [0.29]; MG-QoI15r, -5.2 [0.47]). Consistent improvements in MG-ADL and MG-QoL15r occurred through 4 cycles, regardless of serostatus. Overall, 76.2% of participants had ≥1 adverse event (AE), which were mostly mild/moderate. Frequently reported AEs included injection site erythema, headache, and COVID-19. Injection site reactions were mild/moderate, did not lead to treatment discontinuation, and decreased in incidence with subsequent cycles.

SUMMARY/CONCLUSION: Long-term treatment with efgartigimod PH20 SC was associated with consistent and repeatable improvements in MG-ADL and MG-QoL15r scores in AChR-Ab- patients in ADAPT-SC+ and was well tolerated.

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Ratna Bhavaraju-Sanka - Consultant to argenx BV, Alexion Pharmaceuticals, and PTC Therapeutics Inc

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LONG-TERM SAFETY, TOLERABILITY, AND EFFICACY OF EFGARTIGIMOD IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: CONCLUDING ANALYSES FROM THE ADAPT+ STUDY

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INTRODUCTION: Efgartigimod is a human IgG1 antibody Fc-fragment that reduces total and pathogenic IgG autoantibody levels through neonatal Fc receptor blockade. ADAPT was a 26-week, global, multicenter, randomized, placebo-controlled, phase 3 trial evaluating efgartigimod in patients with generalized myasthenia gravis (gMG). Patients who completed ADAPT could enroll in the ADAPT+ open-label extension study.

OBJECTIVE: To evaluate long-term safety and efficacy of efgartigimod in patients with gMG.

METHODS: Efgartigimod (10 mg/kg IV) was administered in cycles of 4 weekly infusions, with subsequent cycles initiated based on clinical evaluation. Efficacy was assessed using Myasthenia Gravis Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) scores.

RESULTS: Of 167 patients from ADAPT, 151 (90%) entered ADAPT+, and 145 received ≥1 cycle as of January 2022. With 217.5 patient-years of follow-up (mean duration per patient: 548 days), the most common adverse events (AEs; mostly mild or moderate) were headache (25%), COVID-19 infection (15%), nasopharyngitis (14%), and diarrhea (10%). These AEs did not increase in frequency with subsequent cycles. AChR-Ab+ patients (ADAPT/ADAPT+ primary endpoint population) with ≥1 year of follow-up across ADAPT/ADAPT+ (n=95) received a median (range) 5.0 (0.4–7.6) cycles per year. AChR-Ab+ patients (n=111) demonstrated consistent improvements (mean change [SE], week 3 of cycle 1) in MG-ADL (-5.0 [0.33]; repeated up to 14 cycles) and QMG (-4.7 [0.41]; repeated up to 7 cycles) scores.

SUMMARY/CONCLUSION: These ADAPT+ analyses suggest long-term efgartigimod treatment is well tolerated and results in consistent and repeatable reductions in clinical outcomes (MG-ADL and QMG) in patients with gMG.

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TREATMENT OUTCOMES IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS TREATED WITH ECULIZUMAB AND RAVULIZUMAB: A CASE SERIES

Andrew Gordon (Libertyville, IL)

INTRODUCTION: Acetylcholine receptor antibody-positive generalized myasthenia gravis (AChR+ gMG) is an autoimmune disease of the neuromuscular junction that causes generalized muscle weakness. C5 inhibitors (C5i), eculizumab and ravulizumab, are indicated for treating patients with AChR+ gMG. We report real-world outcomes for patients who initiated ravulizumab with or without prior eculizumab treatment.

CASE REPORT: We report outcomes for 11 patients (median age, 65 years) with AChR+ gMG who initiated eculizumab (n=5), 3 of which transitioned from eculizumab to ravulizumab, or were C5i-naïve and initiated ravulizumab (n=6). Prior to initiation of eculizumab or ravulizumab, patients had a median MG Activities of Daily Living (MG-ADL) score of 8 or 9 (range 7 -9; 7-15), respectively. Patients who initiated eculizumab or ravulizumab demonstrated a comparable rapid and sustained reduction in MG-ADL scores (median change: -7 and -7.5, respectively). Myasthenia Gravis Foundation of America post-intervention status improved to class 1 for most (10 of 11) patients. Eculizumab and ravulizumab were generally well-tolerated and safe, with only mild adverse events (AEs) reported. Eculizumab to ravulizumab transition patients maintained efficacy (median MG-ADL score pre- and post-switch: zero) and transition-associated AEs were not observed. The majority of patients tapered corticosteroids within a year of initiating eculizumab (4 of 5) or ravulizumab (4 of 6) therapy. Eculizumab patients (4 of 5) discontinued corticosteroids within an average of 2.11 years.

SUMMARY: The initiation of eculizumab or ravulizumab therapy (including in C5i-naïve or patients transitioned from eculizumab) showed comparable efficacy and safety resulting in sustained disease control in gMG patients while allowing tapering of concomitant corticosteroids.

Disclosures:

Andrew Gordon - Consulting and speaking fees for Alexion; participation in the Registry

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PHARYNGEAL-CERVICAL-BRACHIAL VARIANT OF GUILLAIN-BARRE SYNDROME IN A MIDDLE-AGED PATIENT: A CASE REPORT IN CHÍA, CUNDINAMARCA

Claudia Peña (Bogota, Colombia), Sergio Andres Gonzalez Arteaga (Bogota, Colombia)

INTRODUCTION/BACKGROUND: Guillain-Barre syndrome (GBS) is an acute progressive autoimmune polyradiculoneuropathy. It has an infectious preceding event leading to a hyperactive autoimmune response from the immune system against the myelin coating of neurons in motor nerves. The pharyngeal-cervical-brachial (PCB) variant of GBS involves the neck, upper limb, and oropharyngeal muscles. We present a case of a man in middle age with present PCB variant of GBS.

CASE REPORT: A 49-year-old man, with background gastric cancer, was treated with gastrectomy and chemotherapy in August 2020. In July 2022, after 15 days of high respiratory symptoms, he had upper limb weakness, progressive and continuous dysarthria, and dysphagia to solids. Subsequently, the patient presented paresthesia and weakness in the upper and lower extremities. At the neurological examination, cranial nerve evaluation revealed lower pairs compromised, symmetric upper limb weakness predominant in proximal and distal muscles, upper limb normoreflexia with lower limb hyporeflexia, with an altered gait. Study of the peripheral nerves showed severe motor neuropathy of the upper limbs. Sensory studies were normal. The F-waves study with absent reproducibility. According to clinical and neurophysiological findings, PCB variant of GBS was diagnosed.

SUMMARY/CONCLUSION: PCB variant of GBS has several differential diagnoses, and due to its rapid course and high fatality rate, a high clinical suspicion is needed in framing the diagnosis. Knowledge about how a case may be presented in a clinical setting is important for timely management. This report shows that a rehabilitation program is essential to improve prognosis and functional outcomes.

PHASE 3B EXTENSION STUDY EVALUATING SUPERIORITY OF DAILY VS APPROVED ON/OFF ORAL EDARAVONE DOSING IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

Jeffrey Rothstein (Baltimore, MD), Shari De Silva (Rogers, AR), Lorne Zinman (Toronto, Canada), Marvin Chum (Hamilton, Canada), Adriano Chio (Torino, Italy), Albert C. Ludolph (Ulm, Germany), Gen Sobue (Nagoya, Japan), Manabu Doyu (Nagakute, Japan), Daniel Selness (Jersey City, NJ), Vesna Todorovic (London, United Kingdom), Manabu Hirai (Tokyo, Japan), Takahashi Fumihiro (Tokyo, Japan), Art Wamil (Jersey City, NJ), Stephen Apple (Jersey City, NJ)

INTRODUCTION: IV edaravone (Radicava®/Radicut) was shown to slow the rate of physical functional decline in ALS. This ongoing, multicenter, phase 3b, double-blind, parallel group, randomized extension study is evaluating 2 dosing regimens of Radicava ORS® (edaravone) oral suspension. Oral edaravone was approved by the US FDA for use in patients with ALS in May 2022 and gained approval in late 2022 in Canada and Japan.

OBJECTIVE: Study MT-1186-A04 (NCT05151471) is evaluating and comparing the long-term safety, efficacy, and tolerability of 2 oral edaravone dosing regimens for up to an additional 48 weeks following the end of Study MT-1186-A02 in patients with ALS, comprising a total duration of up to 96 weeks.

METHODS: Study MT-1186-A04 will evaluate 2 dosing regimens of oral edaravone (105-mg dose). Group 1 will have oral edaravone administered once daily for each 28-day cycle. Group 2 will have oral edaravone administered for 10 days followed by placebo for 18 days in each 28-day cycle. Dosing in both groups will continue up to 48 weeks. Study MT-1186-A04 is anticipated to include approximately 300 adult patients who have completed Study MT-1186-A02. The primary objective is to evaluate the efficacy of each dosing regimen based on the randomization date in Study MT-1186-A02 to at least a 12-point Revised ALS Functional Rating Score decrease or death, whichever happens first, over the course of the study.

RESULTS: Ongoing.

SUMMARY/CONCLUSION: This extension study will provide important information on the safety, efficacy, and tolerability of 2 oral edaravone dosing regimens in patients with ALS.

Sponsored by MTPA

Disclosures:

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DYNAMIC CONTRAST-ENHANCED MAGNETIC RESONANCE IMAGING MAY IDENTIFY PATIENTS WITH INFLAMMATORY NEUROPATHIES

Edrich Rodrigues (Melbourne, Australia), Meng Law (Melbourne, Australia), Elspeth Hutton (Melbourne, Australia)

INTRODUCTION: Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) has shown promise in assessment of peripheral neuropathies.

OBJECTIVE: The aim of this study was to use DCE-MRI to obtain perfusion parameters, including the plasma to extravascular volume transfer (Ktrans) and the extravascular fluid volume (Ve) in patients with inflammatory neuropathies and controls.

METHODS: We recruited patients who presented with Guillain-Barre syndrome (GBS) or active chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) (new diagnosis or relapse) for this study between 2019 and 2022. Patients with genetic neuropathies and patients who were undergoing routine MRI scans post lumbar discectomy formed the control group. 3T-MRI examinations of the lumbo-sacral spine were carried out on participants including T1-weighted DCE volume interpolated breath-hold (VIBE) sequences with gadolinium-based contrast agents. Ktrans and Ve maps for motor nerve roots (MR), sensory roots (SR), dorsal root ganglion (DRG), and mixed spinal nerves (MSN) were generated using the Tofts model. We calculated the ratio of the Ktrans of the MSN to that of the MR and similarly that of the SR to the DRG at the L4, L5, and S1 roots bilaterally. A linear mixed model analysis was used to compare differences between the 2 groups.

RESULTS: We analyzed 32 nerve segments from controls (n=7) and 43 nerve segments from patients with GBS/CIDP (n=11). The Ktrans ratio for both motor and sensory roots was higher in the patients with inflammatory neuropathies than controls ($p<0.05$).

SUMMARY/CONCLUSION: DCE-MRI of proximal nerve roots may help complement other modalities in the diagnosis of inflammatory neuropathies.

MAGNETIC RESONANCE NEUROGRAPHY OF SUPRASCAPULAR NEUROPATHY

Yu Jin Im (Seoul, Korea, South), Duk Hyun Sung (Seoul, Korea, South)

INTRODUCTION: Isolated suprascapular neuropathy (SSN) has been considered as entrapment neuropathy at suprascapular (SS) or spinoglenoid (SG) notch, especially in field of peripheral neurosurgery. Evolving in image technique, hourglass-like constriction (HGC) neuropathy is recognized in recent years and HGC in isolated SSN have been reported.

OBJECTIVE: To describe the clinical and imaging features of the intrinsic suprascapular neuropathy.

METHODS: We retrospectively reviewed 18 patients diagnosed with intrinsic SSN based on the MRI or electrophysiologic study. The etiology was classified as intrinsic when no compressive lesion was obvious along the course of the SS nerve on MRI.

RESULTS: The chief complaints of 18 patients (average age 46.2) for visiting outpatient clinic were weakness or atrophy (61.1%) rather than pain (38.9%). In electromyography, 6 patients showed additional HGC neuropathy in other regions of the upper extremity. Brachial plexus (BP) or shoulder MRI demonstrated HGC of SS nerve in 12 patients and number of constrictions were 1-3. In all except 1, HGC of SSN was located between the issuing point from the upper trunk of BP and SS notch. Sixteen of 18 intrinsic SSN patients received conservative management. Twelve patients (70.6%) showed favorable outcomes of motor weakness. Four patients had no recovery but 2 of them had only 2 months of follow-up.

SUMMARY/CONCLUSION: Clinicians should consider HGC neuropathy as a possible cause of SSN. BP MRI should be performed to confirm the HGC in patients with SSN. Patients in our study showed spontaneous recovery with non-operative management. Thus, SS notch release should be reconsidered when an external mechanical problem is absent in MRI.

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DELAYED DIAGNOSIS AMONGST GENERALIZED MYASTENIA GRAVIS PATIENTS: RESULTS FROM A EUROPEAN REAL-WORLD STUDY

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INTRODUCTION: Generalized myasthenia gravis (gMG) is a chronic, neuromuscular disease with symptoms often mistaken for a range of other disorders, complicating diagnosis. A timely diagnosis is important to manage gMG, reduce patient anxiety, improve patient quality of life, and avoid unnecessary healthcare resource use.

METHODS: The Adelphi MG Disease Specific Programme collected cross-sectional data from physicians and their gMG patients across France, Germany, Italy, Spain, and the UK between March-September 2020. Physicians reported patient demographics, diagnostic pathway, and perception of disease impact. Patients voluntarily completed a follow-up form, including the MG-QoL-15r.

RESULTS: One hundred ninety-one physicians provided data for 387 gMG patients with a diagnosis date. Mean age was 52.5 (SD±15.69), mean time from diagnosis to survey was 4.2 years (SD±5.66, Table 1) and 53.9% were female. Mean time from symptom onset to gMG diagnosis was 1.0 years (SD±1.43). One hundred and five patients (27.1%) received a gMG diagnosis more than a year after onset of symptoms. At survey, these patients were more likely to experience moderate/high fatigue (78.1%) and anxiety (75.2%) than those diagnosed within a year (64.7% and 56.2% respectively). One hundred and seventeen patients completed the MG-QoL-15r. Those with delayed diagnoses (n=43) had higher impairment (14.4; SD±5.50) than those diagnosed within a year (12.6; SD±7.84).

CONCLUSION: Physicians reported patients with diagnoses longer than a year experienced more fatigue, anxiety, and prolonged burden on health-related quality of life, leading to unnecessary health care resource utilization in gMG patients. These findings underscore the importance of timely diagnoses of gMG and the need to properly educate all stakeholders.

Disclosures:
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Charlotte Gary - Employee of Janssen-Cilag EMEA
Wim Noel - Employee of Janssen-Cilag EMEA
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CHANGING PRIORITIES AMONG PHYSICIAN REPORTED REASONS FOR CHOICE OF PHARMACOLOGICAL GENERALIZED MYASTHENIA GRAVIS TREATMENTS ACROSS 5 EUROPEAN COUNTRIES

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INTRODUCTION: Generalized myasthenia gravis (gMG) is a chronic, neuromuscular condition. A range of pharmacological treatments are currently prescribed, typically acetylcholinesterase inhibitors (AChEIs), corticosteroids, and non-steroidal immunosuppressants (NS-ISTs).

METHODS: The Adelphi MG Disease Specific Programme collected cross-sectional data from physicians and their patients with gMG across France, Germany, Italy, Spain, and the UK between March-September 2020. Physicians reported treatment history and reasons for treatment selection from a list of 46 preselected options. Reasons were grouped into 5 categories of symptom control, administration, safety, suitability, and general.

RESULTS: One hundred forty-four physicians reported current and historic reasons for choice of maintenance/chronic treatment for 529 gMG patients. Mean age was 54.0 (SD±15.43), 51.0% were female, and average time from diagnosis to survey was 4.1 years (SD±5.27). Control reasons were most frequently selected at first line (99.6%), administration at second line (69.7%), and safety (80.0%), suitability (83.6%), and general (87.3%) at third line or later. Across all lines of treatment, AChEIs were most frequently prescribed (82.0%), followed by corticosteroids (53.3%), NS-ISTs (50.5%), IVIg/ScIg/PLEx (14.7%), and biologics (13.6%). Across treatment categories, control was selected most frequently for AChEIs (97.9%). Administration (68.9%) and safety (73.4%) were selected most frequently for NS-ISTs. Suitability (68.1%) and general (88.9%) were selected most frequently for biologics.

CONCLUSION: These results highlight changing priorities as patients progressed through lines of therapy. Symptom control drove initial treatment choice and AChEI utilization. Administration, safety, and suitability were drivers amongst later lines. Safety and convenience concerns indicate efficacious and safe long-term treatment is required to achieve sustained gMG symptom control.

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SPINAL ACCESSORY NEUROPATHY FROM DELAYED RADIATION INJURY AND SECONDARY BRACHIAL PLEXOPATHY FROM SHOULDER DROOP

Christina Chrisman (Phoenix, AZ), Robin McFarlane (Mesa, AZ)

INTRODUCTION/BACKGROUND: We present a case of delayed radiation injury spinal accessory neuropathy with secondary brachial plexopathy from shoulder droop.

CASE REPORT: The patient is a 60-year-old male presenting with right shoulder weakness and atrophy in the context of repeated lifting and arm extension. He noted right trapezius atrophy and the shoulder rolled forward. Abduction of the right arm beyond 90 degrees was difficult and resulted in radiation of numbness and pain down the arm. He had a history of stage IV squamous cell carcinoma of the right tongue base with metastasis to the neck, resected with lymph nodes and followed by radiation treatment 13 years before presentation. On examination, strength was 4 out of 5 with right shoulder shrug and head turn to the left, otherwise intact. There was atrophy of the right sternocleidomastoid, trapezius, rhomboids, levator scapulae, and serratus anterior. He was unable to abduct his right arm above 90 degrees. Right lateral scapular winging was noted. Reflexes, sensation, and coordination were intact. NCS/EMG revealed right spinal accessory neuropathy with active denervation and fasciculation potentials plus proximal right upper trunk brachial plexopathy. MRI confirmed a brachial plexitis but was negative for malignancy. The patient was sent to physical therapy with treatment aimed at correcting shoulder droop.

SUMMARY/CONCLUSION: Delayed radiation injury to the spinal accessory nerve is an important complication of head and neck cancer which can occur decades later. The presence of fasciculations on EMG points toward radiation injury rather than malignancy. Secondary brachial plexopathy can occur as a complication of drooped shoulder.

GAMMAGARD LIQUID FOR THE TREATMENT OF RELAPSE IN CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY

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INTRODUCTION: GAMMAGARD LIQUID (GGL) is an IVIg 10% therapy.

OBJECTIVE: To evaluate GGL efficacy and safety in patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) who relapsed during facilitated subcutaneous immunoglobulin (fSCIG) 10% or placebo treatment.

METHODS: ADVANCE-CIDP 1 (phase 3, randomized, placebo-controlled study assessing fSCIG 10% efficacy and safety; NCT02549170) comprised 2 epochs. In open-label Epoch-2, eligible adults had confirmed CIDP relapse (≥1-point increase in adjusted Inflammatory Neuropathy Cause and Treatment [INCAT] disability scores from pretreatment baseline) during Epoch-1. Patients received loading GGL doses (2g/kg) then maintenance infusions for 6 months. Outcomes included change in responder rate (patient proportion with ≥1-point decrease in adjusted INCAT score) and clinically meaningful improvement in functional ability (≥1-point decrease in adjusted INCAT scores, ≥8kPa increase in grip strength or ≥4-point increase in Rasch-built overall disability scale scores) from pre-GGL baseline to study completion, and time to functional improvement (≥1-point decrease in adjusted INCAT scores versus pre-GGL baseline). Treatment-emergent adverse events (TEAEs) were also assessed.

RESULTS: Twenty patients (mean age 50.9 years, 45.0% male) received GGL. Responder rate (95% CI) was 95.0% (83.2–100.0%). All patients achieved clinically meaningful functional improvement. Mean change in adjusted INCAT scores was -2.0 points and median time to functional improvement was 25 days. Fourteen patients (70.0%) experienced TEAEs; no serious TEAEs or deaths were reported.

SUMMARY/CONCLUSION: GGL effectively treated CIDP relapse, improving functional ability with a favorable safety profile.

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Todd Levine - Consultant for Alexion, FFF, and Immunovant

Vera Bril - Consultant for Grifols, CSL Behring, UCB Pharma, argenx, Takeda, Alnylam Pharmaceuticals, Octapharma, Pfizer, Powell Mansfield Inc., Akcea, Ionis Pharmaceuticals, Immunovant, Sanofi, Momenta (J&J), Roche, Janssen, AstraZeneca-Alexion, and NovoNordisk; received research support from AstraZeneca-Alexion, Grifols, CSL Behring, UCB Pharma, argenx, Takeda, Octapharma, Akcea, Momenta (J&J), Immunovant, and Ionis

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Konrad Rejdak - Received speaking honoraria and travel expenses for participation in scientific meetings, and participated in advisory boards for Bayer, Biogen, Merck, Novartis, Roche, Sanofi-Genzyme, and Teva Pharmaceuticals

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MECHANICALLY INDUCED SOMATOSENSORY EVOKED POTENTIALS: GENUINE ELECTROPHYSIOLOGICAL RESPONSES OR MOVEMENT ARTIFACTS?

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INTRODUCTION: It is uncertain whether mechanically induced long latency somatosensory evoked potentials (MLLSEP) are genuine electrophysiological responses or artifacts.

OBJECTIVE: To determine if MLLSEP are genuine electrophysiological responses or artifacts related to the mechanical stimulation.

METHODS: LLSEP were recorded in 10 healthy subjects (mean age: 33 years old) in response to the percussion of the second finger with a reflex hammer synchronized with the EMG machine and the electrical stimulation of the second finger. We compared the features of mechanically and electrically induced LLSEP; the features of LLSEP recorded at 3 different body regions (wrist, shoulder, face and scalp (Cz-A1+A2); and the influence of intensity (low, middle, high) and frequency (0.2, 0.1, 0.04 Hz) of mechanical stimulation on the amplitude of LLSEP.

RESULTS: The LLSEP induced by mechanical and electrical stimulation showed similar scalp distribution, morphology, and amplitude (24.03±10.3 μV vs 25.55±12.5 μV, p=0.32). LLSEP induced by mechanical stimulation were recorded only from Cz-A1+A2. No electrical responses were recorded at wrist, shoulder or face sites. The amplitude of mechanically induced LLSEP was not significantly affected by increasing the intensity (low: 21.96±5.1, middle: 20.89±4.3, high: 22.04±5.9 p=0.47) or the frequency (0.2Hz: 19.83±2.84, 0.1Hz: 21.57±7.5, 0.04Hz: 19.05±8.5, p=0.17) of the stimulation.

SUMMARY/CONCLUSION: The similarity between electrical and mechanical LLSEP, the lack of responses at subcortical recording sites closer to the site of stimulation, and the consistency of MLLSEP responses with manipulation of intensity and frequency all support the hypothesis that MLLSEP are less likely to be artifactual and more likely to be bona fide electrophysiological responses.

REAL-WORLD EXPERIENCE WITH ECULIZUMAB IN PATIENTS WITH MYASTHENIA GRAVIS IN JAPAN: ANALYSIS OF 2-YEAR POST-MARKETING SURVEILLANCE DATA

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INTRODUCTION: The terminal complement C5 inhibitor eculizumab is approved in Japan for treatment of adults with anti-acetylcholine receptor antibody-positive (AChRAb+) generalized myasthenia gravis (gMG) whose symptoms are difficult to control with high-dose IVIg therapy or plasma exchange.

OBJECTIVE: To assess the effectiveness and safety of eculizumab in adults with gMG in Japan.

METHODS: In this interim analysis of post-marketing surveillance data, clinically meaningful response (≥3-point reduction in Myasthenia Gravis-Activities of Daily Living total score vs baseline) was evaluated at timepoints up to 104 weeks after eculizumab initiation in the analysis population overall and by a wide range of patient and disease characteristics. Oral corticosteroid use was assessed. Safety was evaluated by recording adverse events.

RESULTS: Data were available for 231 patients; the effectiveness analysis set comprised 223 patients. For patients with both baseline and follow-up data, 99/172 (57.6%), 104/167 (62.3%), 70/108 (64.8%), and 43/61 (70.5%) achieved clinically meaningful response at 12, 26, 52, and 104 weeks, respectively, after eculizumab initiation. Responder rates were similar and maintained through 104 weeks across the analyzed subgroups. In patients receiving oral corticosteroids there was a trend towards reduced corticosteroid use and an increased proportion receiving ≤5 mg/day with continued eculizumab treatment. No new safety signals were observed.

SUMMARY/CONCLUSION: The 2-year analysis findings align with previous real-world data, demonstrating eculizumab's sustained effectiveness and consistent safety profile in adults with AChRAb+ gMG, regardless of patient or disease characteristics. The observed reduction in concomitant oral corticosteroid use, also consistent with other real-world experiences, underscores the benefit of C5 inhibition in these patients.

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ROLE OF TGF-1B GENE POLYMORPHISMS IN THE PATHOGENESIS OF CARPAL TUNNEL SYNDROME IN EGYPTIAN PATIENTS

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INTRODUCTION: Carpal tunnel syndrome (CTS) is a common entrapment neuropathy involving the median nerve. Fibrosis is a hallmark of the pathogenesis of CTS, where transforming growth factor beta 1 (TGF-1β) is thought to play a role in initiating and maintaining the profibrotic pathway.

OBJECTIVE: In this study, we aimed to investigate the role of TGF-1β gene polymorphisms in the development of CTS in Egyptian patients.

METHODS: We evaluated 3 TGF-1β single nucleotide polymorphisms (SNPs), in addition to measuring serum TGF-1β levels in 100 CTS patients diagnosed by electrodiagnosis and 100 healthy controls. TGF-1β SNPs were determined by TaqMan genotyping assay, and serum TGF-1β levels were measured using enzyme linked immunosorbent assay (ELISA).

RESULTS: Serum TGF-1β levels increased significantly and were strongly correlated with development of CTS. The C allele of +915G/C, the T allele of -509C/T, and the G allele of -800G/A occurred more frequently in CTS patients than in healthy controls.

SUMMARY/CONCLUSION: TGF-1β and its SNPs were found to be significantly higher among CTS patients compared to healthy controls, and thus seem to play a role in the development and pathogenesis of CTS.

CLINICAL PROFILE OF MOTOR NEURON DISEASE IN A CENTRAL AMERICAN POPULATION

Sara Loanny Flores Lazo (San Salvador, El Salvador)

INTRODUCTION: The clinical-epidemiological characteristics of motor neuron diseases and their different presentations have been studied in different regions of the world, except Central America, where they have been poorly described. Therefore, we aimed to characterize the clinical profile of the disease in a Salvadoran population.

OBJECTIVE: To identify the clinical profile and accompanying morbid characteristics of motor neuron disease in the Salvadoran population.

METHODS: In this retrospective study, the medical records of patients diagnosed with motor neuron disease were reviewed from a reference center of a third-level hospital in El Salvador from 2015 to 2023. Absolute frequencies of the demographic, clinical, and paraclinical characteristics were calculated.

RESULTS: A total of 56 patients were included, of whom 98% were diagnosed with amyotrophic lateral sclerosis (ALS) and the remaining 2% had multifocal motor neuropathy and primary lateral sclerosis. The mean age at symptom onset was 41.3 years, with a slight predominance of females. Of the 54 patients with ALS, 64.81% had spinal onset and 35.19% had bulbar onset. The mean time from diagnosis to ventilatory support was 22 ± 11 months for bulbar-onset patients and 48 ± 24 months for spinal-onset patients. The mean time from diagnosis to gastrostomy for bulbar onset was 14 ± 8 months.

SUMMARY/CONCLUSION: Salvadoran patients with ALS have a younger age of onset, rapid progression to disability, and assistance dependency. To the best of our knowledge, this is the first study to be conducted in Central America. Therefore, this study contributes to our understanding of the clinical profile of MND/ALS in this region.

ULTRASONOGRAPHIC DIAGNOSIS IN ACUTE SEGMENTAL HERPES ZOSTER PARESIS

Sang Beom Kim (Seoul, Korea, South), Bum Chun Suh (Seoul, Korea, South), Hongmin Ha (Seoul, Korea, South)

INTRODUCTION/BACKGROUND: Segmental herpes zoster (HZ) paresis is characterized by focal, asymmetric motor weakness in the myotome that often do not correspond to the dermatomes affected by the rash. We report a case of upper limb paralysis following HZ infection with ultrasonographic findings.

CASE REPORT: An 81-year-old woman presented with right arm weakness and pain starting after rash on the right arm and shoulder surface. Neurologic examination showed right shoulder flexion/abduction and elbow flexion weakness (MRC III). NCS showed right antebrachial cutaneous, musculocutaneous, and axillary neuropathies. These clinical and neurophysiological findings suggested the suspicion of right C5-6 radiculoplexopathy due to reactivation of HZ virus. Ultrasound (US) study of musculocutaneous, axillary, and suprascapular nerves with cervical roots (C5-6) was performed 2 weeks after the onset. The cross-sectional areas (CSA) of right musculocutaneous, axillary, and suprascapular nerves with cervical roots were significantly larger than left. She was treated with IV steroid with antiviral. We followed the patient 1 month after onset of motor weakness; she was able to flex the elbow actively and abduct the shoulder about 90 degrees, unlike before. In the serial ultrasound study, CSA of right musculocutaneous and axillary nerves decreased from the previous study, but the CSA of the suprascapular nerve remained larger than the left side.

SUMMARY/CONCLUSION: This case report suggests that HZ causes ganglionic or nerve degeneration with initial demyelination resulting in “nerve hypertrophy”. Ultrasonographic diagnosis allows direct observation of nerve damages in acute segmental HZ paresis. Serial ultrasonography may be helpful to predict an improvement earlier than electrophysiological study.

DIAGNOSTIC UTILITY OF NERVE ULTRASONOGRAPHY ON ULNAR NEUROPATHY AT ELBOW WITH NORMAL ELECTRODIAGNOSTIC FINDINGS

Sang Beom Kim (Seoul, Korea, South), Hongmin Ha (Seoul, Korea, South), Bum Chun Suh (Seoul, Korea, South)

INTRODUCTION: Ulnar neuropathy at elbow (UNE) is the second most common entrapment neuropathy. Traditionally, it has been diagnosed by clinical features and electrodiagnostic study (EDX). However, even in patients with clear clinical symptoms, EDX results in unremarkable findings. Recently, high-resolution ultrasonography (US) emerged as an accurate and complementary diagnostic tool for peripheral neuropathy.

OBJECTIVE: The aim of this study is to show that ultrasound can reveal abnormal nerve swelling in patients with UNE with normal EDX findings.

METHODS: A retrospective chart review was performed of 94 patients with suspected UNE between May 2011 and June 2022. The control group of 60 adults without typical UNE symptoms was recruited. All patients underwent US and EDX on both arms. We measured the cross-sectional area (CSA) of ulnar nerve at predetermined sites of arm and elbow. Lesion localizations obtained by US and EDX were compared. Statistical analyses were performed.

RESULTS: Fifty-one clinically suspected UNE patients (54%) displayed abnormal results on both EDX and US. Twenty-nine patients (30%) had abnormal findings on US but normal results on EDX. Four patients (4%) had abnormal findings on EDX and normal on US. Ten patients (10%) had no abnormalities in both tests. Diagnostic sensitivity of US was 85%, compared with 58% of EDX. Specificity of US study was 86% and of EDX 94%.

SUMMARY/CONCLUSION: This study showed the ability of US to provide useful diagnostic information in UNE patients with normal EDX results. US is thought to play an important role in detecting neuropathology that was not revealed by EDX.

UNILATERAL AND BILATERAL CARPAL TUNNEL SYNDROME

Sasha Zivkovic (New Haven, CT)

INTRODUCTION: Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy and affects 4-8% of the general population. Increased prevalence is found during pregnancy, in professions involving manual work, and with polyneuropathies and various multisystemic disorders including amyloidosis. Predictive factors for bilateral CTS have not been established.

OBJECTIVE: To characterize demographic features, comorbidities, and electrodiagnostic findings in patients with unilateral and bilateral CTS.

METHODS: Retrospective chart review of electrodiagnostically confirmed CTS cases.

RESULTS: There were 71 patients with bilateral CTS and 15 with unilateral CTS. Patients with bilateral CTS were 62% women with an average age of 58.27 years and with average BMI of 32.01, including 10 patients with diabetes, 11 with impaired glucose tolerance, and 12 with hypothyroidism. Patients with unilateral CTS were 53% women with an average age of 55.73 years and average BMI of 29.80, including 2 patients with diabetes, 2 with impaired glucose tolerance, and 1 with hypothyroidism. Electrodiagnostic testing of patients with unilateral and bilateral CTS also revealed ulnar neuropathies in 1 and 14 patients and polyneuropathy in 2 and 12 patients, respectively.

SUMMARY/CONCLUSION: The study showed similar demographic characteristics, comorbidities, and additional electrodiagnostic findings in patients with unilateral and bilateral carpal tunnel syndrome. There were no distinguishing features between the 2 groups and bilateral CTS was 4.7-fold more frequent than unilateral CTS, as previously described by other authors. Larger studies are needed to characterize the risk factors for unilateral and bilateral CTS.

PATIENT EXPERIENCE WITH ACUTE HEPATIC PORPHYRIA BEFORE AND AFTER LONG-TERM GIVOSIRAN TREATMENT: A QUALITATIVE INTERVIEW STUDY

Hetanshi Naik (Stanford, CA), T. Michelle Brown (Research Triangle Park, NC), Stephen Meninger (Cambridge, MA), Stephen Lombardelli (Maidenhead, United Kingdom)

INTRODUCTION: Acute hepatic porphyria (AHP) is associated with accumulation of neurotoxic heme intermediates and acute neurovisceral attacks. In phase 1/2 (NCT02949830) and phase 3 (ENVISION; NCT03338816) studies, givosiran treatment led to sustained improvement in annualized attack rate and other measures.

OBJECTIVE: To explore long-term treatment outcomes.

METHODS: Patients with AHP (US, Spain, UK) continuing givosiran after completing open-label extension periods of phase 1/2 or ENVISION studies participated in 1-hour, semistructured, qualitative telephone interviews. Thematic analysis was conducted.

RESULTS: There were 21 interviewees (86% female; mean [range] age, 39.3 [25–61] years; mean [standard deviation] duration of givosiran treatment, 51.8 [7.9] months). Describing their prestudy (prior to phase 1/2 or ENVISION) experience, interviewees reported AHP symptoms in multiple domains, particularly abdominal pain and fatigue (95% for both). AHP symptoms were wide ranging, affecting work/school (100%), family and intimate relationships (95%), and other domains. Most interviewees (90%) had used opioids prestudy. Posttreatment, interviewees reported improvement in symptoms (including pain [100%]) and impacts (particularly family and intimate relationships [95%] and work/school [91%]). Most described their attacks as gone (62%) or less frequent/severe (33%). Among 17 interviewees who took opioids, 59% stopped opioids and 24% used a lower dose. Pain alleviation was most frequently the most important posttreatment improvement (43%). Symptoms still present (but less severe) included muscle weakness and paralysis, fatigue, and neuropathic pain and paresthesia. All interviewees (100%) were “very satisfied” with givosiran treatment.

SUMMARY/CONCLUSION: Results of these qualitative interviews improve understanding of the burden of AHP. Interviewees reported meaningful improvements with continuing givosiran treatment.

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Stephen Meninger - Employed by and owns stock and stock options in Alnylam Pharmaceuticals

Stephen Lombardelli - Employed by and owns stock and stock options in Alnylam Pharmaceuticals

HIRAYAMA DISEASE: A ELECTROPHYSIO-RADIOLOGICAL DOCUMENTARY

Mrinal Acharya (Kharagpur, India)

INTRODUCTION: Hirayama disease (HD), caused by focal ischemic damage to lower cervical AHC, typically affects young men manifesting as unilateral distal upper limb (UL) weakness and atrophy without sensory or pyramidal signs and is initially progressive but eventually becomes non-progressive over time.

OBJECTIVE: To assess the radiological and electrophysiological features of clinically suspected cases of Hirayama disease.

METHODS: We conducted a retrospective analysis on the electrophysiological (bilateral UL-NCS/EMG) studies and dynamic pre- and post-contrast cervicodorsal MRI of 60 cases suspected of Hirayama disease.

RESULTS: Out of the 60 patients, 58 were male. The mean age of the patients was 18.7 (±3.9) years. All suspected HD cases showed lower cervical cord atrophy. However, abnormal cervical curvature (65%), asymmetric cord flattening (80%), anterior shifting of the posterior wall of the cervical dural canal (83%), epidural flow void, and enhancement (97%) were inconsistently observed. Furthermore, some cases also revealed a thoracic extension of epidural enhancement. Reduced compound muscle action potential (CMAP) (< 5mv) was detected in the ulnar (86%) and median (22%) nerve during NCS. Ulnar and median nerve mean amplitude was 3.1 (±2.4) mv and 7.8 (±3.2) mv, respectively. Conduction velocities and sensory studies were normal in all patients. We found variability in the distal and F-wave latencies. Ninety percent of patients show ≤0.6 ulnar/median (U/M) CMAP amplitude ratio. EMG shows evidence of neurogenic changes in ADM and FDI in 96% of patients and there was bilateral involvement in 68% of cases.

SUMMARY/CONCLUSION: Though predominantly unilateral, asymmetric bilateral neurogenic involvement can be commonly found in Hirayama disease.

CAMPTOCORMIA DUE TO ISOLATED THORACOLUMBAR PARASPINAL INCLUSION BODY MYOSITIS

Cynthia De la Rosa Zapata (Greer, SC), Eduardo Cortez-Garcia (Taylors, SC)

INTRODUCTION/BACKGROUND: Sporadic inclusion body myositis (sIBM) is a slowly progressive idiopathic inflammatory myopathy (IIM) and the most common over age 50. sIBM commonly affects the quadriceps and finger flexors. Paraspinal muscle weakness with head drop and/or camptocormia is a rare finding, even more as a presenting feature.

OBJECTIVE: To highlight camptocormia as an uncommon presenting feature of sIBM.

METHODS: Case report

RESULTS/CASE REPORT: A 51-year-old male presented with a 3-year history of mid-lower back pain and difficulty lifting his head, keeping an erect posture, and with fine motor skills. Exam showed mild digit abduction and flexion weakness and torso forward flexion with lateral leaning. Workup demonstrated slightly elevated creatine kinase, serology positive for NT5C1A antibodies, and electrodiagnostic studies showed isolated thoracolumbar, paraspinal myopathy. Left erector spinae muscle biopsy revealed unspecified chronic active acquired inflammatory myopathy. No rimmed vacuoles, congophilic or fibrillary inclusions. Staining for TDP43 and p62 was suspicious but insufficient for pathologic diagnosis of sIBM. Low dose prednisone for 4 months and physical therapy were ineffective. After initial and maintenance IVIg, he subjectively reported improvement of stamina, posture, and paraspinal pain. However, he was lost to follow up.

SUMMARY/CONCLUSION: Muscle biopsy was not definitive for sIBM in our case, which could be related to tissue sampling; however, NT5C1A antibodies, TDP-43, and p62 staining are useful in diagnosis and were present. Often immunosuppressive therapy offers mild/transient benefit. It was encouraging that even with an uncommon presentation of sIBM, our patient reported subjective improvement following IVIg but his lost to follow up limited documentation of corresponding objective changes.

AUTOIMMUNE NODONOPATHY WITH CONCURRENT MEMBRANOUS GLOMERULOPATHY DUE TO ANTI-CONTACTIN 1 AND ANTI-CASPR1 ANTIBODIES

Cynthia De la Rosa Zapata (Greer, SC), Eduardo Cortez-Garcia (Taylors, SC)

INTRODUCTION/BACKGROUND: It is speculated that autoantibodies to paranodal or nodal proteins including anti-contactin 1, neurofascin, and anti-Caspr1 are present in myelinated axons, but also in podocytes and are thus responsible for “neuro-renal syndrome”. Few cases have been reported in literature, although data is still lacking, the consensus is that these cases are poorly responsive to IVIg, but have a favorable outcome to rituximab.

OBJECTIVE: To highlight an uncommon association of chronic inflammatory demyelinating polyneuropathy (CIDP) and membranous glomerulonephritis (MGN) via mutual antibodies.

METHODS: Case report

RESULTS: An 85-year-old male presented with a subacute onset of bilateral lower extremity edema and bilateral fingertip paresthesias. He was diagnosed, via biopsy, with secondary membranous glomerulopathy (PLA2R & THSD7A negative) without obvious cause. He later developed intrinsic hand muscle and severe bilateral lower extremity weakness, progression of paresthesias to the feet, loss of proprioception, and difficult to manage orthostatic hypotension. EDX studies confirmed CIDP. Serologies were positive for anti-contactin 1 and anti-Caspr1 antibodies. Neuro-renal syndrome was suspected. There was no improvement in his MRC sumscore after an initial trial of IVIg. Unfortunately, before starting rituximab he developed acute encephalopathy and acute hypoxic respiratory failure due to COVID-19 infection. Given his severe disability secondary to CIDP and ongoing poor nutritional intake, his family chose comfort measures.

SUMMARY/CONCLUSION: The lack of response to IVIg in our case followed the trend described above. We suspect anti-CD20 treatment could have been beneficial if received prior to his death. Ultimately, prompt diagnosis and treatment for this disease is crucial for a better chance of recovery.

A CASE OF ANTERIOR DURAL TEAR MIMICKING AMYOTROPHIC LATERAL SCLEROSIS

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INTRODUCTION/BACKGROUND: ALS is a heterogeneous disease without reliable biomarkers for diagnosis. To avoid misdiagnosis, it's crucial to exclude other treatable conditions. Here, we report a case of anterior dural tear with cerebrospinal fluid (CSF) leak resulting in compressive extradural fluid collection and cord infarction, mimicking ALS.

CASE REPORT: A 41-year-old personal trainer experienced weakness in the right arm in 2018, followed by similar symptoms in the left arm in 2020, both with antecedent events of shoulder popping from heavy lifting. He was referred to the neuromuscular clinic after receiving a diagnosis of ALS based on an outside NCS/EMG suggesting motor axonopathy in the cervical region. Exam showed severe proximal upper extremity weakness/atrophy and mild involvement distally. There were no sensory abnormalities or pathological reflexes. MRI cervical spine demonstrated anterior extradural fluid collection centered at the cervicothoracic junction, a slight caliber change of the ventral cord margin at C6 with mild cord atrophy, and symmetric bilateral T2 hyperintensity in the anterior horns (“owl-eyes” appearance) spanning C3-C6. Brain MRI revealed an enlarged pituitary gland and an absence of CSF within the optic nerve sheaths, suggesting intracranial hypotension. Subsequent CT myelogram confirmed a large anterior C6 dural tear. A blood patch was recommended by neurosurgical consultation due to the high procedural risk of anterior dural repair at the cervical level.

SUMMARY/CONCLUSION: Ventral myelopathy from an anterior dural tear is a potential cause of slowly progressive upper extremity weakness and atrophy, resembling ALS. It is crucial to exercise clinical and radiological vigilance in order to detect this condition.

SWITCHING TREATMENT FROM ALGLUCOSIDASE ALFA TO CIPAGLUCOSIDASE ALFA/MIGLUSTAT POSITIVELY AFFECTS MOTOR FUNCTION AND QUALITY OF LIFE IN PATIENTS WITH LATE-ONSET POMPE DISEASE

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INTRODUCTION: Late-onset Pompe disease (LOPD) substantially impacts motor function and health-related quality of life (HRQoL). The phase 3 PROPEL trial (NCT03729362) assessed efficacy and safety of cipaglucosidase alfa+miglustat (cipa+mig) versus alglucosidase alfa+placebo (alg+pbo) in mainly enzyme replacement therapy (ERT)-experienced adults with LOPD.

OBJECTIVE: Evaluate the impact of switching from alg+pbo to cipa+mig on motor function and HRQoL in the prespecified population of ERT-experienced patients in PROPEL.

METHODS: PROPEL included assessments of motor function (6-minute walk test; gait, stairs, Gower maneuver, and chair) and patient-reported outcomes (PROs: EQ-5D-5L; Rasch-built Pompe-specific Activity; Subject Global Impression of Change [SGIC]; Patient-Reported Outcomes Measurement Information System [PROMIS]). Group-level analyses estimated between-group differences (least square mean) for motor function and PRO change from baseline to week 52 using analysis of covariance adjusted for baseline age, gender, height, weight, and ERT status. Patient-level responder analyses of PROs compared the proportion of patients satisfying literature-based responder thresholds via chi-square or Fisher's exact tests.

RESULTS: Group-level analyses favored cipa+mig versus alg +pbo in the vast majority of motor function and PRO measures, with nominal significance for walking tests and SGIC's 'ability to move around' and 'energy level.' Patient-level responder analyses showed a greater proportion of patients improved with cipa+mig versus alg+pbo for most PRO measures. Differences in proportions of responders between cipa+mig versus alg+pbo were nominally significant for SGIC's 'overall well-being,' 'ability to move around,' 'muscle function,' and 'energy level.'

SUMMARY/CONCLUSION: These analyses highlight the patient perspective and provide evidence that switching from alg+pbo to cipa+mig benefits patients' motor function and HRQoL.

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NIPOCALIMAB DOSE SELECTION FOR A PHASE 3 STUDY IN ADULT PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: Nipocalimab, a fully human immunoglobulin G1 (IgG1) monoclonal-antibody, blocks neonatal Fc receptors (FcRn) inhibiting IgG recycling and lowering systemic IgG, including pathogenic IgG autoantibodies.

OBJECTIVE: To determine the optimal nipocalimab dose and dosing regimen for the phase 3 study in patients with generalized myasthenia gravis (gMG) using modeling and simulation.

METHODS: Mathematical models linking nipocalimab intravenous dosing with its pharmacokinetics, FcRn occupancy, total IgG reduction, and efficacy (MG-Activities of Daily Living [MG-ADL]) were developed based on phase 1 data in healthy participants and a phase 2 study in gMG patients. Model-based simulations were conducted to identify optimal nipocalimab dose, schedule, and loading-dose for phase 3 study.

RESULTS: Nipocalimab exhibited nonlinear FcRn-mediated disposition and rapid, dose-dependent IgG lowering in phase 1 and phase 2 studies. Phase 2 study dosing ranged from 5 mg/kg every 4 weeks to 60 mg/kg every 2 weeks (Q2W). Dose-dependent improvements in MG-ADL associated with 70% IgG reduction accounted for ~90% of maximum MG-ADL reduction. Model-based simulations indicated 15 mg/kg Q2W maintenance dose achieved >70% target IgG lowering with minimal gains at higher doses. A 30 mg/kg loading dose was incorporated to lower IgG and MG-ADL scores by 2 weeks. This dosing regimen is predicted to have an average steady-state albumin lowering of 12% and total cholesterol and low-density lipoprotein increase of 6% and 8%, respectively, with limited clinical impact expected.

SUMMARY/CONCLUSION: A 30 mg/kg loading dose followed by 15 mg/kg Q2W maintenance dose was identified as optimal for the phase 3 study. Predicted exposure is well below the exposure from 60 mg/kg Q2W dosing regimen in phase 2 study, which was generally safe and well-tolerated.

Disclosures:

Juan-José Pérez-Ruixo - Employee of Janssen Research & Development, LLC and may hold stocks/stock options in Johnson & Johnson

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HANDHELD DYNAMOMETRY CORRELATES SIGNIFICANTLY WITH GLOBAL MANUAL MUSCLE STRENGTH IN PERIPHERAL NEUROPATHY PATIENTS

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INTRODUCTION: Grip strength is commonly used to measure muscle strength. The Jamar dynamometer is a popular device for this purpose, showing good inter- and intra-rater reliability.

OBJECTIVE: To investigate handheld dynamometry in neuropathy.

METHODS: Over 23 months, 147 patients were evaluated, including neuropathy impairment scores and Jamar grip strength.

RESULTS: Of 147 patients, 134 had peripheral neuropathy as a final diagnosis. The remaining 13 had other neurologic diagnoses. The neuropathy categories were length dependent sensorimotor peripheral neuropathy (LDSMPN) (n=87), small fiber neuropathy (SFN) (n=8), sensory neuropathy (SN) (n=9), polyradiculoneuropathy (PRN) (n=5), and combinations (COMBOS) (n=25). Twenty of 25 COMBOS patients had LDSMPN. The mean neuropathy impairment score-weakness subscore (NIS-W) values [SD], paired with Jamar grip strength values (adding left and right hand values [SD]) for each of the neuropathy subgroups were: LDSMPN (3.7 [9.3],144.2 [57.3]), SFN (0.0 [0.0], 153.2 [49.1]), SN (0.0 [0.0], 104.9 [59.4]), PRN (29.6 [25.8], 100.2 [79.0]) and COMBOS (11.2 [28.8], 117.2 [63.7]). Calculable Pearson correlation coefficients between NIS-W and Jamar grip strength for subgroups (r, 95% CI, p value) were: LDSMPN (r=-0.456, [-0.721, -0.074], p<0.0001), PRN (r=-0.667, [-0.975, 0.0523, p=0.5227), COMBOS (r=-0.456, [-0.721, -0.074], p<0.0001).

SUMMARY/CONCLUSION: 1. In LDSMPN, as NIS-W increases, there is a statistically significant decrease in Jamar grip strength. 2. In LDSMPN with other neurologic conditions, a significant negative correlation between NIS-W and Jamar grip strength also exists. 3. Jamar grip strength may be a useful surrogate marker of global muscle strength (as measured by NIS-W) in LDSMPN, in both longitudinal neuropathy assessments and as a clinical research endpoint.

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INTEGRATED ANALYSES OF DATA FROM CLINICAL TRIALS OF DELANDISTROGENE MOXEPARVOVEC IN DUCHENNE MUSCULAR DYSTROPHY

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INTRODUCTION: Delandistrogene moxeparvovec (SRP-9001) is an investigational rAAV vector-based gene therapy, designed to compensate for missing dystrophin in Duchenne muscular dystrophy (DMD) by delivering a transgene encoding SRP-9001 dystrophin, an engineered dystrophin protein that retains key functional domains of the wild-type protein.

OBJECTIVE: To evaluate 1-year functional data in patients following single IV infusion of delandistrogene moxeparvovec versus a propensity-score-weighted external control (EC) cohort.

METHODS: Ambulatory patients with DMD (≥4 to ≤8 years) received a single dose of delandistrogene moxeparvovec (1.33x1014 vg/kg). The dataset included patients treated with delandistrogene moxeparvovec from 3 studies: Study 101 (SRP-9001-101; NCT03375164), Study 102 (SRP-9001-102; NCT03769116), and ENDEAVOR (NCT04626674). The EC cohort (N=131), comprising patients from 3 studies, was used for comparison. The primary endpoint was 1-year change from baseline in North Star Ambulatory Assessment (NSAA) total score. Exploratory endpoints included the effect on timed function tests 1-year post-treatment. Collective safety data are presented.

RESULTS: The integrated analyses evaluated functional data from Study 101 (n=4), Study 102 (n=28), and Cohort 1 of ENDEAVOR (n=20). A statistically significant difference of 2.4 points (p<0.0001) was observed in NSAA change from baseline to Year 1 in treated patients versus the EC cohort (n=105). No adverse events led to study discontinuation and there were no deaths.

SUMMARY/CONCLUSION: Delandistrogene moxeparvovec demonstrated a clinically meaningful change from baseline in NSAA total score at 1 year versus a propensity-score-weighted EC cohort, suggesting a beneficial modification of the DMD disease trajectory. Collective safety data were consistent and manageable across studies.

Disclosures:

Crystal Proud - Consultant for Biogen, Sarepta Therapeutics, AveXis/Novartis Gene Therapies, Genentech/Roche and Scholar Rock; speaker for Biogen; PI of studies sponsored by AveXis/Novartis Gene Therapies, AMO, Astellas, Biogen, CSL Behring, Fibrogen, PTC Therapeutics, Pfizer, Sarepta Therapeutics, and Scholar Rock

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Stefanie Mason - Employee of Sarepta Therapeutics and may have stock options

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APHERESIS AND HYPOKALEMIA IN A MYASTHENIA GRAVIS PATIENT: A CASE REPORT

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INTRODUCTION/BACKGROUND: Myasthenia gravis (MG) is an autoimmune condition involving an immune-mediated attack on the acetylcholine receptors (AChR) that are located on the postsynaptic membrane of the neuromuscular junction. The symptoms of MG can vary widely depending on the severity of the condition. MG can be treated with medications that improve neuromuscular junction transmission, immunosuppressants, and, in severe cases, therapeutic apheresis. This procedure involves removing autoantibodies from the blood of MG patients and then returning the rest of the blood to the patient. Additionally, potassium plays a crucial role in neuromuscular transmission, and alterations in serum potassium levels can affect muscle function and exacerbate MG symptoms.

CASE REPORT: A 38-year-old woman with a history of MG had a myasthenic crisis and was started initially on IVIg therapy with no improvement. Due to the severity of her symptoms, the patient subsequently started apheresis therapy. After multiple rounds of apheresis therapy, her symptoms minimally improved. A metabolic panel was drawn which revealed severe hypokalemia, with a potassium level of 2.7 mEq/L. Upon replenishing her potassium levels along with continuing apheresis, the patient started to see great improvement in her MG symptoms.

SUMMARY/CONCLUSION: This case highlights a unique presentation in an MG patient whose symptoms were refractory to apheresis but improved upon recognition and correction of potassium disturbances. A review of the literature failed to reveal any similar cases. Due to the effect of potassium on neuromuscular transmission, correcting hypokalemia can result in a significant improvement in MG symptoms.

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CHARACTERIZATION OF MYASTHENIA GRAVIS PATIENT POPULATION AND MANAGEMENT PREFERENCES IN COLORADO

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INTRODUCTION: There is limited investigation using real-world population data regarding differences in treatment patterns, outcomes, epidemiologic factors, and disparities in patients with myasthenia gravis (MG).

OBJECTIVE: To characterize longitudinal healthcare utilization of adult MG patients in Colorado including epidemiologic factors, treatments, complications, and hospitalizations.

METHODS: The study sample included adult patients from a large health system in Colorado with MG between January 2019 and December 2021 with at least 4 clinical visits. Data was collected on treatments and population demographics, including age, gender, race, ethnicity, payor, and urban/rural status.

RESULTS: Two hundred seventy patients (50.4% female) with MG were identified. Mean (sd) age was 61.0 (17.6) years. 61.8% of patients had government insurance. 81.5% of patients identified as Caucasian, 5.6% as African American and 13.0% reported Hispanic ethnicity. 75.2% of patients had positive antibodies (AChR and MuSK), with only 3 patients (1.1%) having positive MuSK antibodies. Two hundred sixty-nine patients received oral medications, with 81.5% receiving oral steroids, 87.0% pyridostigmine, 39.3% azathioprine, and 31.9% mycophenolate. Intravenous medications were used less frequently at 46.3% though 28.9% of patients in our cohort received IVIg, many of them chronically. There were 26 thymectomies performed, 19 uses of plasmapheresis, and 1 gastrostomy placement during the study period. Overall, 46.7% of patients were hospitalized for any reason during the time period, 23.7% due to MG.

SUMMARY/CONCLUSION: This study will help inform care and treatment decisions for patients with MG, provide updated epidemiologic information about MG, and give important context to real world practice for patients with MG compared with published guidelines.

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RAVULIZUMAB IN ADULTS WITH GENERALIZED MYASTHENIA GRAVIS: A SUB-ANALYSIS OF THE PHASE 3 CHAMPION MYASTHENIA GRAVIS STUDY ACCORDING TO CHRONIC INTRAVENOUS IMMUNOGLOBULIN USE AT STUDY ENTRY

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INTRODUCTION: The long-acting terminal complement C5 inhibitor, ravulizumab, demonstrated sustained efficacy and was well tolerated in adults with anti-acetylcholine receptor antibody-positive (AChR Ab+) generalized myasthenia gravis (gMG) in the phase 3 CHAMPION MG study. Although intravenous immunoglobulin (IVIg) treatment was only allowed as rescue therapy during the study, many patients had received IVIg before study entry.

OBJECTIVE: To assess response to ravulizumab, according to prior IVIg treatment.

METHODS: Post-hoc sub-analysis of double-blind, placebo-controlled, phase 3 CHAMPION MG study (NCT03920293) of ravulizumab (administered every 8 weeks) in adults with AChR Ab+ gMG, according to prior IVIg use. Changes from baseline to Week 26 in Myasthenia Gravis Activities of Daily Living (MG-ADL; primary endpoint) and Quantitative Myasthenia Gravis (QMG) total scores were analyzed.

RESULTS: Of 175 enrolled patients: 79 had no previous IVIg use (38 placebo; 41 ravulizumab), 96 had received either acute or chronic (any) IVIg (51 placebo; 45 ravulizumab), and 46 had received only chronic IVIg (22 placebo; 24 ravulizumab). The groups had comparable baseline characteristics and demographics. Least squares (LS) mean changes (95% CI) from baseline to Week 26 for ravulizumab vs placebo in patients with no, any, or chronic previous IVIg use, were: -2.1 (-3.6, -0.5), -1.3 (-2.8, -0.6), and -1.1 (-2.6, 0.0), respectively for MG-ADL total scores; and -2.4 (-4.2, -0.7), -1.6 (-3.2, -0.0), and -2.3 (-4.6, 0.1), respectively for QMG total scores.

SUMMARY/CONCLUSION: Improvements in functional ability and muscle strength in patients with AChR Ab+ gMG following ravulizumab treatment were not statistically significantly different between groups according to prior IVIg use.

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Rasha Aguzzi - Employee of and holds stock options in Alexion, AstraZeneca Rare Disease

Glen Frick - Employee of and holds stock options in Alexion, AstraZeneca Rare Disease

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FORMAL BALANCE ASSESSMENT IN PATIENTS WITH DIABETES AS STANDARD OF PRACTICE

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INTRODUCTION: During the lifetime of adults with diabetes, approximately 50% will be affected by diabetic peripheral neuropathy (DPN). While some with DPN are relatively asymptomatic, others report pain, paresthesia, and imbalance. Potential negative complications of DPN include ulcers, falls, and amputations. Due to the increasing number of patients with diabetes and the significant morbidity associated with consequences of DPN, professional associations have been advocating for more screening and preventative disease management.

OBJECTIVE: This retrospective review aims to demonstrate the critical need for formal balance examination by physical therapists (PT) for patients with diabetes.

METHODS: Eighty-nine consecutive patients with diabetes who consented to assessment, underwent a formal balance examination by PT. The mean age was 58.3 years, 51 were female, and mean duration of diabetes was 7.4 years. PT examination included the Sit To Stand 30, Berg Balance Scale, Timed Up and Go, Four Square Step Test, Self-Selected Gait Speed, and 4-Stage Balance Test.

RESULTS: 52.8% reported DPM symptoms, 34.8% reported using an assistive device, 29.2% reported a fall in the past year, 32.5% had a home health aide, 76.8% demonstrated below normal scores on at least 5/6 tests, and 97.8% reported never having been formally tested for balance.

SUMMARY/CONCLUSION: Only 2 of 89 patients had previously been formally tested for balance while more than 75% demonstrated poor balance. Objective balance testing by PT in collaboration with primary care physicians, podiatrists, and endocrinologists is needed. Formal testing identifies patients at risk, helps guide clinical decision making, and serves as an objective reference point.

NOMOGRAM FOR PREDICTION OF PREGNANCY-RELATED CLINICAL WORSENING IN MYASTHENIA GRAVIS PATIENTS

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INTRODUCTION: Myasthenia gravis (MG) is an autoimmune disease mediated by autoantibodies that primarily affects the neuromuscular junction. Female patients constitute a higher proportion of early-onset MG. Given the potential risks of MG exacerbation and the effects on pregnancy, clinical management of pregnancy-associated MG is critical for pregnant women and fetuses.

OBJECTIVE: We aimed to develop and validate a predictive nomogram to assess the pregnancy-related clinical worsening in myasthenia gravis patients.

METHODS: The current study retrospectively reviewed the MG-related clinical scales in 143 pregnancy-related MG patients from Huashan Hospital Fudan University from January 2015 to October 2021. Changes in MG-ADL scale (≥1 point) were defined as MG worsening.

RESULTS: One hundred thirteen patients had MG onset before pregnancy and 30 patients had the first attack of MG during pregnancy or 1 year after childbirth. Among 113 patients with pre-pregnant onset, 52 patients (46.0%) had MG worsening, which frequently occurred in the first trimester of pregnancy and the first trimester after delivery. We then analyzed the differences in clinical variables between the worsening group (n=52) and the non-worsening group (n=61) of pregnancy-related MG. Maternal age of childbirth/abortion (20-32.5 years old) (p=0.001), well-controlled disease duration shorter than 2 years (p=0.001), thymus hyperplasia (p=0.004), thymectomy before pregnancy (p=0.005), and insufficient treatment during pregnancy (p=0.027) were statistically associated with worsening. The Nomogram model has good performance in predicting worsening with a C-index of 0.812 (95% CI: 0.733-0.891) and AUC of 0.812.

SUMMARY/CONCLUSION: The nomogram achieved an optimal prediction of pregnancy-related worsening in MG patients using the baseline clinical characters.

IMPACT OF BASELINE POLYNEUROPATHY SEVERITY ON VUTRISIRAN TREATMENT RESPONSE IN THE PHASE 3 HELIOS-A STUDY

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INTRODUCTION: Hereditary transthyretin-mediated (hATTR) amyloidosis is a progressive, multisystem disease. Vutrisiran, an RNA interference therapeutic, improved neuropathy and quality of life (QOL) versus external placebo in patients with hATTR amyloidosis with polyneuropathy in the HELIOS-A study.

OBJECTIVE: This analysis evaluates the impact of baseline polyneuropathy severity on vutrisiran response.

METHODS: Patients were randomized (3:1) to vutrisiran (25 mg subcutaneous q3m) or patisiran (0.3 mg/kg intravenous q3w), a reference group. This post-hoc analysis divided patients into quartiles with approximately equal number of patients with increasing baseline Neuropathy Impairment Score (NIS): Q1 ≥5.0—≤20.5; Q2 >20.5—≤44.1; Q3 >44.1—≤73.1; Q4 >73.1—≤127. Mean change from baseline to Month 18 was summarized by quartile for efficacy endpoints.

RESULTS: Across baseline NIS quartiles, vutrisiran demonstrated benefit in mNIS+7 versus external placebo (mean change from baseline in mNIS+7 at Month 9/18: Q1, -3.3/-3.0 [vutrisiran] vs +13.8/+18.4 [external placebo]; Q2, -0.6/-3.1 vs +12.1/+24.5; Q3, -2.1/+6.2 vs +16.5/+33.1; Q4, +1.6/+3.2 vs +16.5/+30.7). Vutrisiran also demonstrated benefit versus external placebo across NIS quartiles for QOL (Norfolk QOL-DN), disability (Rasch-built Overall Disability Scale), gait speed (10-meter walk test), and nutritional status (modified BMI). Overall, patients in lower NIS quartiles at baseline maintained better scores at Month 18. The external placebo group progressively worsened in all measures at Month 18.

SUMMARY/CONCLUSION: Vutrisiran demonstrated benefit in key measures, versus external placebo, across all baseline polyneuropathy severities. Patients who initiated vutrisiran earlier in their disease course retained the highest level of neurologic function after 18 months, highlighting the importance of early diagnosis and treatment.

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NEUROFILAMENT LIGHT CHAIN LEVELS SIGNIFICANTLY DECREASE IN RESPONSE TO TREATMENT WITH PATISIRAN OR VUTRISIRAN IN HEREDITARY TRANSTHYRETIN-MEDIATED AMYLOIDOSIS WITH POLYNEUROPATHY

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INTRODUCTION: In hereditary transthyretin-mediated (hATTR) amyloidosis, diagnosis and monitoring treatment response can be challenging. Neurofilament light chain (NfL) is a potential biomarker of disease progression and treatment response in patients with hATTR amyloidosis with polyneuropathy.

OBJECTIVE: To analyze NfL levels in patients from the phase 3 APOLLO and HELIOS-A studies to further assess its potential utility in hATTR amyloidosis.

METHODS: NfL plasma levels were measured at different time points in healthy controls and in a subset of patients from the APOLLO or HELIOS-A studies, who gave consent and had available samples.

RESULTS: NfL levels at baseline were slightly higher in APOLLO (69.4 pg/mL) than in HELIOS-A (58.2 pg/mL). In the APOLLO placebo arm, NfL levels significantly increased from baseline at 4 months (+19.0 pg/mL, $p<0.001$) and 18 months (+36.3 pg/mL, $p<0.001$). However, in the APOLLO patisiran arm, NfL decreased from baseline at 4 months (-20.0 pg/mL, $p<0.001$) and 18 months (-23.2 pg/mL, $p<0.001$). Similarly, in HELIOS-A, NfL in patisiran and vutrisiran groups decreased from baseline at 4 months (-9.7 and -11.0 pg/mL, respectively; $p<0.05$) and these decreases were maintained at 18 months (-16.4 and -19.9 pg/mL, respectively; $p<0.001$).

SUMMARY/CONCLUSION: NfL may serve as a biomarker of treatment response as early as 4 months following initiation of patisiran or vutrisiran. The observed decreases in NfL from baseline are maintained through 18 months of treatment, in contrast to the significant increase observed in untreated patients, making it potentially useful for monitoring disease progression and treatment response in hATTR amyloidosis with polyneuropathy.

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Jennifer Barnes - Former Alnylam Pharmaceuticals employee and stock owner

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ROLE OF VIDEO-ELECTROENCEPHALOGRAM IN TILT TABLE TESTING TO DISTINGUISH DIFFERENT DEGREES OF CEREBRAL HYPOPERFUSION DURING SYNCOPE

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INTRODUCTION: Tilt table test is commonly used in the diagnostic evaluation of patients who have experienced syncope or syncope-like events causing loss of consciousness (LOC). There is limited literature available on the utility and cost-effectiveness of a combined video-electroencephalogram (vEEG) tilt table testing in evaluation of such patients.

OBJECTIVE: To report vEEG and tilt table analyses in two 18-year-old patients with recurrent syncope-like events.

METHODS: Chart review, vEEG and tilt table findings. EEG and tilt table analyses were performed independently.

RESULTS: With upright tilt to 70 degrees, the mean heart rate increased by 30 bpm in patient 1 and by 18 bpm in patient 2. Both patients demonstrated a vasodepressor response at ~9 and 12 minutes respectively, associated with bradycardia and hypotension. Clinically, both patients appeared to be unconscious and both patients had some ‘twitching’ movements. The vEEG review of patient 1 demonstrated evolution of normal alpha background into theta and diffuse delta activity, followed by generalized EEG suppression, associated with bilateral arm tonic-clonic activity mimicking a seizure, consistent with convulsive syncope. The vEEG of patient 2 demonstrated maintenance of normal alpha background throughout the vasodepressor phase, hence indicating that the unconsciousness was likely functional.

SUMMARY/CONCLUSION: These 2 cases demonstrate the diagnostic value of vEEG in tilt table testing for evaluation of syncope or syncope-like events with LOC. A future prospective study would be required to establish clinical utility and cost-effectiveness of this approach.

THYMOMA-ASSOCIATED MYASTHENIC CRISIS: A MULTICENTER RETROSPECTIVE COHORT STUDY

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INTRODUCTION: Myasthenic crisis (MC) is a life-threatening condition for patients with myasthenia gravis (MG). Thymoma-associated MC (TMC) accounted for about 30% of total MC episodes. There is still limited evidence regarding the outcome of TMC.

OBJECTIVE: To investigate the clinical features and in-hospital clinical outcomes of TMC.

METHODS: We performed a retrospective cohort study in TMC patients recruited from 9 independent tertiary neuromuscular centers from Jan 2015 through Oct 2022. A total of 156 MC episodes from 149 MG patients who were anti-acetylcholine receptor (AChR) antibody-positive were finally included. Next, these patients were divided into 2 groups: the TMC group (n=60 episodes, 58 patients) and the non-thymoma-associated MC (n=96 episodes, 91 patients). Subgroup analysis was performed by stratifying TMC patients according to the time of MC occurrence (with the concurrence of thymoma versus postoperative myasthenic crisis [POMC]). Group comparison was assessed using the t-test or Wilcoxon test for continuous variables and the $\chi 2$ test or Fisher's exact test for categorical variables.

RESULTS: Compared with non-thymoma-associated MCs, TMCs had a significantly shorter disease duration from onset to the crisis (17.95±40.9 vs 51.31±60.61 months, $p<0.0001$) and a longer hospital stay (39.24±22.09 [6-111] vs 33.2±23.42 days [7-120]; $p= 0.0317$). Within the TMC group, the hospital stay was significantly longer in MCs with thymoma concurrence compared to that in POMC (47.68±24.9 [6-111] vs 34.21±18.87 days [12-82]; $p=0.0257$).

CONCLUSION: TMC was associated with a more aggressive disease progression and longer hospital stays. The identification of the precise MC subtypes may provide some hints in tailoring the therapeutic strategies to improve the prognosis.

BETHLEM MYOPATHY CLINICAL VIEW WITH ULTRASONOGRAPHY AND ELECTRODIAGNOSIS: A CASE REPORT

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INTRODUCTION/BACKGROUND: Bethlem myopathy is a muscle disorder characterized by muscle weakness and contractures. Its onset is during childhood with manifestations such as mild proximal weakness and distal joint laxity. It can be accompanied by alterations such as hip dysplasia, equinovarus deformities, and torticollis. This case report includes the clinical symptoms and the relationship with the variant in the COL6A1 gene, compatible with Bethlem myopathy 1 of autosomal dominant inheritance, and its relationship with studies such as NCS, EMG, and ultrasonography.

CASE REPORT: An 8-year-old male patient with a family history of progressive weakness presented with proximal muscle weakness from an early age, delayed motor development, toe walking, motor dysphagia, hyporeflexia, distal hypermobility, and contractures. Blood laboratory showed elevated creatine kinase, NCS, and EMG with a muscle fiber primary disease. Muscle ultrasound revealed multiple hyperechogenic foci related to fatty infiltration. Genetic confirmation with COL6A1 gene variant: c. 788G>A, p. Gly263Asp, heterozygous, with phenotype compatible with Bethlem myopathy 1 of autosomal dominant inheritance.

CONCLUSION: Bethlem myopathy is collagen VI damaged. This case report shows the neurophysiology studies and ultrasonography as a complement to diagnostic confirmation through genetic studies because of dominant inheritance. However, some cases of autosomal recessive inheritance have been reported. Muscle ultrasound visualizes fatty infiltration, predominantly in the upper limb muscles. Therefore, it denotes the importance of a complementary assessment with neuromuscular ultrasound and NCS/EMG studies.

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EFFECT OF SARS-COV-2 PANDEMIC ON OUTCOMES AND ASSOCIATED RISK FACTORS OF GUILLAIN-BARRE SYNDROME PATIENTS

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INTRODUCTION: Evidence suggests an increase in neurological complications, such as Guillain-Barre syndrome (GBS), following SARS-CoV-2 infection, however, the differences in GBS patient outcomes and related risk factors before and during the pandemic have not been characterized.

OBJECTIVE: To investigate outcomes and associated risk factors among those diagnosed with GBS prior to and during the SARS-CoV-2 pandemic.

METHODS: A retrospective analysis on 29 million hospitalizations from 2016 to 2020 was conducted using the national inpatient sample. A discharge sample weight was applied to provide national estimates for over 145 million hospitalizations. The sample's mean age was 58 years, with 96,880 hospitalizations for GBS. GBS incidence before and after pandemic onset was compared, along with mortality, patient demographics, and select comorbidities.

RESULTS: When comparing time periods before and after pandemic onset, the incidence of GBS increased significantly (18.6% vs 19.6%, p<0.00001). Among those with GBS, there was a significant increase in obese patients (19.10% vs 22.00%, p<0.001) and those with chronic lung disease (19.20% vs 20.50%, p<0.001). There was no significant change in chronic autoimmune conditions among GBS patients (4.80% vs 4.90%, p=0.75). However, during the pandemic, chronic autoimmune conditions among GBS patients significantly increased odds of mortality when compared to the pre-pandemic period (p<0.001, OR=1.794 CI [1.337, 2.407]).

SUMMARY/CONCLUSION: This study demonstrates that GBS incidence increased significantly during the SARS-CoV-2 pandemic, and among those with GBS, a significantly greater number of patients also had obesity or chronic lung disease. Chronic autoimmune disease patients with GBS had significantly higher odds of mortality during the pandemic compared to before.

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EFFECTS OF SARS-COV-2 PANDEMIC ON HOSPITALIZATIONS AND ASSOCIATED RISK FACTORS FOR MYASTHENIA GRAVIS EXACERBATION

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INTRODUCTION: A relationship has been demonstrated between SARS-CoV-2 infection and subsequent exacerbation of neurological conditions, however, the differences in hospitalizations and related factors for myasthenia gravis (MG) before versus during the pandemic have not yet been characterized.

OBJECTIVE: To investigate trends in hospitalizations and associated risk factors for acute MG exacerbation before and after onset of the SARS-CoV-2 pandemic.

METHODS: A retrospective analysis on 46,620 hospitalizations for MG from 2016 to 2020 was conducted using the National Inpatient Sample database. The mean patient age was 63 years with 1745 (3.7%) cases of death reported. Trends were elucidated from the differences in MG exacerbation incidence, mortality, and various comorbidities prior to the pandemic versus during.

RESULTS: There was significantly higher mortality among those hospitalized for MG during the pandemic compared to the time period prior (3.40% vs 5.40%, p<0.001), although there was no significant difference between the incidence of MG (0.031% vs 0.031%, p=0.37). A significantly greater number of MG patients presented with comorbidities during the pandemic, namely hypertension (63.90% vs 68.20%, p<0.001), obesity (22.00% vs 27.20%, p<0.001), chronic autoimmune disease (5.90% vs 6.60%, p=0.017), thyroid disease (23.40% vs 24.60%, p=0.017), and diabetes mellitus (32.20% vs 33.40%, p=0.023).

SUMMARY/CONCLUSION: This study suggests that there was a significant increase in mortality among those hospitalized with MG during the pandemic, despite no significant change in the incidence of MG. A significantly higher prevalence of each of the following comorbidities in MG patients was also observed: hypertension, obesity, chronic autoimmune disease, thyroid disease, and diabetes mellitus.

IDENTIFICATION OF PERINATAL FACTORS RELATED TO ELEVATED CREATINE KINASE IN NEWBORNS

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INTRODUCTION: Creatine kinase (CK) newborn screening may help identify infants with certain neuromuscular disorders, such as muscular dystrophy and congenital myopathies, and is of increasing importance as therapeutic interventions for these diseases become available. CK levels are subject to multiple factors and a paucity of information of how maternal, perinatal, and post-natal birth factors affect CK levels remains.

OBJECTIVE: We aim to identify how newborn demographics, labor, and delivery influence elevated serum CK levels during newborn screening (NBS).

METHODS: >8,000 newborns and their mothers were enrolled in our study. CK-MM levels for newborns were measured on already-existing dried bloodspot (DBS) samples in conjunction with routine NBS. Review of electronic medical records was performed to analyze maternal and perinatal variables and factors.

RESULTS: Demographic factors that correlated to CK levels included male sex and gestational age more than birth weight, and shorter time until sample collection. Labor marked by oxytocin induction or augmentation was correlated to higher CK levels. Vaginal deliveries in which assistive maneuvers were utilized or shoulder dystocia occurred showed elevated CK levels. C-sections resulted in higher CK levels when: (A) delivery was urgently indicated, (B) indication was due to failure to process, and (C) a trial of labor prior was present. Maternal fever correlated to higher newborn CK levels. Lower Apgar score and intensive resuscitation were associated with higher CK.

SUMMARY/CONCLUSION: Multiple factors can result in elevated perinatal CK levels; the presence of these for an infant undergoing newborn screening for congenital muscular dystrophies and myopathies can help to aid interpretation of these tests.

NOVEL BAG3 VARIANT IDENTIFIED IN A CASE OF ADULT-ONSET MYOFIBRILLAR MYOPATHY

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INTRODUCTION/BACKGROUND: Myofibrillary myopathies (MFM) are a heterogeneous group of disorders characterised by myofibrillar dissolution and accumulation of protein degradation products in myofibres. BCL2-associated anthanogene 3 (BAG3)-related MFM has been reported to present with sensorimotor neuropathy and cardiomyopathy. We report a case of a 54-year-old man with a progressive sensorimotor axonal neuropathy with respiratory involvement who was found to have a novel BAG3 variant.

CASE REPORT: A 54-year-old man presented with a 6-month history of increasing dyspnoea with severe restrictive ventilatory dysfunction evident on pulmonary function testing. He has a 5-year history of progressive sensorimotor disturbance in his limbs with muscle cramps and gait impairment leaving him wheelchair-bound. Examination revealed marked wasting and florid fasciculations in the upper and lower limbs, distal greater than proximal weakness, absent reflexes, and a stocking-and-glove distribution sensory disturbance. Electrodiagnostic studies confirmed a severe length-dependent sensorimotor axonal neuropathy with active and chronic denervation on electromyography. Singleton whole exome sequencing identified a heterozygous missense variant of unknown significance in BAG3 [NM_004281.3:c.625C>G, p.(Pro209Ala)]. Other variants in BAG3 at the same amino acid residue [p.(Pro209Leu) and p.(Pro209Gln)] have been reported to be associated with BAG3-related MFM. Subsequent muscle biopsy demonstrated chronic denervation and reinnervation of myofibres with pseudodystrophic changes, suggestive of an underlying myofibrillar myopathy. He was managed supportively with nocturnal bilevel positive airway pressure and discharged into supported accommodation.

SUMMARY/CONCLUSION: This is a case of adult-onset myofibrillary myopathy suspected to be due to a novel missense BAG3 variant located in a previously reported BAG3 mutation hotspot (Proline 209).

THE MATILDA EFFECT: ARE WOMEN UNDERRECOGNIZED FOR NATIONAL AWARDS IN NEUROMUSCULAR AND ELECTRODIAGNOSTIC MEDICINE?

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INTRODUCTION: Acknowledging the problem of gender disparity, institutions and organizations, including the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM), have committed to equity, diversity, and inclusion. Notwithstanding this commitment, studies repeatedly demonstrate that women are much less likely to receive awards and recognitions in medicine and scientific research compared to their male counterparts. The problem of women being underrecognized is so pervasive that the moniker The Matilda Effect was coined in 1993. Whether women are less likely to be recognized with AANEM awards is unknown.

OBJECTIVE: To evaluate whether there is a gender disparity in the AANEM's annual distinguished physician, distinguished researcher, and lifetime achievement awards.

METHODS: Retrospective observational study. A list of winners was obtained from the AANEM website and gender was assigned based on searches of public professional websites. Data were analyzed using descriptive statistics.

RESULTS: Of 87 awards given from 1957-2022, 7 (8%) were awarded to women and 80 (92%) to men. Three women had received the distinguished physician award, accounting for 10.3% of awardees; 2 women had each won the distinguished researcher and lifetime achievement awards, accounting for 7.1% and 6.7% of awardees, respectively. Both women lifetime achievement winners were after 2020. Further, each of these women previously won in another category, meaning only 5 individual women had been acknowledged overall, compared to 65 individual men.

SUMMARY/CONCLUSION: For the AANEM, the gender gap in awards and recognitions falls far short of parity. Further efforts to address systemic barriers contributing to this disparity are warranted.

COMPARISON OF TOLERABILITY AND SAFETY OF HYALURONIDASE-FACILITATED SUBCUTANEOUS IMMUNOGLOBULIN 10% AND 20% THERAPIES AFTER SINGLE SUBCUTANEOUS ADMINISTRATION IN HEALTHY ADULTS

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INTRODUCTION: Hyaluronidase-facilitated subcutaneous immunoglobulin (fSCIG) 20% (immunoglobulin G [IgG] 20% with recombinant human hyaluronidase) is under investigation for the treatment of primary immunodeficiency disease and offers potentially beneficial reductions in infusion times and volumes versus fSCIG 10%.

OBJECTIVE: To compare the tolerability and safety of fSCIG 10% and 20% following single-dose subcutaneous administration.

METHODS: Data from 2 phase 1 open-label studies of fSCIG 10% (Study 1 [NCT04578535]) and 20% (Study 2 [NCT05059977]) in healthy adults aged 19–50 years were analyzed. Participants received single doses of fSCIG 10% (Study 1; 0.4g/kg [n=8] or 1.0g/kg [n=10]; ≤25±1-week follow-up) or fSCIG 20% (Study 2; 3 treatment arms [0.4g/kg or 1.0g/kg with in-line warming, or 1.0g/kg unwarmed; n=8 per arm]; ≤12±1-week follow-up).

RESULTS: Mean total IgG doses given were similar between fSCIG 20% and 10% at the same dose strength, while mean total IgG volumes were lower with fSCIG 20% than 10% for both dose strengths (e.g. unwarmed fSCIG 20% vs fSCIG 10% 1.0g/kg: 355.0mL vs 667.0mL). Mean time to deliver total IgG volume was shorter with fSCIG 20% than 10% at both dose strengths. In both studies, all infusions were tolerated and all participants experienced treatment-emergent adverse events (TEAEs). All TEAEs were mild in severity; the majority were infusion site reactions. No serious TEAEs were reported.

SUMMARY/CONCLUSION: The single-dose tolerability and safety profiles of fSCIG 20% and 10% are comparable, supporting further investigation of fSCIG 20% in target patient populations.

Study/writing funding: Takeda Development Center Americas, Inc/Takeda Pharmaceuticals International AG.

Disclosures:

Zhaoyang Li - Employee of Takeda Development Center Americas, Inc and a Takeda shareholder

Noor Khaskhely - Employee of Takeda Development Center Americas, Inc and a Takeda shareholder

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COMPARISON OF THE SINGLE-DOSE PHARMACOKINETICS OF HYALURONIDASE-FACILITATED SUBCUTANEOUS IMMUNOGLOBULIN 10% AND 20% IN HEALTHY ADULTS

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INTRODUCTION: Hyaluronidase-facilitated subcutaneous immunoglobulin (fSCIG) 10% is approved to treat primary immunodeficiency disease. fSCIG 20%, a higher-concentration immunoglobulin therapy in development, may benefit patients through smaller infusion volumes and shorter infusion times.

OBJECTIVE: To compare single-dose pharmacokinetics of fSCIG 10% and 20%, and evaluate the effect of warming on fSCIG 20% pharmacokinetics.

METHODS: Data from 2 phase 1, open-label studies in healthy adults (19–50 years) were used. In Study 1, participants receiving fSCIG 10% with immunoglobulin G (IgG) doses of 0.4 (n=8) or 1.0 g/kg (n=10) on Day 1 were selected for comparison (NCT04578535). In Study 2, participants received fSCIG 20%, with in-line warmed (0.4 or 1.0 g/kg) or unwarmed (1.0 g/kg) IgG doses on Day 1 (n=8 per treatment arm; NCT05059977). Baseline-uncorrected serum total IgG concentrations at the same dose on Days 1 and 4 and Week 4 (Day 29/30) and total IgG exposure (area under curve up to Day 29/30 [AUCDays1–29/30]) were compared for fSCIG 10% and 20% at both doses using group t-tests ($p<0.05$ statistically significant).

RESULTS: At 0.4 and 1.0 g/kg doses, there were no statistically significant differences between serum total IgG concentrations of fSCIG 10% and 20% at the same timepoint and dose strength. There were no statistically significant differences between AUCDays1–29/30 for serum total IgG for fSCIG 10% and 20% at the same dose strength, regardless of fSCIG 20% warming.

SUMMARY/CONCLUSION: fSCIG 10%, warmed fSCIG 20%, and unwarmed fSCIG 20% provided comparable total IgG concentrations and total exposures in healthy adults.

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Iftekhar Mahmood - Consultant to Takeda Development Center Americas, Inc

Zhaoyang Li - Employee of Takeda Development Center Americas, Inc and a Takeda shareholder

REFERENCE VALUES OF ELECTROMYOGRAPHY STUDIES OF THE MASSETER AND TEMPORAL MUSCLES

Andersson Rozo (Cucuta, Colombia)

INTRODUCTION: The masseter and temporal muscles are very important in the chewing process, plus, they are often affected in myoarticular and neurological diseases, among others.

OBJECTIVE: To present the results of EMG made with an electrode needle of the masseter and temporal muscles at the moment of mastication, evaluating the parameters in amplitude and duration of the potentials.

METHODS: Twenty-six persons with prior dental assessments that ruled out congenital abnormalities, chewing problems, and normal dynamometry at the time of the occlusion, to whom an EMG was performed with a needle in the masseter and temporalis muscles. We analyzed the values of maximum and minimum amplitude, as well as the duration, locating in percentiles and quadrilles, seeking to determine the values that may need to be normal in this sample.

RESULTS: In the temporal muscle, it was found that the usual duration is between 4.75 and 6.487 msec, while the amplitude is between 1572.05 uV and 1038.03 uV. For the masseter muscle, it was observed that the usual duration is between 4.03 and 6.767 msec, while the amplitude would be between 2838.43 uV and 1864.635 uV.

SUMMARY: This study shows values for our population considering the duration and amplitude of the motor unit action potentials of the temporal and masseter muscles, which concur with those previously established as normal. Studies from other parts of the world show that the duration is less than in the extremities, but the amplitude is similar, while the tendency to values is below the average.

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A CASE SERIES: COVID-ASSOCIATED CHANGES IN PERIPHERAL MYELIN PROTEIN 22 NEUROPATHIES

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INTRODUCTION/BACKGROUND: The risk of inflammatory neuropathies such as Guillain-Barre syndrome (GBS) in patients with hereditary demyelinating neuropathies is not well-characterized, and no cases have been described following COVID infection. We describe 2 patients with hereditary neuropathy due to peripheral myelin protein 22 (PMP22) defects who developed acute to subacute ascending numbness and weakness following COVID infection or vaccination.

CASE REPORT: The first patient is a 64-year-old man who developed ascending weakness and worsening balance over 1 month following a COVID booster and subsequently stabilized. Examination showed length-dependent sensorimotor deficits. EMG showed a chronic uniformly demyelinating polyneuropathy with fibrillations and positive sharp waves in bilateral tibialis anterior and ulnar-innervated muscles. Genetic testing showed PMP22 duplication. The second patient is a 64-year-old man who developed ascending numbness and weakness over 1 week following COVID infection, followed by slow improvement over the course of 2-3 months. Examination showed distal > proximal left arm weakness, right ulnar-distribution weakness and numbness, left > right foot drop, and a length-dependent pattern of sensory loss up to the knees. EMG showed severe entrapment neuropathies with a superimposed sensorimotor polyneuropathy. Genetic testing showed PMP22 deletion. Nine months later, his strength normalized and his sensory exam improved.

SUMMARY/CONCLUSION: Prior cases of GBS have been reported with the temporal association after COVID-19 infection, vaccinations, and boosters. Our cases describe worsening of neuropathy symptoms following COVID infection and vaccination in patients with hereditary demyelinating neuropathy which mimics acquired demyelinating neuropathy in tempo and electrophysiology but did not require immunotherapy.

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NEGATIVE NERVE BIOPSY IS ONLY AS ACCURATE AS LOCALIZATION: CLINICAL, ELECTRODIAGNOSTIC, AND MRI FINDINGS IN THE DIAGNOSIS OF SCIATIC NEUROPATHY DUE TO CUTANEOUS GRANULOMATOUS MYCOSIS FUNGOIDES

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INTRODUCTION/BACKGROUND: Infiltrative neuropathies are a rare manifestation of lymphoproliferative disorders. To our knowledge, there have only been 2 reported cases of infiltrative mononeuropathy due to granulomatous mycosis fungoides (GMF). Here we present a case of non-traumatic sciatic neuropathy as a rare complication of reportedly stable/resolving cutaneous GMF.

CASE REPORT: A 55-year-old woman with skin biopsy-confirmed cutaneous GMF was hospitalized for subacute progression of painful left foot drop. Outpatient EMG performed 10 months prior demonstrated a chronic peroneal neuropathy thought to be at or proximal to the fibular head. She underwent non-diagnostic superficial peroneal nerve biopsy and unrevealing MRI lumbar spine. She was discharged with presumed vasculitis. In our clinic we noted inversion and plantarflexion weakness localizing to the sciatic nerve. Repeat EMG demonstrated interval loss of sural sensory nerve action potential (SNAP) and active denervation in the short head of the biceps femoris, confirming clinical localization. MRI of her femur showed enhancing induration of subcutaneous soft tissue involving the sciatic nerve. Core biopsy of the soft tissue confirmed GMF.

SUMMARY/CONCLUSION: Diagnostic momentum bias on the basis of her months-old initial EMG resulted in peroneal nerve biopsy and omission of sciatic nerve imaging. Involvement of the sciatic nerve may have been fascicular, involving the peroneal greater than tibial division leading to a false localization at the fibular head. This case demonstrates the importance of considering proximal fascicular lesions in the localization differential for apparent distal mononeuropathies.

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IDENTIFICATION OF MYASTHENIA GRAVIS EXACERBATIONS, CRISES, AND SYMPTOM BURDEN USING RULES-BASED NATURAL LANGUAGE PROCESSING APPLIED TO NEUROLOGIST CLINICAL NOTES

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INTRODUCTION: Myasthenia gravis (MG) is an autoantibody mediated neuromuscular disorder characterized by exacerbations, crises, and heterogeneous symptom patterns. This study examined the use of natural language processing (NLP) to identify MG exacerbations and symptomatology using neurologist clinical notes.

METHODS: A retrospective, cross-sectional analysis was conducted using de-identified transcriptions for 3,085 MG patients and 5,183 neurology encounter notes from 2017 to 2022. A rules-based NLP model was developed to create an analyzable dataset focused on MG clinical status and relevant symptoms. The F1 score (a balanced measure of the model's performance regarding recall and precision) was reported.

RESULTS: F1 reflecting robust model performance at 0.97. Of the 3,085 MG patients, documented changes in MG clinical status included exacerbation (12.6%), crisis (4.4%), and worsening (4.5%). Percentage of patients who reported specific symptoms included ptosis (34.7%), diplopia (30.0%), dysphagia (23.1%), fatigue (22.4%), dyspnea (20.2%), dysarthria (16.6%), generalized weakness (11.3%), extremity weakness (9.1%), face-bulbar weakness (7.5%), respiratory distress-failure (5.5%), and neck weakness (3.9%). Physicians commonly reported patient symptoms "worsening" (37.9%).

CONCLUSIONS: NLP based on neurologist clinical notes illustrates the wide variety of MG symptoms patient suffer from (e.g., ocular, bulbar, appendicular, and respiratory) and fluctuating clinical trajectories as reflected by exacerbations and symptom worsening. Given the paucity of MG clinical scale use in the real-world, NLP can be an important tool to enhance understanding of this complex and heterogeneous disease.

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IDENTIFICATION OF GENERALIZED MYASTHENIA GRAVIS AND ANTIBODY STATUS USING RULES-BASED NATURAL LANGUAGE PROCESSING APPLIED TO NEUROLOGIST CLINICAL NOTES

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INTRODUCTION: Myasthenia gravis (MG) is an autoantibody mediated neuromuscular disorder in which treatment can be informed by generalization and autoantibody subtype. Using rules-based natural language processing (NLP), we assessed the feasibility of identification of meaningful MG subpopulations from physician notes.

METHODS: Retrospective, cross-sectional analysis using de-identified notes from 3,085 MG patients and 5,183 neurology encounters (2017- 2022). A rules-based NLP model was developed to create an analyzable dataset focused upon MG generalization and autoantibody status with an F1 score (a balanced measure of the model's performance regarding recall and precision).

RESULTS: F1 reflecting robust model performance at 0.97. Of the 3,085 MG patients, generalized MG was formally documented in 10.6% of cases (ocular MG 8.2%, bulbar MG 2.4%) and 78.8% (n=2476) patients were unspecified. The 2,474 unspecified MG patients had relevant MG symptoms documented including respiratory (22.8%), ocular (46.8%), bulbar (31.4%), appendicular (9.1%), general weakness (10.6%), and axial (3.9%). Serology documentation included acetylcholine receptor autoantibody positive (14.3%), seronegative (7.9%), MuSK autoantibody negative (1.4%), and MuSK autoantibody positive (0.9%).

CONCLUSIONS: NLP applied to neurologist notes was used to categorize MG patients into meaningful subpopulations with regards to generalization and autoantibody status. Where generalization was not documented, NLP identified relevant MG symptoms with the potential to further clarify MG generalization in over 65% of patients. Serology status was poorly documented. Optimizing specific, meaningful MG population identification can provide greater understanding of clinical needs and enable targeting of optimal treatments.

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REAL-WORLD CHARACTERIZATION OF CHALLENGES RELATED TO THE IDENTIFICATION AND MANAGEMENT OF MYASTHENIA GRAVIS CRISIS

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INTRODUCTION: Myasthenia gravis (MG) can present with a spectrum of severity including myasthenic crisis defined by the need for mechanical ventilation. Using natural language processing (NLP) and note abstraction, we characterized the myasthenic crisis classification compared to documentation, patterns of onset, and challenges with standard MG therapies.

METHODS: Cross-sectional, retrospective analysis using NLP and note abstraction applied to de-identified medical transcriptions of neurologist notes (2017-2022).

RESULTS: Among the 3085 MG patients, 137 (4.4%) myasthenic crisis patients were identified, 100 with the term “crisis” (of whom 36 did not receive mechanical ventilation by documentation) and 37 with no “crisis” term but with mechanical ventilation attributed to MG. Nineteen MG patients had more than 1 crisis, of whom 11 (58%) had repeat events less than 1 month apart. Myasthenic crisis trigger documentation was present in 33 (24%) cases. Among myasthenic crisis cases, documented challenges with standard MG treatments were common (44%) including adverse effects (29%), poor response (12%), interaction with co-morbidity (11%), and poor access (e.g., PLEX not available) or difficulties with insurance (4.3%).

CONCLUSIONS: NLP was able to identify patients with myasthenic crisis, a serious manifestation of MG that is heterogeneous with respect to neurologist documentation and onset with some patients suffering single episodes without trigger or recurrent episodes. Myasthenic crisis management can be complicated by intolerance and/or poor response to standard MG treatments, highlighting the need for more effective therapies with better tolerance in difficult to treat patients.

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PERIPHERAL NERVOUS SYSTEM MANIFESTATIONS OF SJÖGREN SYNDROME

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INTRODUCTION/BACKGROUND: Sjögren syndrome is an inflammatory autoimmune disease which affects multiple organ systems. Common symptoms include dry eyes, dry mouth, myalgias, and fatigue. Extra-glandular symptoms are also possible including neuropathy, nephropathy, or hematological abnormalities.

CASE REPORT: We present a case of a 50-year-old female with a 10-year history of Sjögren syndrome confirmed with SSA antibodies. She presented to the hospital with 2 months of gradual sensory loss and subjective weakness affecting the lower extremities more than the upper extremities to the point that she is now using a walker for ambulation. She had a similar presentation 2 years prior which was thought to be due to Sjögren syndrome and was treated successfully with prednisone, mycophenolate, and hydroxychloroquine. Her current episode is more severe and longer duration than her first episode. On exam, she was noted to have profound loss of proprioception in the lower extremities with mildly reduced sensation to other modalities including pinprick, temperature, and vibration, in a length-dependent manner. Strength is preserved with utilization of visual cues. She was empirically started on IVIg while awaiting further diagnostics and had substantial symptomatic improvement.

SUMMARY/CONCLUSION: There are varying neurological presentations of Sjögren syndrome with peripheral neuropathy being the most common. On NCS/EMG it is most common to find evidence of large fiber axonal sensorimotor neuropathy. In rare cases, sensory ataxic neuropathy has been identified in patients with Sjögren syndrome due to involvement of the dorsal root ganglion. In such cases, there should be strong consideration for a paraneoplastic process. First line treatment for sensory ataxic neuropathy includes IVIg and steroids.

COMORBIDITIES IN PATIENTS WITH MYASTHENIA GRAVIS IN THE USA: A RETROSPECTIVE CLAIMS DATABASE ANALYSIS

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BACKGROUND: Patients with myasthenia gravis (MG) often have comorbidities that contribute to their overall disease burden. These comorbidities can be at risk of exacerbation due to the conventional treatments prescribed for MG.

OBJECTIVE: To characterize the comorbidity burden in patients with MG in the USA.

METHODS: This US retrospective observational cohort study utilized de-identified patient data (01/01/2006-06/30/2019) from the IQVIA insurance claims database. Eligible patients were ≥ 18 years old; had ≥ 2 claims (≥ 30 days apart) with MG diagnoses ICD9 or ICD10 codes; and had ≥ 1 year of continuous enrollment before and after MG diagnosis. Extracted data included demographic and clinical characteristics, comorbidities, treatment history, and follow-up.

RESULTS: Data for 3,516 patients with MG were identified (51.2% male; mean age [standard deviation], 55.8 [13.9]; age range, 18-84 years). The most prevalent comorbidities were cardiovascular and endocrine disorders, including hypertension (41.9%), hyperlipidemia (37.1%), fatigue (24.8%), uncomplicated diabetes (18.2%), cerebrovascular disease (17.6%), and hypothyroidism (15.4%). Patients were often prescribed conventional MG therapies, which have the potential to exacerbate existing comorbid conditions. Within 1 year prior to initiation of corticosteroids, 42.7% and 18.6% of patients had claims for hypertension and uncomplicated diabetes, respectively. Similarly, 14.3% of patients prescribed azathioprine and 6.5% of patients prescribed chronic intravenous immunoglobulin had claims for thromboembolism and malignancy, respectively, within 1 year prior to treatment initiation.

CONCLUSIONS: This study demonstrates the high rates of comorbidities in patients with MG and the importance of considering their potential impact in treatment choice discussions.

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Daniel Basoff - Employee and stockholder of Alexion, AstraZeneca Rare Disease

Anju Parthan - Employee and stockholder of Alexion, AstraZeneca Rare Disease

Raj Bandaru - Employee and stockholder of Alexion, AstraZeneca Rare Disease

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Matthew Kent - Employee of Genesis Research Group, which has received funding from Alexion, AstraZeneca Rare Disease

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REPEATED CYCLES OF ROZANOLIXIZUMAB TREATMENT IN PATIENTS WITH MUSCLE-SPECIFIC KINASE AUTOANTIBODY-POSITIVE GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: The phase 3 MycarinG (MG0003/NCT03971422) study demonstrated efficacy of one 6-week cycle of rozanolixizumab in acetylcholine receptor autoantibody-positive and muscle-specific kinase autoantibody-positive (MuSK Ab+) generalized myasthenia gravis (gMG). Patients could then enroll in open-label extensions MG0004 then MG0007, or MG0007 directly.

OBJECTIVE: To evaluate the efficacy and safety of rozanolixizumab in patients with MuSK Ab+ gMG over repeated cycles of treatment.

METHODS: MG0004 (NCT04124965) evaluated ≤52 weeks of weekly rozanolixizumab infusions. In MG0007 (NCT04650854), after an initial cycle, cycles were administered on symptom worsening (investigator's discretion). Data were pooled across MycarinG, MG0004 (first 6 weeks), and MG0007 (interim analysis): efficacy pool, patients with ≥2 symptom-driven cycles; safety pool, ≥1 cycle including observation periods across MycarinG (symptom-driven) and MG0007 (fixed/symptom-driven).

RESULTS: One hundred twenty-seven (12 MuSK Ab+) patients received ≥2 symptom-driven cycles of rozanolixizumab. Slightly greater changes from baseline to Day 43 in mean MG-ADL score were observed in the MuSK Ab+ subgroup, compared to the overall population: Cycle 1, −7.0 (baseline 10.9; n=12) and −3.7 (baseline 8.9; n=127); Cycle 2, −5.7 (baseline 10.8; n=12) and −3.9 (baseline 9.0; n=127); Cycle 3, −4.7 (baseline 10.6; n=7) and −3.4 (baseline 8.9; n=98); Cycle 4, −4.2 (baseline 9.8; n=6) and −3.8 (baseline 8.9; n=75), respectively. Similar patterns were seen in MGC and QMG. Fourteen out of 18 (77.8%) MuSK Ab+ patients reported ≥1 treatment-emergent adverse event; most were mild to moderate in severity.

SUMMARY/CONCLUSION: Rozanolixizumab efficacy in patients with MuSK Ab+ gMG was maintained over repeated cycles, with an acceptable safety profile, consistent with findings in the overall population.
Funding: UCB Pharma.

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SUBCUTANEOUS ROZANOLIXIZUMAB IN PEDIATRIC PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: CLINICAL STUDY DESIGN

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INTRODUCTION: Rozanolixizumab has demonstrated clinically meaningful and statistically significant efficacy in adults with generalized MG (gMG). The phase 2/3 MG0006 study (roMyG) and phase 3 long-term extension MG0008 (roMyG+) aim to assess the safety, tolerability, pharmacokinetics/pharmacodynamics (PK/PD), and activity of rozanolixizumab in pediatric patients with gMG.

METHODS: MG0006 will include patients aged 2 to <18 years with acetylcholine receptor autoantibody-positive (AChR Ab+) or muscle-specific tyrosine kinase receptor autoantibody-positive (MuSK Ab+) gMG, moderate-severe symptoms and MGFA classification II-IVa requiring additional therapy. Participants will receive 1 rozanolixizumab treatment cycle (6 subcutaneous doses at 1-week intervals) with weight-tiered dosing, followed by an ≤8-week observation period. Patients who complete MG0006 or complete the dosing period and have gMG symptom worsening before the end of the 8-week observation period are eligible for MG0008, in which participants will receive ≤3 rozanolixizumab treatment cycles, based on gMG symptom worsening at the investigator's discretion. Primary safety endpoints in both studies include serious treatment-emergent adverse events (TEAEs), TEAEs leading to permanent rozanolixizumab withdrawal, and AEs of special monitoring. PK/PD analyses are rozanolixizumab concentration and change from baseline (CFB) in total IgG and AChR/MuSK Ab levels. Secondary endpoints include CFB in Myasthenia Gravis Activities of Daily Living total score and Quantitative Myasthenia Gravis total score, to the end of Week 6 of the first (MG0006) or subsequent (MG0008) cycles.

SUMMARY/CONCLUSION: The MG0006 and long-term extension MG0008 studies will evaluate the safety, PK/PD, and activity of subcutaneous rozanolixizumab in pediatric patients. Recruitment is ongoing.
Funding: UCB Pharma.

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SEVERE PREDOMINANTLY MOTOR AXONAL POLYNEUROPATHY AND MYELOPATHY SECONDARY TO NITROUS OXIDE TOXICITY

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INTRODUCTION/BACKGROUND: Nitrous oxide is a commonly used recreational drug that can cause myeloneuropathy. We describe a patient with an unusually severe, predominantly motor, acute axonal polyneuropathy plus myelopathy following nitrous oxide abuse.

CASE REPORT: A 30-year-old woman with history of substance abuse presented with acute bilateral leg weakness and numbness. The patient had consumed a large amount of nitrous oxide prior to the onset of symptoms, which progressed for 5 days before she was admitted. There were no bowel or bladder symptoms. At presentation, she was unable to form coherent sentences. Her examination revealed reduced sensation and severe weakness in the lower extremities, with the upper extremities spared. MRI of the brain was normal. MRI of the cervical and thoracic spine showed symmetric bilateral increased T2 signal abnormalities in the posterior columns. Vitamin B12 levels were undetectable. A diagnosis of subacute combined degeneration due to severe vitamin B12 deficiency in the setting of nitrous oxide toxicity was made. The patient was treated with high dose intravenous vitamin B12 and rehabilitation. The patient had gradual improvement over weeks to months. An EMG 1 year following the initial admission demonstrated a severe, predominantly motor, axonal polyneuropathy affecting the lower extremities with sparing of the sural nerve responses. At this point, patient had no residual sensory symptoms but continued to have spasticity and bilateral foot drop.

SUMMARY/CONCLUSION: Nitrous oxide toxicity should be considered in the differential diagnosis of motor-predominant polyneuropathies and also as a potential cause for acute paraplegia/paraparesis mimicking Guillain-Barre syndrome.

EFFECT OF RNA INTERFERENCE ON CARDIOMYOPATHY AND POLYNEUROPATHY OUTCOMES IN PATIENTS WITH V122I VARIANT HEREDITARY TRANSTHYRETIN-MEDIATED (HATTR OR ATTRV) AMYLOIDOSIS

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INTRODUCTION: Hereditary transthyretin-mediated (ATTRv) amyloidosis is caused by variants in the transthyretin gene. The V122I variant is historically associated with cardiomyopathy, yet evidence of a mixed phenotype including neuropathy is emerging.

OBJECTIVE: Assess the efficacy of RNA interference (RNAi) therapeutics targeting variant and wild-type transthyretin in V122I patients, which has not been reported.

METHODS: In an observational phase 4 study of US patients (NCT04201418), the impact of patisiran, an RNAi therapeutic, on cardiac (Kansas City Cardiomyopathy Questionnaire-Overall Summary [KCCQ-OS], New York Heart Association [NYHA] class, N-terminal pro-brain natriuretic peptide [NT-proBNP]), neuropathy (polyneuropathy disability [PND] score), quality of life (Norfolk Quality of Life-Diabetic Neuropathy [QOL-DN]), and autonomic outcomes (Composite Autonomic Symptom Score 31-item [COMPASS-31], modified body mass index [mBMI]) was assessed in 45 patients with V122I ATTRv amyloidosis over 12 months.

RESULTS: Thirty-two patients completed the study. Mean (SE) KCCQ-OS improved by 5.6 (2.1) points, 81% (25/31) stabilized or improved in NYHA class, and 100% (5/5) had stable (<300 ng/L increase from baseline) NT-proBNP (mean [SE] change, + 20.7 [20.9] ng/L). Patients improved in Norfolk QOL-DN (mean [SE] change, –4.6 [4.0]), COMPASS-31 (–11.2 [5.2]), orthostatic intolerance (–5.3 [4.6]), and mBMI (73.0 [67.5]); 94% (30/32) improved or stabilized their PND score. Patients improved as early as Month 6 in NT-proBNP, KCCQ-OS, and PND score. Patisiran was generally well-tolerated, consistent with the established safety profile.

SUMMARY/CONCLUSION: In this study, patisiran-treated V122I ATTRv amyloidosis patients improved or stabilized in cardiac and neurologic outcomes, consistent with results of randomized controlled studies of RNAi therapeutics in ATTR amyloidosis.

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Steven Roblin - Employee and stockholder of Alnylam Pharmaceuticals

Elena Yureneva - Employed by Alnylam Pharmaceuticals

Lin-Na Chou - Former contractor of Alnylam Pharmaceuticals

Patrick Jay - Employee and stockholder of Alnylam Pharmaceuticals

Kelley Capocelli - Employee and stockowner of Alnylam Pharmaceuticals

Miriam Freimer - On advisory board for Alexion, argenx, UCB Research; receives funding from Acceleron, Alnylam, Amicus, Catalyst, Avidity, Ionis, Immunovant, Jansenn, Roche, UCB, and NIH

POVETACICEPT (ALPN-303), A POTENT DUAL BAFF/APRIL ANTAGONIST, FOR THE TREATMENT OF MYASTHENIA GRAVIS AND OTHER ANTIBODY-RELATED DISEASES

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INTRODUCTION: Povetacicept is an Fc fusion protein of an engineered TACI domain with significantly more potent dual inhibition of APRIL and BAFF than wild type (WT) TACI-Fc (e.g., telitacicept).

OBJECTIVE: To evaluate povetacicept for pharmacodynamics (PD) and efficacy in a murine experimental autoimmune myasthenia gravis (EAMG) model, and for safety, pharmacokinetics (PK), and PD in adult healthy volunteers (HV).

METHODS: Mice were immunized with acetylcholine receptor (AChR) and treated after disease onset with povetacicept, Fc control, or telitacicept, twice weekly for 7 injections. HV were studied in single ascending dose cohorts of intravenous (IV) or subcutaneous (SC) povetacicept or placebo (NCT05034484). Safety, PK, and circulating immunoglobulins (Ig) and leukocyte populations were assessed.

RESULTS: Povetacicept-treated EAMG mice demonstrated significantly lower clinical disease scores and serum anti-AChR IgG antibody levels than controls. In adult HV, povetacicept was well tolerated in all cohorts evaluated as single IV or SC doses of up to 960 mg. It exhibits dose-related PK, and its expected PD effects, including reductions in circulating Ig and antibody-secreting cells, appear greater than those reported for WT TACI-Fc-treated HV. There were no imbalances of infections between placebo and povetacicept groups, no serious adverse events, no infusion-related or injection site reactions other than grade 1 injection-site pain, and no adverse trends in safety laboratories.

SUMMARY/CONCLUSION: Povetacicept demonstrates promising efficacy in a preclinical EAMG model and has demonstrated acceptable safety and tolerability and exhibits expected PD effects in adult HV. Future studies of povetacicept in MG and other autoantibody-related neurological diseases are therefore strongly supported.

Disclosures:

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HEREDITARY TRANSTHYRETIN AMYLOIDOSIS WITH POLYNEUROPATHY: A CASE REPORT

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INTRODUCTION/BACKGROUND: Hereditary transthyretin amyloidosis (hATTR) with polyneuropathy is an uncommon genetic disorder that arises from a mutation in the transthyretin protein. It causes impaired peripheral nerve and organ function, with diverse clinical manifestations and genetic variability. Due to its infrequent occurrence and lack of clear family history, misdiagnosis is common, leading to diagnostic delays that can last several years.

CASE REPORT: A 67-year-old right-handed man complained of bilateral lower extremity numbness, tingling, and pain that had persisted for about a year. His medical history included bilateral carpal tunnel syndrome (CTS) and hypothyroidism. The numbness and tingling radiated from the knees down into the feet and involved all toes. Pain involved the right knee extending into the right lateral thigh with a sharp character and maximum pain intensity of 5/10. EMG showed moderate sensorimotor polyneuropathy with axonal and demyelinating features. Extensive bloodwork to find possible common causes of polyneuropathy showed negative results. Genetic testing revealed a heterozygous p.Phe84Leu mutation variant, indicating autosomal dominant hATTR. At that time, the patient recalled several family members had CTS. A cardiac work-up for cardiomyopathy was negative. The patient was placed on patisiran infusion with a vitamin A supplement. We scheduled a follow-up in 2-3 months to see if he had any improvement.

SUMMARY/CONCLUSION: The diagnosis of hATTR presents a challenge due to its low prevalence and nonspecific clinical presentations. We suggest that genetic testing be considered in patients with idiopathic neuropathy. Further evaluation is warranted to exclude amyloid involvement in other organ systems.

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USING REAL-WORLD EVIDENCE TO UNDERSTAND THE DIAGNOSTIC JOURNEY OF PEOPLE LIVING WITH MYASTHENIA GRAVIS AND ITS IMPACT ON MENTAL HEALTH

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INTRODUCTION: Understanding individuals' needs within a community necessitates active listening regarding the patient experience. A proprietary artificial intelligence (AI) engine was applied to social media conversations on mental health (MH) for individuals with myasthenia gravis (MG), an autoimmune disease that causes fatigue and skeletal muscle weakness. MG is associated with poorer MH, but it is not well understood how MH might be affected by diagnostic stage.

OBJECTIVE: To reveal differences in MH conversations before and after beginning the MG diagnostic journey.

METHODS: This AI platform used natural language processing to identify prevalent conversational terms/concepts. We evaluated 3 public MG subreddits with 6169 posts/replies from 528 active members from 2013-2022, and an additional 1800 posts/replies from these members across 12 MH-related subreddits.

RESULTS: AI identified conversations with a high probability (>0.80) of discussing 'mental health'; these were used in cluster analyses to evaluate topic prevalence. 'Diagnosis' was a frequent topic. Conversations were filtered for before and after users contributed to MG subreddits. Anxiety terms occurred more in 'pre-dx' statements (13.1%) but depression terms more in 'post-dx' statements (14.2%). Regarding affect, 'pre-dx' statements were weighted mostly on 'trust' words (16.9%) vs 'sadness' words in 'post-dx' statements (17.2%).

SUMMARY/CONCLUSION: We explored MG community member profiles before and after joining MG subreddits. Anxiety in group 'pre-dx' might reflect individuals trying to understand their symptoms, whereas depression in group 'post-dx' could be driven by the diagnostic journey outcome. These findings can be invaluable for elucidating intersections of MH and disease management, which typically is not explored in traditional approaches.

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Anthony Amatucci - Employee and shareholder of Horizon Therapeutics

Kristina Davidson - Employee and shareholder of Horizon Therapeutics

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REGIONAL DISPARITIES IN TREATMENT OUTCOMES AMONG PATIENTS WITH GUILLAIN-BARRE SYNDROME

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INTRODUCTION: Studies have shown the presence of regional disparities in both access to care and treatment outcomes among hospitalized patients. However, the impact of location on treatment outcomes among patients hospitalized with Guillain-Barre syndrome (GBS) has not been fully characterized.

OBJECTIVE: To investigate regional disparities in treatment outcomes among hospitalized GBS patients.

METHODS: A retrospective analysis of 96,880 hospitalizations from 2016 to 2020 for patients hospitalized with GBS was conducted using the National Inpatient Sample database. The mean age was 58 years, with 50,645 (52.3%) males and 46,210 (47.7%) females. 2,830 (2.9%) deaths were reported. Outcomes among patients receiving care in rural communities (RC) were compared to patients in urban communities (UC). Patient demographics and comorbidities were included in the logistical regression analysis.

RESULTS: Among hospitalized GBS patients, RC had no significant difference in mortality compared to UC (2.9% vs 2.9%, p=1). Among those who died with GBS, RC had a significantly higher proportion of males (54.3% vs 43.1%, p<0.01), white patients (82.4% vs 72.4%, p<0.001), low-income status (82.4% vs 53.4%, p<0.001), lung disease (37.1% vs 22%, p<0.001), and thyroid disease (20% vs 13.6%, p<0.05). UC had a significantly higher amount of autoimmune disease (6.2% vs 0.0%, p<0.001) and peripheral vascular disease (8.3% vs 2.9%, p<0.05) than RC.

SUMMARY/CONCLUSION: Our results suggest that there is no significant difference in mortality between RC and UC. However, further studies are needed to investigate how patient comorbidity profiles impact outcomes between RC and UC.

RACIAL DISPARITIES IN TREATMENT OUTCOMES AMONG PATIENTS WITH CEREBRAL PALSY

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INTRODUCTION: Studies have shown the existence of racial disparities in both the delivery and outcomes of care among hospitalized patients. However, the impact of race and income on treatment outcomes among patients with cerebral palsy (CP) within the inpatient setting has not been fully characterized.

OBJECTIVE: To investigate potential racial disparities in treatment outcomes among hospitalized CP patients.

METHODS: A case-controlled retrospective analysis of 392,420 hospitalizations from 2016 to 2020 for patients with CP was conducted using the National Inpatient Sample database. The mean age was 45.6 years, with 218,250 (55.6%) males and 174,135 (44.4%) females. There were 10,355 deaths (2.6%) reported. Outcomes among Black and Hispanic (BH) patients were compared to all other race categories (nBH). A broad range of patient demographics and comorbidities were included in our analysis.

RESULTS: Among hospitalized CP patients, BH compared to nBH had significantly less mortality (2.4% vs 2.9%, $p<0.01$), lower mean age (39.2 vs 48.5 years, $p<0.05$), and significantly higher non-elective admissions (90.5% vs 89.9%, $p<0.036$), length of stay (7.1 vs 6.5 days, $p<0.05$), and care at a teaching hospital (78.6% vs 71.4%, $p<0.001$). There were significantly higher levels of hypertension (35.3% vs 30.6%, $p<0.001$), substance use disorders (2.2% vs 1.6%, $p<0.001$), and thyroid disease (16.4% vs 8.6%, $p<0.001$) among nBH patients hospitalized with CP.

SUMMARY/CONCLUSION: Our results suggest BH patients had significantly longer length of stay compared to nBH, however, BH had significantly less mortality. Further studies are needed to further characterize the racial disparities in treatment outcomes among patients with CP.

NERVE CONDUCTION STUDIES IN PATIENTS WITH FAMILIAL DYSAUTONOMIA

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INTRODUCTION: Nerve conduction studies (NCS) can help to characterize peripheral neuropathy in patients with familial dysautonomia (FD).

OBJECTIVE: To define NCS abnormalities in patients with FD.

METHODS: NCS were evaluated in 35 patients with FD (28.3±13 years old) and 34 age-matched healthy controls (30.2±10 years old). Motor and sensory responses were assessed in ulnar, peroneal, and sural nerves. T-tests were used for between group comparisons.

RESULTS: As compared to controls, patients with FD showed: 1) significantly increased latencies in motor peroneal (5.5±2.1 vs 4.4±0.7 ms, $p=0.03$), motor ulnar (3.1±0.6 vs 2.8±0.4 ms, $p=0.02$), sural (2.4±0.3 vs 2.2±0.2 ms, $p=0.04$), and sensory ulnar (2.5±0.6 vs 2.1±0.3 ms, $p=0.02$) nerves; 2) significantly decreased conduction velocities of motor peroneal (40.5±5.4 vs 52±4.7 m/s, $p=0.001$), motor ulnar (48.8±4.7 vs 59.1± 4.8 m/s, $p=0.00$), sural (42.7±6.7 vs 48.9±2.8 m/s, $p=0.001$), and sensory ulnar (47.1±7.6 vs 53±4.4 m/s, $p=0.001$) responses; 3) significantly decreased amplitudes of motor peroneal (4.8±3.3 vs 9.1± 3.8 mV, $p=0.001$), sensory sural (15.5±8.7 vs 30.8±9.7 uV, $p=0.001$), and sensory ulnar (25.3±3.2 vs 40.6±2.8 uV, $p=0.04$) responses. The ulnar motor responses showed similar amplitudes in patients and controls (16.4±4.4 vs 15.5±3.9 uV).

SUMMARY/CONCLUSION: Patients with FD have axonal and demyelinating abnormalities in both sensory and motor fibers. Demyelination of motor fibers appears to be less severe than in other hereditary neuropathies but, nevertheless, apparent in many patients with FD. Decreased motor and sensory amplitudes indicate a reduced number of axons. Sensory responses are more affected than motor responses. Lower limbs are more affected than upper limbs.

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NERVE CONDUCTION STUDIES IN ANGELMAN SYNDROME

Suemin Yoon (Chicago, IL), Elizabeth Berry-Kravis (Chicago, IL), Rabia Malik (Chicago, IL)

INTRODUCTION: Results of nerve conduction studies (NCS) have not been previously published for patients with Angelman syndrome (AS). As AS is associated with reduced central myelin, there have been concerns that myelin might not be normal in the peripheral nerve. In the recent clinical trial of GTX-102, a dose-dependent adverse effect of leg weakness was seen secondary to acute polyradiculopathy. Therefore, it was important to establish whether NCS showed any abnormalities at baseline in these patients.

OBJECTIVE: To assess whether any peripheral nerve abnormalities are associated with AS.

METHODS: Baseline nerve conduction studies were performed for 10 patients with AS. Right ulnar, sural, and superficial peroneal sensory as well as right ulnar, common peroneal, and tibial motor responses were obtained with surface electrodes under anesthesia. Right ulnar, peroneal, and tibial F waves were obtained when the patients were awake.

RESULTS: Ten children, between the ages of 4 and 8, with AS were studied. The amplitudes, latencies, and conduction velocities obtained were all within normal limits for studied sensory and motor nerves. The F waves were present and persistent in all patients.

SUMMARY/CONCLUSION: NCS in AS are normal and can be measured under anesthesia. F waves can be obtained without anesthesia. These studies provide reassurance against concerns for any peripheral myelination defects in AS, and provide a useful baseline for evaluation of potentially concerning lower extremity weakness in future trials of ASOs or gene therapy delivered by lumbar intrathecal infusion.

Disclosures:

Elizabeth Berry-Kravis - Site PI for Ultragenyx Pharmaceutical Inc

Rabia Malik - Consultant trial design for GeneTx Biotherapeutics

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PAIN-RELATED EVOKED POTENTIALS: NORMATIVE DATA

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INTRODUCTION: The development of the planar concentric electrode for stimulation allowed the advance in the clinical applicability of pain-related nociceptive evoked potentials (PREP), a non-invasive and reliable electrophysiological procedure that can assess A-delta fiber signal transmission without major expense.

OBJECTIVE: The availability of normative data allows establishing physiological criteria and inferring pathological variations, so our objective was to determine PREP latencies and amplitudes in a healthy adult population in southern Brazil.

METHODS: We studied 20 healthy volunteers, with a mean age of 38 years. PREP were elicited bilaterally by stimulation in the hands (medial phalanx of the second digit) and feet (back). Potentials were recorded above Cz by an electrode placed superficially referred to the linked ear lobes.

RESULTS: In the 10 women with a mean age of 37.4 years, the mean latency of the N1 wave after hand stimulation was 143.79 ms with an amplitude of 2.93 uV, after foot stimulation the latency was 192.42 ms with an amplitude of 2.47 uV. In the 10 men studied, mean age of 38.8 years, N1 in the hands was 134.59 ms with an amplitude of 4.19 uV and in the feet 184.15 ms and 2.63 uV.

CONCLUSION: The average latency of the N1 wave in our study was 139.19 ms with 3.56 uV of amplitude, after stimulation of the hand, and 188.29 ms and 2.55 uV of amplitude when the foot was stimulated. Knowing PREP normative data can help clarify an important diagnostic gap in increasingly prevalent and challenging conditions, such as small fiber neuropathies.

ANALYSIS OF INDICATIONS FOR ELECTRONEUROMYOGRAPHIC STUDIES

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INTRODUCTION: Complementary examination of interest to several areas of health and medical specialties, the EDX constitutes an extension of the clinical neurological examination and an important aid in the positive diagnosis, differential diagnosis, and/or prognosis of numerous diseases that affect both the central or peripheral nervous system, the neuromuscular junction, and the muscles.

OBJECTIVE: To determine the main medical specialties that request EDX and their main indications in a center in southern Brazil.

METHODS: We carried out a descriptive and retrospective study of patients evaluated at an electrodiagnostic center during the period from January 1, 2016 to December 31, 2018. Data, age, gender, specialty of the requesting physician, justification for the indication or diagnostic hypothesis, and type of examination were tabulated and statistically analyzed.

RESULTS: During the study period, 4093 people over 16 years of age were assessed, with an average of 51 years of age, 67.9% female. There were 1876 exams requested by orthopedists (45.8%), 579 by neurologists (14.14%), and 554 (13.53%) by neurosurgeons. The hypotheses most commonly formulated were neuropathic pain, fibromyalgia, polyneuropathy, and mononeuropathy, the most frequent being carpal tunnel syndrome.

CONCLUSION: The correct indication of these procedures leads to an optimization of the technical and human resources involved, and as a result a correct management of patients, the most important focus in this chain of medical care. The results of our study showed that most EDX exams are ordered by a specialist and that, among these, the majority of requests come from orthopedists, neurologists, and neurosurgeons.

BICKERSTAFF BRAINSTEM ENCEPHALITIS IN A YOUNG PATIENT: A CASE REPORT IN BOGOTA, COLOMBIA

Andrea Bonfante (Bogota, Colombia), Luisa Guzman (Bogota, Colombia), Josue Moreno (Bogota, Colombia)

INTRODUCTION/BACKGROUND: Bickerstaff brainstem encephalitis is a rare neurological disorder characterized by the presence of ophthalmoplegia, ataxia, and altered consciousness. The pathophysiology is still not understood. It was considered a variant of Miller Fisher syndrome, however, it differs due to the presence of central nervous system involvement. We present a case of a young man who presented Bickerstaff brainstem encephalitis.

CASE REPORT: Our patient was a healthy 20-year-old man. In March 2022, after a 15-day history of headache, behavioral changes, and social withdrawal, he presented with progressive lower limb weakness and dysphagia. Findings at neurological examination were somnolence, bradypsychia, ophthalmoparesis, facial diplegia, dysphagia, dysphonia, and symmetric weakness in lower limbs with areflexia and ataxic gait. Cerebrospinal fluid protein was normal; MRI of the brain with gadolinium showed focal hyper signals on T2 sequences, located in pons-bulb junction, the tectal region midbrain and thalamus. Study of peripheral nerves showed acute axonal motor neuropathy of the upper and lower limbs. Serum anti-GQ1b was negative but it was taken during plasmapheresis. According to clinical and neurophysiological findings, Bickerstaff brainstem encephalitis was diagnosed.

SUMMARY/CONCLUSION: Bickerstaff brainstem encephalitis has several differential diagnoses that require high clinical suspicion due to its low prevalence, progressive course, and usually benign outcome with adequate management and rehabilitation process.

DESIGN OF A PHASE 2 CLINICAL PROGRAM FOR THE DEVELOPMENT OF PGN-EDO51 IN PARTICIPANTS WITH DUCHENNE MUSCULAR DYSTROPHY

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INTRODUCTION: PepGen's Enhanced Delivery Oligonucleotide (EDO) cell-penetrating peptide technology is engineered to optimize tissue delivery and cellular uptake of therapeutic oligonucleotides. Delivery of oligonucleotides is a major challenge that limits their efficacy. PGN-EDO51 is being evaluated for the treatment of Duchenne muscular dystrophy (DMD) amenable to exon 51 skipping. A phase 1 safety study in healthy male volunteers showed high levels of exon skipping at tolerable doses.

OBJECTIVE: The PGN-EDO51 program is designed to evaluate the safety and tolerability of multiple intravenous doses of PGN-EDO51. Secondary and exploratory objectives include evaluation of PK in plasma and muscle, exon skipping, production of dystrophin, and selected functional assessments.

METHODS: The study will enroll males ≥10 years with confirmed DMD amendable to exon 51 skipping. PGN-EDO51 will be administered at ascending doses through multiple cohorts. Participants will receive PGN-EDO51 at Baseline and Weeks 4, 8, and 12. Open muscle biopsies (biceps) will be performed at Baseline and Week 13 for measurement of dystrophin, exon 51 skipping, and PGN-EDO51 concentration. Functional assessments and patient-reported outcomes will be assessed at baseline and Week 16. An independent data and safety monitoring board will oversee dose escalation.

RESULTS: The design of the study will be presented, including planned safety measures (vital signs, electrocardiograms, clinical chemistry, urinalysis, and biomarkers), measurements of pharmacodynamic effect (exon skipping, dystrophin), and exploratory outcomes.

SUMMARY/CONCLUSION: This phase 2, multicenter, multiple-ascending dose study will support continued development of PGN-EDO51 for the treatment of DMD and will be initiated in 2023.

Disclosures:

Jane Larkindale - Holds stock options in PepGen Inc; received an honorarium from NINDS for participation in an advisory committee

Michelle Mellion - Employee and stock options in PepGen Inc

Jennifer Cormier - Employee and stock options in PepGen Inc

Sarah Vacca - Employee and stock options in PepGen Inc

Jennifer Shoskes - Employee and stock options in PepGen Inc

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PERIPHERAL NERVE INVOLVEMENT IN NEURONAL INTRANUCLEAR INCLUSION DISEASE: PROSPECTIVE CLINICAL AND NEUROPHYSIOLOGICAL STUDIES

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INTRODUCTION: Neuronal intranuclear inclusion body disease (NIID) has a broad spectrum of clinical manifestations. Central nervous system involvement in NIID has been widely concerned, while peripheral nerve involvement has not been well elaborated.

OBJECTIVE: To assess the clinical and electrophysiological features of peripheral neuropathy in NIID.

METHODS: Thirty-four patients diagnosed with NIID were recruited in one center. Clinical symptoms and detailed neurological examinations were recorded. All patients underwent standard peripheral nerve motor and sensory NCS, F-wave, and needle EMG.

RESULTS: There were 12 males and 22 females, with a mean age of 62.79±9.59 years. Eight patients (23.5%) presented muscle weakness caused by peripheral neuropathy. Twenty-five patients (73.5%) had decreased tendon reflexes. Six patients (17.6%) had sensory disturbance associated with peripheral neuropathy. Under electrophysiological examination, 32 patients (94.1%) showed abnormal NCS and/or needle EMG. Five patients showed slow-down motor and sensory nerve conduction velocity, prolonged distal motor latency and F latency.15 patients showed isolated prolonged F latency. The other 12 patients had slow-down motor and sensory conduction velocity with decreased compound motor action potential/sensory nerve action potential amplitude, and 2 of them showed spontaneous potentials and chronic neurogenic changes on needle EMG. The incidence of prolonged F wave latency of the tibial nerve was 84% (mean 58.30±7.57m/s) and that of the ulnar nerve was 65% (mean 29.35±3.51m/s).

SUMMARY/CONCLUSION: Although only one-fourth of patients present corresponding clinical manifestations, 94% of NIID patients have peripheral polyneuropathy, characterized by myelin dysfunction on electrophysiology. F-wave detection is helpful to detect subclinical peripheral neuropathy.

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CELLULAR AND IN VIVO PRECLINICAL PHARMACODYNAMICS AND PHARMACOLOGY OF NIPOCALIMAB, A HIGH-AFFINITY, FULLY HUMAN ANTI FCRN BLOCKING THERAPEUTIC ANTIBODY

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INTRODUCTION: The molecular, cellular, and in vivo pharmacology of nipocalimab are shown to be well aligned with pharmacodynamic and pharmacological effects observed in myasthenia gravis (MG) patients.

OBJECTIVE: To characterize nipocalimab's mechanism of action, pharmacodynamics, and pharmacology in preclinical models.

METHODS: Nipocalimab in vivo receptor occupancy (RO) was assessed in a fluorescence-activated cell sorting assay in human aortic endothelial cells. In vivo, RO in circulating monocytes and total serum immunoglobulin G (IgG) were evaluated in human FcRn transgenic mice (Tg32 strain) or cynomolgus monkeys after intravenous infusions of up to 100 or 300 mg/kg nipocalimab, respectively.

RESULTS: Nipocalimab exposure at picomolar concentrations results in full RO within 30 minutes and inhibits IgG recycling in endothelial cells. In vivo, full RO was established within 2 hours in mice and 4 hours in monkeys and maintained at picomolar concentrations. Onset of IgG lowering due to inhibition of IgG recycling was detected within 1-2 days and maintained during the period of full FcRn saturation. Duration of RO in peripheral blood monocytes in both species was dose dependent, as was the duration of IgG clearance, suggesting a relationship between RO and maintenance of increased IgG clearance rate. Nipocalimab in vivo FcRn RO and IgG recycling correlated well with in vivo RO and IgG lowering.

SUMMARY/CONCLUSION: Nipocalimab is a potent FcRn blocker inducing rapid and sustained lowering of IgG and IgG autoantibodies in preclinical studies. These results are consistent with findings from the phase 1 healthy volunteer (NCT02828046) and phase 2 VIVACITY studies in gMG patients (NCT03772587).

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Amit Choudhury - Employee or contractor of Janssen Pharmaceutical Company and may own stock or stock options in Johnson & Johnson

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OVERVIEW OF THE SAFETY PROFILE FROM EFGARTIGIMOD CLINICAL TRIALS IN PARTICIPANTS WITH DIVERSE IMMUNOGLOBULIN G-MEDIATED AUTOIMMUNE DISEASES

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INTRODUCTION: Efgartigimod is a first-in-class human immunoglobulin G (IgG) Fc fragment that inhibits the neonatal Fc receptor (FcRn) and outcompetes endogenous IgG binding. This results in reduced recycling and increased degradation of IgGs, including pathogenic IgG autoantibodies. FcRn inhibition by efgartigimod is a rational therapeutic option for IgG-mediated autoimmune disorders.

METHODS: Intravenous efgartigimod safety was assessed in generalized myasthenia gravis (gMG) in phase 2 and 3 (ADAPT) trials and a 3-year open-label extension (ADAPT+) trial, in primary immune thrombocytopenia (ITP) in a phase 3 trial (ADVANCE), and in pemphigus (vulgaris and foliaceus) in an open-label phase 2 trial. These studies examined different dosing regimens of efgartigimod (10–25 mg/kg), including cyclical dosing in gMG and continuous weekly dosing in ITP and pemphigus.

RESULTS: Across all indications and doses studied, efgartigimod demonstrated a consistent safety profile, with comparable treatment-emergent adverse event (TEAE) rates to placebo (ADAPT 77.4% efgartigimod/84.3% placebo; ADVANCE 93.0% efgartigimod/95.6% placebo; and pemphigus 85% efgartigimod). Most TEAEs were mild to moderate in severity. Discontinuation rates due to adverse events were consistently low (ADAPT 3.6% efgartigimod group/3.6% placebo; ADVANCE 3.5% efgartigimod/2.2% placebo; and 3% of pemphigus study participants). Efgartigimod was well tolerated in ADAPT+, with no increase in TEAE incidence rates, including infections, with repeated efgartigimod cycles (up to 19). Efgartigimod treatment did not reduce albumin levels or increase cholesterol levels.

SUMMARY/CONCLUSION: Efgartigimod is well tolerated across indications and doses studied. Most TEAEs, including infections, were mild or moderate in severity and did not increase in frequency with recurrent dosing.

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EARLY DIAGNOSTIC AND PROGNOSTIC VALUE OF REPETITIVE NERVE STIMULATION IN AMYOTROPHIC LATERAL SCLEROSIS

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INTRODUCTION: Previous studies have shown the decremental responses to low-frequency repetitive nerve stimulation in patients with ALS, but the decrement percentages were usually lower than the diagnostic standard.

OBJECTIVE: Our study applied repetitive nerve stimulation to assess the function of neuromuscular junction in patients with ALS and expected to find new diagnostic cut-off values within the clinical background of ALS.

METHODS: We conducted a prospective study, in which clinically suspected ALS patients were enrolled. Comprehensive electrophysiological examinations were performed on ALS patients and their clinical data was recorded in detail. Patients without ALS and neuromuscular junction diseases were included as controls.

RESULTS: The decrement percentages of upper limb nerves in ALS patients were not correlated with the rate of disease progression and the stage of disease but were negatively correlated with the upper limb functional score. The decrement percentage was significantly higher in the nerve which was located in the site of onset and in the nerve, whose matching muscle was positive in EMG test. In our study, new diagnostic cut-off values within the clinical background of ALS were 5.1% for accessory nerve, 5% for axillary nerve, and 3.9% for median nerve.

CONCLUSION: Neuromuscular junction injury plays an important role in the development of ALS and may be also involved in the development of “split hand”. The decrement percentage of median nerve has relatively higher specificity and sensitivity in the diagnosis of ALS and may be used in the prediction of “split hand” phenomenon in ALS patients.

LONG-TERM SAFETY, TOLERABILITY, AND EFFICACY OF SUBCUTANEOUS EFGARTIGIMOD PH20 IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: INTERIM RESULTS OF THE ADAPT-SC+ STUDY

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INTRODUCTION: In the ADAPT-SC study, subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20) was shown to have noninferior total IgG reduction to efgartigimod IV, resulting in similar clinical improvement in patients with generalized myasthenia gravis (gMG). Patients completing ADAPT-SC or enrolled in efgartigimod IV open-label extension (OLE) ADAPT+ were eligible for the ongoing OLE, ADAPT-SC+.

OBJECTIVE: Evaluate long-term safety, tolerability, and efficacy of efgartigimod PH20 SC in patients with gMG enrolled in the ADAPT-SC+ OLE.

METHODS: Efgartigimod PH20 SC 1000 mg was administered in cycles of 4 weekly injections. Subsequent cycles were initiated ≥28 days from the last dose based on clinical evaluation. Myasthenia Gravis Activities of Daily Living (MG-ADL) score assessed clinical efficacy.

RESULTS: As of March 2022, 164 participants received ≥1 dose of efgartigimod PH20 SC, with an average of ≈3 treatment cycles over a mean (SD) study duration of 170 (59) days, resulting in 72 patient-years of observation. Adverse events (AEs) were predominantly mild/moderate. Most frequent AEs were injection site erythema (25.6%), headache (15.2%), and COVID-19 (11.6%). Injection site reactions were mild/moderate, did not lead to treatment discontinuation, and decreased in incidence with subsequent cycles. Improvement from cycle baseline in MG-ADL total score (mean [SE] improvement at week 4: -4.0 [0.25]) was observed in cycle 1, with consistent and repeatable improvements seen in subsequent cycles. Observed improvements were similar to those seen with efgartigimod IV during ADAPT/ADAPT+.

SUMMARY/CONCLUSION: Results suggest that treatment with multiple cycles of efgartigimod PH20 SC was well tolerated and efficacious, consistent with efgartigimod IV in ADAPT/ADAPT+.

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THE GENERALIZED MYASTHENIA GRAVIS DIAGNOSTIC JOURNEY AND TREATMENT INITIATION: EUROPEAN AND US REAL-WORLD PERSPECTIVES FROM PHYSICIAN AND PATIENT SURVEYS

Jenny Park (Deerfield, IL), Gregor Gibson (Bollington, United Kingdom), Emma Chatterton (Bollington, United Kingdom), Anthony Amatucci (Deerfield, IL), Elizabeth Crane (Deerfield, IL), Cornelia Fuller (Deerfield, IL), Kristina Patterson (Deerfield, IL), Hari Patel (Deerfield, IL)

INTRODUCTION: Generalized myasthenia gravis (gMG) is a rare, chronic autoimmune disease that causes debilitating and potentially life-threatening muscle weakness. Patients may endure multiple exams and referrals before diagnosis, delaying treatment.

OBJECTIVE: This study characterizes and compares the European and US gMG patient journeys from symptom onset to diagnosis and treatment initiation.

METHODS: Data was drawn from an Adelphi Disease Specific Programme, a survey of providers and patients with gMG in France, Germany, Italy, Spain, the UK, and the US, collected from March to September 2020.

RESULTS: Of the 557 patients with gMG included, mean age was 53.2 (SD: 15.9) years, 50.3% were female, and 36.9% were from the US. The mean time from symptom onset to gMG diagnosis was 9.8 (SD: 13.7) months. Most common symptoms included ocular myasthenia (59.4%), ptosis (58.9%), and general fatigue (58.7%). Most patients consulted primary care physicians (62.1%) and were then diagnosed by neurologists (79.9%). Providers, on average, used 8.7 (SD: 4.2) tests to aid gMG diagnosis. Among those previously misdiagnosed (26.9%), the most common misdiagnoses were chronic fatigue syndrome (34.7%) and multiple sclerosis (14.7%). Treatment initiation was, on average, 3.2 (SD: 7.7) months following diagnosis. Acetylcholinesterase inhibitors (73.8%) were the most commonly initiated, followed by steroids (42.9%) and immunosuppressive therapies (36.0%). Geographic differences between countries were noted.

SUMMARY/CONCLUSION: In this international survey, patients with gMG were diagnosed 10 months following symptom onset and initiated treatment 3 months following diagnosis. Optimizing the diagnosis and treatment pathways may improve health outcomes among patients with gMG.

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Jenny Park - Employee and stockholder of Horizon Therapeutics

Gregor Gibson - Employee of Adelphi Real World

Emma Chatterton - Employee of Adelphi Real World

Anthony Amatucci - Employee and stockholder of Horizon Therapeutics

Elizabeth Crane - Employee and stockholder of Horizon Therapeutics

Cornelia Fuller - Employee and stockholder of Horizon Therapeutics

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Hari Patel - Employee and stockholder of Horizon Therapeutics

NON-NEUROMUSCULAR PATHOLOGIES IN PATIENTS PRIMARILY REFERRED FOR NEUROMUSCULAR ULTRASOUND: REPORT OF TWO CASES

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INTRODUCTION: Neuromuscular ultrasound (NMUS) is a diagnostic tool used to identify structural abnormalities in nerves and/or muscles. However, in some instances scanning may reveal non-neuromuscular pathologies as the primary cause of the patient's symptoms.

OBJECTIVE: To present 2 cases with different non-neuromuscular pathologies encountered during neuromuscular ultrasound.

CASE REPORTS: The first case was a 52-year-old female with chronic painful small swelling at the dorsal forearm and numbness along the lateral side of the forearm. Ganglion cyst with possible pressure on the superficial radial nerve was suspected. Scanning did not reveal ganglion cyst nor nerve abnormality. Instead, an oblong, vascular, non-pulsating, non-compressible, predominately hypoechoic nodule was observed in the subcutaneous tissue. Histopathological findings after surgical excision were consistent with arteriovenous malformation. The second case was a 27-year-old female who was referred for NMUS of the right suprascapular nerve. The patient had a previous history of right suprascapular nerve entrapment, for which she underwent nerve release. Post-surgery, the patient did not significantly improve and complained of persistent right upper shoulder pain. No sonographic abnormalities were found in the suprascapular nerve. However, scanning the painful area revealed a small, round, well defined, hypoechoic, and avascular nodule running in the fascia overlying the upper trapezius. The patient underwent surgical excision and subsequent histopathological assessment revealed lobulated capillary hemangioma. The 2 patients reported complete improvement of the symptoms post-surgical excision.

SUMMARY/CONCLUSION: The 2 case reports highlight the importance of meticulous scanning of all tissue layers when no pathologies are found in nerves and/or muscles to avoid missing non-neuromuscular pathologies.

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A PHASE 2/3 PLACEBO-CONTROLLED, PARALLEL GROUP, RANDOMIZED WITHDRAWAL STUDY EVALUATING EFFICACY AND SAFETY OF NIPOCALIMAB IN ADULTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY: ARISE STUDY

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INTRODUCTION: Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare autoimmune disease of the peripheral nervous system characterized by progressive weakness and impaired sensation.

OBJECTIVE: The ARISE study (NCT05327114) evaluates the efficacy and safety of nipocalimab, an anti-neonatal Fc receptor monoclonal antibody in adults with CIDP.

METHODS: The study consists of the following periods: (1) Screening (≤4 weeks)/Run-in (≤12 weeks), which includes identification of patients with active CIDP; (2) Stage A (open-label, 12 weeks), in which participants receive nipocalimab loading dose, then once every 2 weeks (q2w); (3) Stage B (double-blind, placebo-controlled, ≤52 weeks), in which participants are randomized 1:1 to nipocalimab q2w versus placebo; (4) Open-label extension (variable duration), in which participants receive nipocalimab q2w. Key inclusion criteria: adults ≥18 years with CIDP, progressing/relapsing forms, confirmed by independent adjudication committee; CIDP disease activity score ≥3; and adjusted Inflammatory Neuropathy Cause And Treatment disability score 2-9. Exclusion criteria: patients with pure sensory CIDP or chronic immune sensory polyradiculopathy, or other diagnoses that better explain their clinical presentation. Primary endpoint: time to first occurrence of a relapse event in Stage B. Secondary efficacy endpoints include time to initial response to nipocalimab and percentage of nipocalimab responders in Stage A, and change from baseline in functional measures (grip strength, MRC sum score) in Stage B. Other secondary endpoints include safety/tolerability, pharmacokinetics, immunogenicity, and pharmacodynamics of nipocalimab.

RESULTS: The study is currently enrolling patients, targeting approximately 300 patients, with primary study completion date anticipated in 2026.

SUMMARY/CONCLUSION: This ongoing phase 2/3 study will assess the efficacy, safety, pharmacokinetics, and pharmacodynamics of nipocalimab in adults with CIDP.

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Hong Sun - Employee of Janssen Pharmaceuticals and may hold stock in Johnson & Johnson, Inc

SENSITIVITY OF ULTRASOUND OF PARASPINAL MUSCLES AND CORRELATION WITH MRI IN RADICULOPATHY

William Buxton (Santa Monica, CA)

INTRODUCTION: Needle EMG of the paraspinal muscles is considered a confirmatory component of an electrodiagnostic evaluation of cervical and lumbosacral radiculopathies. However, it is not always possible, most often due to anticoagulation, and there are concerns about risk of pneumothorax when performed at the T1 spinal level. Ultrasound is showing promise as an alternative to needle EMG and can be performed in more individuals and at more spinal levels than EMG.

OBJECTIVE: To determine the sensitivity of ultrasound of the paraspinal muscles in radiculopathy, as well as to determine correlation with imaging findings.

METHODS: Paraspinal ultrasound was performed in 28 patients, including 36 cervical radiculopathies and 27 lumbar radiculopathies in which the limb EMG supported a diagnosis of radiculopathy. Ultrasound was performed with the paraspinal muscles at rest, observing for spontaneous activity at rest.

RESULTS: Using limb EMG as the gold standard by which sensitivity was calculated, ultrasound of the paraspinal muscles yielded a sensitivity of 64% for cervical radiculopathies and 48% for lumbar radiculopathies. When MRI reports were available, correlation with root compression was also calculated and reached significance ($p<0.05$) by two-tailed T-test for cervical radiculopathy but not for lumbar.

SUMMARY/CONCLUSION: Ultrasound of the paraspinal muscles may represent a viable alternative to needle EMG of paraspinal muscles in evaluation of radiculopathy.

QUANTITATIVE SONOGRAPHIC ASSESSMENT OF MUSCLE THICKNESS IN CARPAL TUNNEL SYNDROME

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INTRODUCTION: Carpal tunnel syndrome (CTS) is a common entrapment syndrome. Sonographic assessment of median nerve cross-sectional area (CSA) has a high accuracy for diagnosis.

OBJECTIVE: To determine whether quantitative sonographic assessment of abductor pollicis brevis muscle thickness (APB-MT) can aid in diagnosis in severe cases with motor involvement.

METHODS: We prospectively recruited subjects attending the EMG laboratory at Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, from December 2021 to March 2023. All subjects underwent electrophysiological evaluation of the upper limbs, followed by quantitative sonographic assessment of median nerve CSA at the wrist, and APB-MT in at least 1 hand. Optimal threshold, AUC, sensitivity, and specificity for diagnosing CTS were determined.

RESULTS: Forty-four subjects, mean age 54 (±17) years, 66% females, were included. Eighty-seven hands were examined, 30 with CTS. In patients with CTS, lower APB-MT was associated with lower median motor amplitudes. Optimal threshold, AUC, sensitivity, and specificity for diagnosing all CTS cases using median CSA were 13.05 mm2, 0.87, 75%, and 85%, and by using APB-MT 0.36 cm, 0.56, 43%, and 74% respectively. Values for diagnosing patients with severe CTS using median CSA were 15.20 mm2, 0.97, 100%, and 92%, and by using APB-MT 0.29 cm, 0.79, 57%,, and 98% respectively. Loss of dexterity and/or grip weakness were associated with larger median CSA ($p=0.004$), but not with thinner APB ($p=0.66$).

SUMMARY/CONCLUSIONS: Quantitative assessment of APB-MT provides an additional useful diagnostic parameter in cases with severe CTS, although with inferior performance compared with median CSA.

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QUANTITATIVE SONOGRAPHIC ASSESSMENT OF MUSCLE THICKNESS PREDICTS SURVIVAL IN AMYOTROPHIC LATERAL SCLEROSIS

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INTRODUCTION: Muscle thickness assessed quantitatively by ultrasound correlates with clinical and electrophysiological indices in various neuromuscular disorders, including ALS.

OBJECTIVE: To explore the ability of sonographic assessment of muscle thickness to predict mortality in ALS patients compared with manual muscle testing (MMT) and ALS Functional Rating Scale (ALSFRS).

METHODS: We prospectively recruited ALS patients attending the neuromuscular clinic at Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, from December 2018 to November 2019. All patients underwent routine clinical assessment and quantitative sonographic assessment of muscle thickness in 8 relaxed and 4 contracted limb muscles. We calculated the average monthly decline rate of MMT and ALSFRS scores from disease onset and of relaxed and contracted muscle thickness (using predicted values based on a previous study in healthy subjects). To explore mortality prediction, we generated ROC curves, determined AUC, and calculated optimal cutoff points using Youden Index. Subsequently, we determined the hazard ratio (HR) for 1- and 2-year mortality using Cox regression analysis, including covariates (age, sex, BMI, diagnostic delay, and site of disease onset).

RESULTS: Eighty-six ALS patients, mean age 62 (±13), 44% females, were included. Significant increased 1-year mortality was associated only with greater decline in contracted muscle thickness (OR-8.1), while significant increased 2-year mortality was associated with greater decline in MMT (OR-3), ALSFRS (OR-3.7), relaxed (OR-2.6), and contracted (OR-4.4) muscle thickness.

SUMMARY/CONCLUSIONS: Greater decline in limb muscle thickness is associated with significant increased mortality in ALS and has the potential to serve as an additional biomarker in clinic and research.

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COMBINED RITUXIMAB AND EFGARTIGIMOD FOR GENERALIZED MYASTHENIA GRAVIS

Arjun Seth (Chicago, IL), Qihua Fan (Richmond, VA)

INTRODUCTION/BACKGROUND: Efgartigimod was approved for generalized myasthenia gravis (gMG) in December 2021. There is no data on combined use of efgartigimod and rituximab. We describe 2 cases of AChR+ gMG in which efgartigimod was safely and successfully used in combination with rituximab.

CASE SERIES: Two patients presented with AChR+ gMG. The first was diagnosed at age 12, underwent thymectomy but had refractory oculobulbar symptoms with recurrent intubations and required chronic weekly to biweekly plasmapheresis, prednisone, and azathioprine. She had no response to eculizumab. She was started on efgartigimod and received rituximab 2 weeks later. Efgartigimod cycles were repeated every 50 days, azathioprine was stopped, and prednisone was reduced. Nine months later, her bulbar function has normalized and she continues on rituximab every 6 months, efgartigimod every 50 days, and low-dose prednisone. The second patient presented with 7 months of progressive ophthalmoparesis, ptosis, and extremity weakness. He received rituximab followed by 1 cycle of efgartigimod and exam normalized by the third week of efgartigimod with successful transition to rituximab monotherapy.

SUMMARY/CONCLUSION: Efgartigimod was developed as a long-term therapy for treatment refractory cases of AChR+ gMG with a significant benefit being rapid treatment efficacy. As prior use of rituximab was an exclusionary criterion in the ADAPT trial, these cases demonstrate that 1) combination therapy is safe and 2) efgartigimod can be used as bridge therapy to alterative long term disease modifying therapies which typically take several months to show clinical efficacy.

Disclosures:

Qihua Fan - Speaker for Alnylam; consultant for PRIME

100TH ANNIVERSARY OF THE CUTANEOUS SILENT PERIOD TEST: CURRENT RELEVANCE IN CLINICAL NEUROPHYSIOLOGY

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INTRODUCTION: The cutaneous silent period (CSP) is the transient suppression of continuous EMG activity induced by sensory nerve stimulation. In 1922, physiologist Paul Hoffmann described the basis for a neurophysiological test that allows us to assess the integrity of the structures of the spinal cord and of the A-delta fine sensory fibers.

OBJECTIVE: Describe the historical aspects of CSP and its role in current clinical neurophysiology.

METHODS: This is a narrative review study that investigated the PubMed databases with the descriptor: cutaneous silent period and we reviewed the monograph "Untersuchungen über die eigenreflexe (sehnenreflexe) menschlicher muskeln" - Investigations into the self-reflexes (tendon reflexes) of human muscles- published by Springer-Verlag in 1922.

RESULTS: With the postulate of a monosynaptic transmission, Hoffmann made a significant contribution to the elucidation of functional principles in the central nervous system. This also applies to the interpretation of the post-reflective, temporary decrease in the tonic basic innervation, which he interpreted as the inhibitory reflex of the spinal cord and which later received great attention under the term “silent period”. There were 201 articles found, published from 1971 to January 2023.

CONCLUSION: Despite the limited amount of articles, the authors agree with Kofler et. al., who showed that the potential clinical utility of CSP depends on the possibility of evaluating segments and components of sensory nerves that are not exhaustively evaluated by standard EDX methods. CSP may have a diagnostic role in the evaluation of small-fiber neuropathies, diseases of the central nervous system, and the functional diagnosis of intramedullary lesions.

“AXONAL” LANDRY-GUILLAIN-BARRE-STROHL SYNDROME IN THE LATIN AMERICAN BOOK OF 1976

Otto Hernandez Fustes (Curitiba, Brazil), Olga Judith Hernandez Fustes (Curitiba, Brazil)

INTRODUCTION: Guillain-Barre syndrome (GBS) was initially defined as an acute inflammatory demyelinating polyneuropathy, but the incidence of axonal GBS has increased in recent years, as well as studies focusing on optimizing diagnosis and treatment.

OBJECTIVE: Our objective was to report the axonal injury in the “Landry-Guillain-Barre-Strohl syndrome” described in the homonymous book published 50 years ago by Latin American authors.

METHODS: This is a narrative review study that investigated the PubMed databases with the descriptors “Axonal GBS” and “Axonal Landry-Guillain-Barré-Strohl syndrome,” title of the book written by 3 Cuban doctors in 1972 and published in 1976.

RESULTS: In 1972, then resident of neurology Otto Hernández Cossio finished writing the clinical descriptions of the 76 patients included in the book, which together with the pathological examinations by Drs. Joaquim Galarraga Inza and Rafael Estrada Gonzalez compose the 273-page book. After 11 pathological studies the authors reveal an early axonal reaction; it is difficult to determine the primary or secondary nature of the degenerative lesions found.

CONCLUSIONS: In literature reviews, the first cases of axonal GBS proven by pathological studies showing axonal degeneration in nerve roots and distal nerves were described in 1986. Our work is a homage to the 4 physicians who in the 19th and early 20th century described it masterfully, as did the 3 Latino neuroscientists who published the first book using the eponym with the names of the 4 original authors and described axonal injuries.

LATE-ONSET P.VAL142ILE TRANSTHYRETIN AMYLOIDOSIS MIXED PHENOTYPE IN AN ELDERLY PERSON IN A NON-ENDEMIC AREA: A CASE REPORT IN COLOMBIA

Daniel Manrique Hernandez (Bogota, Colombia), Claudia Peña (Bogota, Colombia)

INTRODUCTION/BACKGROUND: Hereditary amyloidosis TTR-related (hATTR) is a rare disease associated with several point mutations in the transthyretin (TTR) gene, characterized by heterogeneous clinical features, including polyneuropathy, cardiomyopathy, vitreous opacity, and nephropathy. We presented a case in an older man with features of peripheral neuropathy, small fiber, and cardiac compromise in ATTRv.

CASE REPORT: A 76-year-old man with a history of intermittent numbness and paresthesias developed weakness in his hands to the point where he could no longer do up buttons or open jars. The cardiac test reported amyloidosis findings, a left ventricular ejection fraction of 55%. Neurological examination revealed mild to moderate bilateral median nerve compressive mononeuropathy, severity, and distribution of postganglionic sudomotor, adrenergic, and cardiovagal function. Quantitative sensory test indicated a severe pan-modality sensory loss in upper and lower limbs. A genetic test of TTR was performed and identified TTR: c. 424G>A, p. Val142Ile, in heterozygous interpretation like pathogenic variant mixed phenotype. Tafamidis was administered at 61 mg per day to stabilize the TTR tetramer. Nowadays, he participates in a rehabilitation domiciliary program with aerobic exercise and muscle-strengthening objectives.

SUMMARY/CONCLUSION: Diagnosing hATTR is often very difficult especially in the early stages when the symptoms are absent or unclear or overlap with other clinical conditions. Neuropathy is a hallmark of ATTRv, representing one of the most disabling and progressive conditions. Overall, it is essential for a multidisciplinary approach to manage symptoms and other conditions to improve the quality of life of the patients.

EFGARTIGIMOD TREATMENT OF GENERALIZED MYASTHENIA GRAVIS: A REAL-WORLD SINGLE-CENTER EXPERIENCE

Long Davalos Loo (Cincinnati, OH), Jonathan Smith (Cincinnati, OH), Jacqueline Janecek (Cincinnati, OH), Hani Kushlaf (Cincinnati, OH)

INTRODUCTION: The current efficacy and safety data come from the ADAPT phase 3 clinical trial. There is a need for real-world data regarding the safety and efficacy of efgartigimod.

OBJECTIVE: To report our single-center experience on the efficacy and safety of efgartigimod in acetylcholine receptor (AChR) antibody positive generalized myasthenia gravis (gMG).

METHODS: We performed a retrospective chart review of all patients with gMG who received efgartigimod at the University of Cincinnati until February 1st, 2023. We collected demographic, baseline and posttreatment efficacy, and adverse effects data.

RESULTS: Seven AChR antibody-positive patients were treated with efgartigimod. Three patients completed 2 cycles and 4 patients completed 1 cycle. Five (71%) were women; the median age was 57 (range 33-72). The median baseline MG-ADL score was 8 (range 5-14), and MGFA classification ranged from IIa to IIIb. Five patients (71%) showed clinical improvement as measured by the MG-ADL. The median MG-ADL improvement after the first cycle was 5 (range 5-6). Responders were able to discontinue IVIg (3), plasmapheresis (1), prednisone (1), and pyridostigmine (1). In 3 responders, symptoms worsened less than 4 weeks after completing the first cycle. One patient had angioedema; no other side effects reported. One responder had an MG crisis 3-4 weeks after the first cycle.

SUMMARY/CONCLUSION: Efgartigimod was well-tolerated. Most patients (71%) treated with efgartigimod had a favorable response. The improvement was short-lived (<4 weeks) in 60% of the patients, perhaps reflecting the baseline severity of gMG and raising the question of the need for shorter intercycle intervals.

THE SPECTRUM OF CONDUCTION SLOWING IN AMYOTROPHIC LATERAL SCLEROSIS

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INTRODUCTION: Abnormal motor nerve conduction studies in ALS are attributed to loss of large axons and distal axonopathy, however conduction slowing can be the result of other conditions.

OBJECTIVE: To determine the range and distribution of conduction slowing in ALS and the limits of conduction slowing beyond which the diagnosis of exclusive axonopathy is uncertain.

METHODS: The electrodiagnostic data of 76 patients with chronic inflammatory demyelinating polyneuropathy (CIDP) were used to create 12 novel equations using regression analysis that determine a range of the expected slowing of a primary demyelinating polyneuropathy. Demyelinating range confidence intervals were defined by assessing conduction velocity (CV), distal latency (DL), and F-latency in relation to distal compound muscle action potential (CMAP) amplitude of median, ulnar, fibular, and tibial nerves. These equations were used to evaluate conduction slowing in 95 patients with ALS. Transformed CMAP amplitude was used as an independent variable whereas transformed DL, CV, and F were used as dependent variables.

RESULTS: CV slowing, prolonged DL, and abnormal F latency were observed respectively in 22.2%, 19.6%, and 46.7% of the studied nerves. When slowing occurred, it affected more than 1 segment of the motor nerve, suggesting that loss of large axons is the main mechanism of slowing. No ALS patient had more than 2 nerves with CV slowing in the confidence-interval defined by the regression equations or AAN criteria for acquired demyelination diagnosis.

SUMMARY/CONCLUSION: The presence of more than 2 motor nerves with CV slowing in the demyelinating range defined by the regression analysis or AAN criteria in ALS patients suggests an alternative diagnosis or superimposed demyelination.

THE PROFILE OF CONDUCTION SLOWING IN DIABETIC DISTAL SYMMETRIC POLYNEUROPATHY

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INTRODUCTION: Conduction slowing beyond what is expected from pure axonal loss has been reported in diabetic distal symmetric polyneuropathy (DSP) and has been attributed to an additional demyelinating component.

OBJECTIVE: To evaluate the use of novel regression equations to investigate the profile of conduction slowing in diabetic DSP.

METHODS: Electrodiagnostic data from CIDP patients was plotted and transformed and linear regression analysis was performed to create confidence intervals to determine abnormal nerve conduction ranges of distal latency (DL), conduction velocity (CV), and F latency for compound muscle action potential (CMAP). These ranges were then used to evaluate abnormal nerve conduction values in 219 patients with diabetic DSP and 219 non-diabetic axonal DSP.

RESULTS: The mean CV was significantly slower in diabetic DSP than in the non-diabetic DSP group for all tested nerves. There was a significantly higher number of patients fulfilling the regression equation above criteria in the diabetic group compared to the axonal non-diabetic group (47.0% vs 23.3%; $p<0.0001$). There are significantly more patients with more than 2 motor nerves with CV in the demyelinating range in the diabetic DSP group compared to the axonal non-diabetic group (25.6% vs 7.8%; $p<0.0001$). Furthermore, there are significantly more patients that fulfilled an additional criteria of at least 1 motor nerve with the corresponding F response in the demyelinating range by AAN criteria in the diabetic DSP group compared to the axonal non-diabetic group (21.0% vs 4.1%; $p<0.0001$).

SUMMARY/CONCLUSION: Regression analysis identified conduction slowing in diabetic DSP beyond what is expected from exclusive axonal loss. Combining regression analysis of conduction slowing with adequate clinical evaluation may improve the identification of demyelination in diabetic DSP.

A LONG WINDY ROAD TO CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

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INTRODUCTION/BACKGROUND: Eighteen percent of chronic inflammatory demyelinating polyneuropathy (CIDP) patients present atypically. Retrospective studies show atypical forms of CIDP often progress to typical CIDP after a mean disease duration of 5.5 years. We present a case series of patients that didn't initially meet European Federation of Neurologic Society/Peripheral Nervous Society electrodiagnostic criteria for CIDP and then later progressed to typical CIDP.

CASE REPORT: 1) A 62-year-old man initially presented with subacute weakness, areflexia, and non-length-dependent sensory symptoms at age 55. Initial electrodiagnostic studies were normal and cerebrospinal fluid (CSF) analysis showed albuminocytologic dissociation. He initially responded well to IVIg but continued to have frequent relapses which were successfully treated with IVIg. Five years later, his electrodiagnostic studies were repeated and were consistent with definite CIDP. He currently receives IVIg monthly. 2) A 68-year-old man initially presented with an acute onset of sensory ataxia at age 60. Initial electrodiagnostic studies showed evidence of demyelinating changes in the sensory nerves with relative sparing of the motor nerves. CSF analysis showed albuminocytologic dissociation and he was started on IVIg. He had a relapsing course for over 3 years when electrodiagnostic testing was repeated and was now consistent with typical CIDP. His symptoms are currently well controlled on IVIg every 3 weeks and low dose oral prednisone.

SUMMARY/CONCLUSION: Atypical CIDP frequently eludes early diagnosis but can be more accurately identified as the disease progresses. In our cases, continued suspicion for potential typical CIDP remained high despite initial non-diagnostic nerve conduction studies which eventually led to our patients' correct diagnosis.

CHANGE IN CONCOMITANT THERAPIES FOR GENERALIZED MYASTHENIA GRAVIS IN PATIENTS RECEIVING ECULIZUMAB: A RETROSPECTIVE ANALYSIS OF REGISTRY DATA

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INTRODUCTION: A range of treatments are available for patients with generalized myasthenia gravis (gMG) such as typical immunosuppressive therapies and complement C5 inhibitors, including eculizumab.

OBJECTIVE: To assess concomitant therapy use at and after eculizumab initiation in patients with gMG.

METHODS: US patients enrolled in a global gMG registry that collects data on eculizumab use were included if they were treated with eculizumab for ≥ 1 year and had data on concomitant therapy use 12 months before eculizumab initiation. Azathioprine (AZA), mycophenolate mofetil (MMF), IVIg/plasma exchange (PLEX), and oral corticosteroid use at initiation of and during eculizumab treatment were analyzed. Data cutoff was July 5, 2022.

RESULTS: Of the 94 patients included, 25 (27%), 40 (43%), 25 (27%), and 4 (4%) were receiving 0, 1, 2, or 3 concomitant therapies investigated at eculizumab initiation, respectively. Nine (10%) patients received AZA, 26 (28%) MMF, 19 (20%) IVIg/PLEX, and 47 (50%) oral corticosteroids. In 57 (61%) patients, the number of concomitant therapies did not change after eculizumab initiation. The number of concomitant therapies decreased in 24 (26%) patients. Thirteen (14%) patients received more treatments after eculizumab initiation. Of the patients using each treatment at eculizumab initiation, AZA was discontinued in 2/9 (22%) patients, MMF in 8/26 (31%), IVIg/PLEX in 5/19 (26%), and oral corticosteroids in 11/47 (23%).

CONCLUSIONS: One or more concomitant therapy was discontinued in approximately one quarter of patients with gMG treated with eculizumab, providing evidence from clinical practice that eculizumab may enable patients with gMG to reduce concomitant therapies.

Disclosures:

Michael Pulley - Received compensation from Alexion, argenx, Immunovant, CSL/Behring, Catalyst, and UCB

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Richard Nowak - Received support from the National Institutes of Health, Genentech, Alexion Pharmaceuticals, argenx, Annexon Biosciences, Ra Pharmaceuticals (now UCB S.A.), the Myasthenia Gravis Foundation of America, Momenta Pharmaceuticals, Immunovant, Grifols, S.A., Cabaletta Bio, CSL Behring, and Viela Bio (Horizon Therapeutics plc)

Ema Rodrigues - Employee of Alexion Pharmaceuticals and has received stock or an ownership interest from Alexion Pharmaceuticals, Inc

Houari Korideck - Was an employee of Alexion, AstraZeneca Rare Disease at time of study

Brian Werneburg - Employee of Alexion, AstraZeneca Rare Disease

Pushpa Narayanaswami - Received research support from PCORI, Momenta/Janssen, Alexion/AstraZeneca, and Ra/UCB; served on advisory boards for Janssen, DMC Chair, and Sanofi; has been a speaker for argenx, Alexion, and UCB

C5B-9 UPREGULATION IN PATIENTS WITH SPORADIC INCLUSION BODY MYOSITIS

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INTRODUCTION: Sporadic inclusion body myositis (sIBM) is an idiopathic inflammatory myopathy characterized by slowly progressive skeletal muscle weakness with characteristic pathologic features on skeletal muscle biopsy. Auto-antibodies to cN1A aid in differentiating sIBM from other inflammatory myopathies and suggest an adaptive immune response may also play a role in sIBM pathophysiology. While literature does not suggest that IBM is a complement-mediated disease, case reports describe C5b-9 staining in muscle biopsies of patients newly diagnosed with sIBM.

OBJECTIVE: Review the prevalence of C5b-9 upregulation and the correlation between NT5C1A serology and sIBM muscle biopsies.

METHODS: We performed a retrospective chart review of 20 patients with sIBM with muscle biopsies from 2010-2022. Biopsies were reviewed for the presence of vacuoles, cytochrome-oxidase (COX) fibers, succinate-dehydrogenase (SDH) fibers, inflammation, C5b-9 upregulation, and MHC-class I. We assessed phenotypic correlation to C5b-9 upregulation and the presence of positive NT5C1A serology.

RESULTS: Out of 20 muscle biopsies, 17 patients were found to have C5b-9 upregulation. NT5C1A was positive in 7 patients, negative in 8 patients, and not assessed in 5 patients. All patients presented with limb and facial weakness, grip involvement, or quadriceps atrophy.

SUMMARY/CONCLUSION: This review reveals the possibility of a complement-mediated role in the pathophysiology of sIBM. A correlation can be seen between C5b-9 upregulation and sIBM without correlation to NT5C1A. Recognizing this association will allow further investigation focused on C5b-9 upregulation with a possible role in therapeutics.

FACILITATED SUBCUTANEOUS IMMUNOGLOBULIN 10% FOR CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY: INTERIM RESULTS FROM A LONG-TERM SAFETY AND TOLERABILITY STUDY

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INTRODUCTION: Facilitated subcutaneous immunoglobulin (fSCIG; human immunoglobulin G [IgG] 10% with recombinant human hyaluronidase) is under investigation as a maintenance therapy for patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

OBJECTIVE: To evaluate long-term safety and efficacy of fSCIG in patients with CIDP.

METHODS: ADVANCE-CIDP 3 (NCT02955355) is a long-term extension of ADVANCE-CIDP 1 (NCT02549170), a phase 3, double-blind, randomized, placebo-controlled study that evaluated efficacy and safety/tolerability of fSCIG as maintenance therapy for CIDP. Patients completing 6 months without relapse in ADVANCE-CIDP 1 could enter ADVANCE-CIDP 3 and receive open-label fSCIG treatment. The primary outcome is safety. Efficacy is an exploratory outcome including evaluation of CIDP relapse.

RESULTS: This interim analysis included 79 patients (mean age 53.9 years, 54.4% male) with total follow-up of 169 patient-years; 2595 infusions were administered. Median exposure was 23 months (range: 0–61 months). Most adverse events (AEs) were mild or moderate, local and self-limiting, and consistent with the established fSCIG safety profile. Overall, 1166 AEs (40 severe; 18 serious) occurred in 70 patients (88.6%). Of these, 661 AEs (19 severe; 2 serious) were related to fSCIG. Systemic AEs (e.g., hemodynamic alterations) were infrequent. Overall, 5 patients relapsed; the 6-month relapse rate was 1.5%.

SUMMARY/CONCLUSION: ADVANCE-CIDP 3 demonstrates favorable long-term safety and tolerability of fSCIG and a low relapse rate, supporting its use as a maintenance treatment for CIDP.

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Henning Andersen - Received research support (CSL Behring, NMD Pharma, Sanofi Genzyme) and speaker honoraria (Alexion); served as consultant on advisory boards (Alexion, Sanofi Genzyme, UCB Pharma, Amicus Pharmaceuticals and Lundbeck)

Vera Bril - Received funding from Grifols, CSL Behring, UCB Pharma, argenx, Takeda, Alnylam Pharmaceuticals, Octapharma, Pfizer, Powell Mansfield, Akcea, Ionis Pharmaceuticals, Immunovant, Sanofi, Momenta (J&J), Roche, Janssen, AZ-Alexion, and NovoNordisk

Ivana Basta - Received lecture honoraria from Pfizer, Teva Actavis, Berlin Chemie Menarini, Mylan, Adoc, and Salveo, and research grants from Kedrion and Octapharma

Konrad Rejdak - Received speaking honoraria and travel expenses for participation in scientific meetings and participated in advisory boards with Bayer, Biogen, Merck, Novartis, Roche, Sanofi-Genzyme, and Teva Pharmaceutical

Erin Greco - Employee of Takeda Development Center Americas, Inc and is a Takeda shareholder

Shabbir Hasan - Employee of Takeda Development Center Americas, Inc and is a Takeda shareholder

James French - Employee of Takeda Development Center Americas, Inc and is a Takeda shareholder

Leman Yel - Employee of Takeda Development Center Americas, Inc and was a Takeda shareholder at the time of study

Hakan Ay - Employee of Takeda Development Center Americas, Inc and is a Takeda shareholder

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A CASE OF TREATMENT WITH EFGARTIGIMOD IN A PATIENT WITH GENERALIZED MYASTHENIA GRAVIS AND LRP4 ANTIBODIES

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INTRODUCTION/BACKGROUND: Efgartigimod is a human IgG1 antibody Fc-fragment that reduces total and pathogenic IgG autoantibody levels through neonatal Fc receptor blockade. We describe the effect of efgartigimod treatment in a case of LRP4+ generalized myasthenia gravis (gMG).

CASE REPORT: A 66-year-old male with LRP4+ gMG presented with persistent symptoms, including double vision, eyelid droop, and difficulty speaking/swallowing. The patient's history included stroke and rheumatoid arthritis, and current medications included methotrexate 20 mg weekly, prednisone 10 mg daily, and sulfasalazine 500 mg 3 times daily. His MG-ADL total score was 10 (max 24), and MG-QoL15R score was 19 (max 30). Since LRP4 autoantibodies are predominantly IgG1/3, we hypothesized that this patient would benefit from efgartigimod. Efgartigimod 10 mg/kg was administered intravenously in cycles of 4 once-weekly infusions, with subsequent cycles initiated based on clinical evaluation. Clinical improvements were observed 35 days after cycle 1 (MG-ADL, 5; MG-QoL15r, 10) and he received a second cycle. Following cycle 2 his vocal/swallowing issues mostly resolved and he tapered prednisone to 5 mg daily. Some exertional dyspnea, diplopia, eyelid droop, and mild limb weakness persist (MG-ADL, 5; MG-QoL15r: 16). A third cycle of efgartigimod is underway.

SUMMARY/CONCLUSION: This patient's MG-ADL and MG-QoL15R scores improved after the first cycle of efgartigimod, enabling a return to some normal activities, and were maintained through a second cycle. This suggests efgartigimod may be an effective treatment option for patients with LRP4+ gMG, though further study is warranted. The patient is currently receiving a third cycle of efgartigimod; follow-up on this patient will be presented.

Disclosures:

Eduardo De Sousa - Served as a medical advisor and/or speaker for Alexion, argenx BV, CSL Behring, and Grifols

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CORTICOSTEROID MANAGEMENT IN NEUROMUSCULAR DISEASE: A CANADIAN SURVEY

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INTRODUCTION: Systemic corticosteroids (CS) are first-line therapy for many neuromuscular diseases. Although long-term use is associated with many adverse effects, guidelines regarding the prevention and management of CS complications in neurology are lacking, introducing potential practice variation.

OBJECTIVE: We aimed to evaluate Canadian neuromuscular neurologist practices for screening, management, and treatment of CS-related complications.

METHODS: A web-based anonymous questionnaire was disseminated to 99 Canadian neuromuscular neurologists addressing: patterns of screening, prevention, monitoring, and treatment of CS-induced adverse effects, such as infection and osteoporosis.

RESULTS: Seventy-one percent completed the survey. Of those, 52% perform screening blood work prior to initiating CS, 56.3% screen for infections, and 18.3% screen for osteoporosis. The majority monitor glycemic control and blood pressure. 28.6% never use pneumocystis jiroveci pneumonia prophylaxis and 28.6% routinely recommend vaccination. Eighty percent recommend calcium supplementation to prevent bone complications. Thirty-six percent were unaware of any existing guidelines for the management of CS complications and 91% felt that there was a need for neurology-specific guidelines. Additional data and details of responses will be presented.

SUMMARY/CONCLUSION: There is substantial variability in the management of CS-associated adverse effects among neuromuscular neurologists. This suggests a need for neurology-specific guidelines to help standardize practice.

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REAL-WORLD INSIGHTS INTO DIFFERING CLINICAL PRESENTATION OF MYASTHENIA GRAVIS PATIENTS ON PHARMACOLOGICAL TREATMENT IN THE USA AND FIVE EUROPEAN COUNTRIES

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OBJECTIVES: Myasthenia gravis (MG) is an autoantibody mediated condition with varied clinical presentation. This study reports differences in patient presentation and initial pharmacological treatment.

METHODS: Data was drawn from the Adelphi MG Disease Specific Programme, a cross-sectional survey of physicians and their MG patients in France, Germany, Italy, Spain, UK, and USA between March – September 2020. Physicians provided patient demographics, symptomology, and treatment history. Descriptive statistics were reported.

RESULTS: Two hundred ten physicians provided data for 1,021 MG patients diagnosed within 10 years of the survey. Mean age was 53.1 years (standard deviation; SD, 16.4), 49.9% were female, and mean time since diagnosis was 2.7 years (SD, 2.3). Three groups were created based on patients' symptomatic presentation at diagnosis: 'ocular only' (n=312, 30.6%), 'bulbar' (with/without ocular; n=221, 21.6%), and 'limb' (with/without ocular and/or bulbar; n=468, 45.8%). Most patients received acetylcholinesterase inhibitors first line (ocular only: 85.9%, bulbar: 73.8%, limb: 70.5%). Bulbar and limb patients received nonsteroidal immunosuppressants (bulbar: 32.4%, limb: 33.6%, ocular: 17.9%) or corticosteroids (bulbar: 37.1%, limb: 42.1%, ocular: 24.7%) more often than ocular only patients. Use of biologics as first line was higher in bulbar (5.2%) and limb (7.2%) than ocular (2.7%) as was use of immunoglobulins (bulbar: 4.8%, limb: 7.2%, ocular: 2.7%).

CONCLUSION: These data show MG patient presentation impacts initial treatment selection, with limb and bulbar patients typically receiving more advanced therapies. Additional analysis will examine underlying differences in patient characteristics, management, and subsequent treatments received by these patients.

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CHARACTERISTICS OF PROGRESSIVE MYASTHENIA GRAVIS PATIENTS IN REAL WORLD PRACTICE IN THE USA AND FIVE EUROPEAN COUNTRIES

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OBJECTIVES: Myasthenia gravis (MG) is a chronic autoantibody mediated disease which progresses from ocular symptoms to generalized limb, bulbar or respiratory muscle involvement. This study compares MG patients with documented progression to those with more stable disease.

METHODS: Cross-sectional data were drawn from the Adelphi MG Disease Specific Programme on MG-treating physicians and their patients in France, Germany, Italy, Spain, UK, and USA between March – September 2020. Physicians provided patient characteristics including Myasthenia Gravis Foundation of America (MGFA) classifications at diagnosis and at survey. Progression was defined as advancing to a higher MGFA class within 2 years of diagnosis. Descriptive statistics were reported.

RESULTS: One hundred sixty-three physicians provided data on 516 MG patients, mean time since diagnosis was 12.2 months (standard deviation±7.0). Of these patients, 16.9% (n=87) experienced progression. Ocular (93.1%) and bulbar symptoms (83.9%), fatigue (77%), and limb weaknesses (65.5%) were more evident in progressors compared to those whose MGFA class remained stable or improved (ocular 78.8%; bulbar 49.7%; fatigue 45.9%; limb weakness 44.8%). The number of treatment lines received was higher for progressors (mean 1.4; n=84, stable/improved; 1.2; n=402), however; treatment received at time of survey was similar (progressors vs stable/improved; acetylcholinesterase inhibitors 74.7% vs 77.3%; non-immunosuppressants 32.9% vs 31.4%; corticosteroids 31.6% vs 31.4%; biologics 8.9% vs 8.4%).

CONCLUSION: Despite experiencing a greater number of MG symptoms, patients with progression were not treated more aggressively than those who were stable. Work is needed to understand drivers and best treatment approaches for stable patients and for those with progression.

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HEALTHCARE UTILIZATION AND COSTS OF ADULTS WITH MYASTHENIA GRAVIS AND COMMON COMORBIDITY OR DISEASE ACTIVITY PROFILES

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INTRODUCTION: Generalized myasthenia gravis (gMG) is associated with elevated healthcare resource utilization (HRU) and costs, which may vary by comorbidities and disease activity profiles.

OBJECTIVE: To understand variability in HRU and costs across patients with newly diagnosed gMG, specifically those with common comorbidities and acute symptomatic events.

METHODS: Adults with gMG were identified from the IQVIA PharMetrics® Plus database (01/2017-12/2021). The first MG diagnosis was the index date. Subgroups included those with a 12-month pre-index cardiometabolic or psychiatric comorbidity or a post-index MG exacerbation/crisis. Post-index per-patient-per-month (PPPM) HRU and costs were described.

RESULTS: 2,739 patients with gMG were selected (mean age: 56.2 years; female: 50.6%), including 1,859 with cardiometabolic comorbidity, 1,308 with psychiatric comorbidity, and 419 with MG exacerbation/crisis. Mean PPPM number of inpatient days was 0.71 for overall gMG, 0.91 for cardiometabolic, 0.97 for psychiatric, and 3.06 for MG exacerbation/crisis subgroups. Mean PPPM number of outpatient visits was 2.66 for gMG, 2.96 for cardiometabolic, 3.28 for psychiatric, and 3.91 for MG exacerbation/crisis subgroups. Mean PPPM total healthcare costs were $5,567 in gMG cohort, $6,659 in cardiometabolic, $7,443 in psychiatric, and $17,330 in MG exacerbation/crisis subgroups. Inpatient costs drove total costs accounting for 47.0%, 49.9%, 48.2%, and 63.1% in the gMG cohort, cardiometabolic, psychiatric, and exacerbation/crisis subgroups, respectively.

SUMMARY/CONCLUSION: Within gMG, underlying cardiometabolic and psychiatric conditions are associated with elevated HRU and costs; patients with MG exacerbations/crisis are particularly costly. There is a clinical and economic need to manage comorbidities and acute symptomatic events associated with MG.

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GUILLAIN-BARRE LIKE SYNDROME WITH PLEOCYTOSIS FOLLOWING NELARABINE TREATMENT

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INTRODUCTION/BACKGROUND: Nelarabine is a purine analog chemotherapy medication used for the treatment of refractory or relapsed T-cell leukemia and T-cell lymphoma patients. A major but rare side effect due to nelarabine is severe neurotoxicity that can present as peripheral neuropathy, Guillain-Barre like syndrome, or seizures. Guillain-Barre like syndrome due to nelarabine has been documented, but few case reports have included CSF findings and electrodiagnostic studies to help characterize the syndrome.

CASE REPORT: A 9-year-old female with T-cell leukemia and no known central nervous system (CNS) progression had worsening distal and proximal weakness and paresthesias, which progressed to inability to ambulate or lift her arms 3 weeks after nelarabine treatment. She had a lumbar puncture showing a pleocytosis with lymphocytic predominance and elevated protein. Other causes of pleocytosis like infection and CNS progression were ruled out with CSF testing. EMG and NCS were conducted and showed a severe sensorimotor primarily demyelinating polyradiculoneuropathy with active denervation. She received IVIg over 3 days, with improvement of distal weakness and progressed to significant dysesthesia on the third day of treatment, requiring initiation of neuropathic pain medication.

SUMMARY/CONCLUSION: Neurotoxicity due to nelarabine can have severe presentations including Guillain-Barre like syndrome. CSF studies in past cases have shown elevated protein, while pleocytosis is rare. When pleocytosis is present, it is important to evaluate other possible causes including infection and CNS progression of malignancy. Electrodiagnostic studies are not commonly reported in patients with nelarabine neurotoxicity and characterization can be helpful in providing a diagnosis.

TOLERANCE OF THE NOVEL DRUG RELYVRIO IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

Lindsay Malatesta (Nashville, TN)

INTRODUCTION/BACKGROUND: ALS is a devastating neuromuscular disease with 2 minimally effective available FDA-approved medications. Relyvrio is an oral suspension medication consisting of 3 grams of sodium phenylbutyrate and 1 gram taurursodiol approved in September 2022. Significant side effects of diarrhea, abdominal pain, nausea, and dizziness were reported during the study in up to 25% of patients.

CASE REPORT: We describe the experience of 24 ALS patients with interest in Relyvrio.

SUMMARY/CONCLUSION: Twenty-four patients started Relyvrio. Seven patients were women (29%). The average age of the patients was 62 years (range 48 to 80 years). Four patients (2 women, 2 men) stopped taking Relyvrio due to adverse effects. These patients reported weakness or fatigue, diarrhea, bad taste, nausea, and abdominal pain. Out of the patients remaining on Relyvrio, 45% reported adverse effects that include bad taste (10), abdominal pain (3), dizziness (1), and diarrhea (6) at similar rates reported in the trial except dizziness which was less frequent. Two of 24 experienced swelling in their hands and feet which was not listed as a common adverse effect but is a significant adverse effected noted in this case series. Overall, 54% of patients who began Relyvrio experienced adverse effects, but only 16% of patients discontinued the drug. The main adverse effect causing discontinuation was diarrhea. The frequency of side effects was higher than riluzole or edaravone. Discussion of potential adverse effects prior to starting Relyvrio is essential and could contribute to better adherence to therapy. Monitoring the tolerance of the novel drug Relyvrio in a larger population after longer treatment time is necessary.

Disclosures:

Lindsay Malatesta - Served on advisory board for Amylx0035

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RAPIDLY PROGRESSIVE AMYOTROPHIC LATERAL SCLEROSIS FOLLOWING IMMUNE CHECKPOINT INHIBITOR COMBINATION THERAPY

Kyoko Kohno (Nashville, TN), Lindsay Malatesta (Nashville, TN)

INTRODUCTION: We describe a patient who developed rapidly progressive ALS after treatment for metastatic renal cell cancer with combination therapy (cabozantinib, nivolumab, and ipilimumab).

CASE REPORT: We present a case of a 66-year-old male with a history of metastatic renal cell carcinoma, status post nephrectomy with adrenalectomy and splenectomy who received combination therapy with cabozantinib (multi-receptor tyrosine kinase inhibitor), nivolumab (anti-PD-1), and ipilimumab (anti-CTLA-4). After being on this combination therapy for 15 months, the patient developed significant muscle fasciculations, weight loss, and right leg weakness and brisk reflexes. He remained on monotherapy with nivolumab for only 6 more weeks without symptom improvement. High dose corticosteroid therapy and plasma exchange were initiated followed by IVIg as adverse effect from immune therapy was suspected, but he continued to clinically deteriorate. After 8 months, the patient was quadriplegic, status post percutaneous endoscopic gastrostomy and dependent on non-invasive ventilation.

SUMMARY/CONCLUSION: To our knowledge, this is the first reported case of ALS developing after receiving combination therapy with immune checkpoint inhibitors. A literature review reveals that such a combined treatment could result in subacute immune-mediated motor polyneuropathy amongst myositis, myocarditis, and myasthenia gravis. Unlike other potential adverse effects, ALS will not respond to therapies and has no known cure. As these immune therapies are increasingly used in metastatic cancers, clinicians should be aware of the associated risks of causing neuromuscular disorders.

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Lindsay Malatesta - Served on advisory board for Amylx0035

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IDIOPATHIC INFLAMMATORY MYOPATHIES AND MALIGNANCY SCREENING: A SURVEY OF THE CURRENT PRACTICES AMONGST CANADIAN NEUROLOGISTS AND RHEUMATOLOGISTS

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INTRODUCTION: There is a well-established association between idiopathic inflammatory myopathies (IIM) and malignancy, however, there are no evidence-based guidelines amongst neurologists and rheumatologists on the choice and timing of investigations.

OBJECTIVE: Our aim was to better understand and characterize the current gaps and uncertainties amongst neurologists and rheumatologists with malignancy screening in IIM patients.

METHODS: An online survey consisting of 18 multiple-choice questions related to IIM malignancy screening practice was distributed to adult neurologists and rheumatologists in Canada. Quantitative and descriptive analysis of the data was performed using statistical software programs.

RESULTS: The majority of respondents (96%, n=68) performed malignancy screening, however there was variability in practice including delegation and choice of screening tests, influence of patient-specific factors, and time and length of repeat testing. Only 18% of respondents were confident in their malignancy screening practices. Between neurologists and rheumatologists, there were differences in the number of IIM patients seen, consideration of patient-specific factors, and choice of screening investigations.

SUMMARY/CONCLUSION: There is a lack of consensus and confidence in the choice and timing of investigations, with neurologists and rheumatologists differing in their approach to malignancy screening. Further research is required to better understand the relationship between IIM and malignancy to create expert-led consensus guidelines.

UTILITY OF THE COMBINATION OF MEDIAN NERVE SOMATOSENSORY EVOKED POTENTIAL AND AUDITORY BRAINSTEM RESPONSE IN THE EARLY DIAGNOSIS OF BICKERSTAFF BRAINSTEM ENCEPHALITIS

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INTRODUCTION: Early diagnosis of Bickerstaff brainstem encephalitis (BBE) is challenging. We have had a preliminary impression that the median nerve somatosensory evoked potentials (SEPs) are abnormal, although auditory brainstem responses (ABRs) are normal in many patients with BBE.

OBJECTIVE: To document the utility of the median nerve SEPs and ABRs for the early diagnosis of BBE.

METHODS: We retrospectively reviewed our EMG database for 20 years. Patients with BBE who underwent median nerve SEPs and ABRs within 2 weeks after onset were enrolled. The latency of P13/14 onset (P13/14o), interval between P13/14o and N20 onset (N20o), and N20 amplitude were evaluated in SEPs. Z-scores of evaluated parameters were calculated from multiple regression of the control data, and those exceeding ±2.5 were considered abnormal.

RESULTS: Enrolled were 14 patients with BBE. MRI was normal in all patients. The mean duration from admission to neurophysiological examinations was 3.7±3.7 (range, 0–11, median 2) days. SEPs were abnormal in 13 patients (93%): N20 was lost in 5 patients (36%). Abnormalities that can localize the lesion intracranially, i.e. normal P13/14o latency with prolonged P13/14o-N20o interval or depressed/lost N20, were observed in 11 patients (79%). ABRs were abnormal in only 3 patients (21%), and normal ABRs with abnormal SEPs were noted in 10 patients (71%).

SUMMARY/CONCLUSION: The combination of abnormal SEPs with normal ABRs is characteristic for BBE and is useful for its early diagnosis, especially because SEPs can document a lesion that cannot be visualized by MRI.

A CASE OF ANTI-MI2 DERMATOMYOSITIS AFTER COVID VACCINATION

Leila Darki (Los Angeles, CA), Said Beydoun (Los Angeles, CA)

INTRODUCTION/BACKGROUND: Vaccination against COVID-19 is crucial, however, with higher numbers of vaccinated individuals, autoimmune reactions following vaccination are seen more extensively. There are growing numbers of case reports with seropositive dermatomyositis (DM) after COVID-19 vaccination. The underlying mechanisms to trigger autoimmunity is unknown but is likely due to molecular mimicry and epitope sharing, or direct effect by the vaccine adjuvant. Most reported DM cases have been anti-MDA5 positive. Herein, we describe a case of anti-Mi2 DM with temporality after the second dose of Moderna COVID-19 vaccine. To our knowledge this is the 3rd reported case of Mi2 DM after COVID vaccination.

CASE REPORT: The patient is a 49-year-old female with subacute proximal upper and lower extremities weakness, dysphagia, and rash within 2 weeks after the 2nd dose of Moderna COVID-19 vaccination. She had typical DM rashes and severe proximal and neck flexor muscles weakness. Creatine kinase (CK) was 7800 units/L. EMG demonstrated evidence of irritable myopathy. MI-2 antibody was positive. Muscle biopsy demonstrated perifascicular atrophy, inflammatory infiltrate, and necrosis. There was no underlying malignancy. The patient was started on high-dose corticosteroids and intravenous immunoglobulin (IVIg) with gradual improvement of her symptoms and CK level.

SUMMARY/CONCLUSION: This observation highlights the crucial need for further studies, clinical and pathological evaluations of additional cases to understand vaccine interaction with the host immune response and possible other key factors like genetic susceptibility and to define whether this observation is coincidental or there is a causal relationship.

PATIENTS IN THE POMPE REGISTRY WHO SWITCHED FROM ALGLUCOSIDASE ALFA TO AVALGLUCOSIDASE ALFA: REAL-WORLD EXPERIENCE

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INTRODUCTION: Avalglucosidase alfa (AVAL), a recombinant human acid α-glucosidase enzyme replacement therapy, has received marketing authorization in several countries for infantile-onset (IOPD) and/or late-onset Pompe disease (LOPD); US approval: August 2021 for LOPD patients aged ≥1y.

OBJECTIVE: Characterize demographic/clinical characteristics of IOPD and LOPD patients who switched from alglucosidase alfa (ALGLU) to AVAL enrolled in the ongoing international, observational, voluntary Pompe Registry (NCT00231400).

METHODS: For this analysis, patients had ≥1 ALGLU record immediately pre-switch to AVAL. Demographic/treatment histories were collected. Respiratory, ambulatory, and biomarker data were assessed pre-/post-switch for LOPD only (IOPD excluded due to small cohort). Patients who received ALGLU for <5 and ≥5y pre-switch were compared.

RESULTS: As of December 2, 2022, 89 switch patients were identified (LOPD, 81 [91%]; IOPD, 8 [9%]). LOPD: United States, 72 (89%); male, 43 (53%). IOPD: Europe, 5 (63%), female 5 (63%). Patients switched at mean±standard deviation age of 44.9±21.94 (range: 1.0-83.0)y for LOPD and 11.0±5.15 (range:3.0-17.6)y for IOPD. Most had ≥5y experience on ALGLU pre-switch (LOPD, 55 [68%]; IOPD, 6 [75%]). For LOPD, last assessments pre-switch were upright forced vital capacity % predicted: 59.1±22.48 (n=69), 6-minute walk test: 359.1±149.86 m (n=41), urine glucose tetrasaccharide/hexose tetrasaccharide: 9.7±17.29 mmol/mol creatinine (n=56), and serum creatine kinase: 517.6±465.69 U/L (n=65). Mean changes among LOPD patients with both pre- and up to 1-y post-switch assessments showed stabilization in respiratory and ambulatory function and biomarker improvement.

SUMMARY/CONCLUSION: The Pompe Registry continues to accrue data for patients switching from ALGLU to AVAL, which will support our understanding of AVAL's effectiveness on respiratory and ambulatory outcomes and biomarker levels in the real world. Funding: Sanofi.

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A RARE CASE OF A PATIENT WITH PURE AUTONOMIC FAILURE AND C9ORF72+ AMYTROPHIC LATERAL SCLEROSIS: CASE REPORT

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INTRODUCTION/BACKGROUND: We describe the association between C9ORF72 gene mutation and 1 of the synucleinopathies, which is pure autonomic failure (PAF). This association which has never been described before.

CASE REPORT: A 73-year-old man had a diagnosis of PAF since 2003. His sister and mother had a history of frontotemporal dementia (FTD). In early 2020, he started to develop progressive weakness of his upper extremities suggestive of ALS which was confirmed with EMG. Gene testing was positive for GGGGCC hexanucleotide repeat in C9ORF72 > 145. The diagnosis of familial ALS was made. Shortly after, his brother was also diagnosed with ALS. In terms of his PAF, he started to notice some worsening of his orthostatic hypotension (OH) as well.

SUMMARY/CONCLUSION: Although it was argued that C9ORF72 disease and α-synucleinopathy are 2 distinct pathologic entities, the common co-existence of 2 proteinopathies may suggest a common pathologic pathway. Several reports described the association between C9ORF72 gene mutation and Parkinson disease (PD); however, it is still unclear whether patients with C9ORF72 gene mutation develop parkinsonism due to C9ORF72 causing an α-synucleinopathy (as in idiopathic PD) or due to another C9ORF72 extramotor pathology. Unlike PD, the co-existence of PAF and C9ORF72+ ALS has never been described in literature. With the known detrimental effect of αSyn aggregation on motor neurons, it is crucial to understand the relationship between C9ORF72 mutation and various types of synucleinopathies for proper management.

INVESTIGATING OUTCOMES OF TREATMENT IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY: A NEW YORK STATE PLANNING AND RESEARCH COOPERATION (SPARCS) STUDY

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INTRODUCTION: Treatment options and their effectiveness in reducing overall mortality remain a question of high-interest in studying the outcomes of chronic inflammatory demyelinating polyneuropathy (CIDP).

OBJECTIVE: To identify the effectiveness of treatment on mortality in CIDP.

METHODS: We used the New York State Planning and Research Cooperation (SPARCS) database to retrospectively collect all patients with CIDP from 1998-2018. Mortality data was collected using discharge status as either expired or sent to hospice. Multivariate analysis with binary logistic regression adjusted for comorbidities, gender, and age. Pearson Chi Squared test was used to test for significance.

RESULTS: From 1998-2018, 8,096 patients with CIDP were identified. One hundred sixty-nine patients were treated with only plasmapheresis (2.0%), 602 patients were treated with only steroids (7.4%), 27 were treated with only immunosuppressants (0.3%), 1,802 were treated with only IVIg (22.2%), and 538 were treated with a combination therapy (6.6%). There was no significant difference in gender (p=0.119) or age (p=0.585) between those who were treated and those who were not treated. Multivariable binary logistic regression showed there was no significant difference in the likelihood of death whether a patient was ever treated or not treated (OR: 1.011; 95% CL: 0830-1.232; p=0.912).

SUMMARY/CONCLUSION: In CIDP patients with a history of treatment with plasmapheresis, steroids, immunosuppressants, IVIg, or a combination at any time, when confounding for all comorbid conditions, gender and age did not significantly affect mortality when compared to patients who did not. Work is in progress for subgroup analysis and identifying other risk factors for mortality including hospital admission and socioeconomic status.

DOES ELEVATED CREATINE KINASE INCREASE THE RISK OF DEVELOPING POST-ACUTE SEQUELAE OF COVID-19 IN ENCEPHALOPATHIC COVID-19 PATIENTS?

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INTRODUCTION: Elevated creatine kinase (CK) levels have been demonstrated as a poor prognostic factor of outcomes in acute COVID-19 infection but its role as a marker of post-acute sequelae of COVID-19 (PASC) is unclear.

OBJECTIVE: To investigate whether elevated CK is a prognostic factor in SARS-CoV-2 related encephalopathy in development of PASC.

METHODS: A retrospective chart review was performed on hospitalized encephalopathic patients who developed COVID-19 infection during March-May of 2020 at an urban tertiary care center. Patients were divided into subgroups according to elevated CK levels (E-CK) vs non-elevated CK levels (N-CK) with elevated defined as >200 u/L. Follow-ups between 4 weeks and 1 year from initial visit were analyzed for development of new or persisting symptoms to determine incidence of PASC.

RESULTS: Of the 43 encephalopathic COVID-19 infection patients reviewed, 25 and 18 patients were found to be in the E-CK and N-CK groups, respectively (average serum CK level of 1485 u/L vs 87.11 u/L, p=0.0026). Among the E-CK group, 14 patients (56%) had follow-up at least 4 weeks post admission in the outpatient setting vs 13 patients (72.22%) in the N-CK group (p>0.05), with an average total follow-up time of 477.37 days post initial admission in the E-CK group and 466.7857 days for N-CK (p>0.05). In the follow-up E-CK group, 6 patients (42.85%) reported any one of the PASC symptoms whereas in the follow-up N-CK group, 9 patients (69.23%) reported any one of the PASC symptoms (RR=0.73, 95%CI [0.32-1.69], p=0.47).

SUMMARY/CONCLUSION: Encephalopathic patients who had elevated CK levels on COVID-19 infection admission did not have an increased risk of developing PASC.

TYPE 2 DIABETES EFFECT ON AMYOTROPHIC LATERAL SCLEROSIS ONSET: A NEW YORK STATE PLANNING AND RESEARCH COOPERATION STUDY

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INTRODUCTION: Previous literature has suggested that patients with type 2 diabetes have an older age of onset of ALS when compared to non-diabetic ALS patients, suggesting a protective effect.

OBJECTIVE: To identify whether there are significant differences in the age at diagnosis of ALS in the presence of comorbid conditions.

METHODS: The New York State Planning and Research Cooperative System (SPARCS) database was utilized to gather ALS patient data. The comorbid conditions of congestive heart failure, ischemic stroke, and end stage renal disease were compared to the separate cohort of patients with type 2 diabetes (DM2) and ALS.

RESULTS: There were 6,489 patients with ALS identified. Of these, 2,043 had hypertension (32.9%), 357 had congestive heart failure (5.5%), 39 had ischemic stroke (0.6%), 13 had end stage renal disease (0.2%), and 697 had DM2 (10.7%). There was no significant difference between gender and appearance of comorbid conditions of ALS patients (p=0.314). Patients with comorbid conditions were significantly older than those without comorbid conditions (69.69±11.04 vs 62.32±13.73; p<0.001). Similar findings were observed in DM2 patients compared to non-diabetic patients (67.88±11.24 vs 64.55±13.51; p<0.001).

SUMMARY/CONCLUSION: Similar to ALS patients with DM2, patients with other comorbid conditions are significantly older when diagnosed with ALS compared to patients without comorbid conditions. This is most likely related to the fact that aging is associated with more comorbid conditions rather than these comorbid conditions including type 2 diabetes delaying or protecting from ALS.

RETROSPECTIVE STUDY OF SELECT ADVERSE EVENTS OF SPECIAL INTEREST ASSOCIATED WITH CORTICOSTEROID USE IN MYASTHENIA GRAVIS

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INTRODUCTION: Myasthenia gravis (MG) is an autoantibody-driven disease. Oral corticosteroids (OCS) remain the initial medication for patients requiring immunotherapy despite known toxicities.

OBJECTIVE: To assess the risk of select adverse events of special interest (AESIs) during real-world OCS use in MG patients.

METHODS: US adults with newly diagnosed MG between 01/2015 and 06/2022 were identified from the Optum Clinformatics database. Periods of OCS exposure and non-exposure were defined for each patient. AESIs were identified based on the Glucocorticoid Toxicity Index using International Classification of Diseases (ICD) codes. Frailty models were fitted to assess risks of recurrent AESIs during OCS-exposed periods versus non-exposed periods as hazard ratios (HR). OCS dose and concomitant medications were included as time-variating covariates along with time-fixed baseline characteristics.

RESULTS: Among the 3,839 newly diagnosed MG patients identified, 1,781 (46%) were treated with OCS after diagnosis. The patients had median 1 episode (interquartile range [IQR] 1-3) of OCS exposure with median duration of 45 days (IQR 14-142). The crude incidence rate of any AESI was 1.57 (95% CI: 1.5–1.65) per patient-year during OCS exposure and 0.57 (0.56–0.59) during non-exposure. Adjusted frailty models identified significantly increased hazard of any AESI during OCS exposure for all OCS dosages, low: 2.45 (2.24-2.67), medium: 2.24 (2.03-2.46), high: 2.56 (2.32-2.82). Increased hazards were also observed for each of the AESIs evaluated including cardiac and bone events.

SUMMARY/CONCLUSION: OCS exposure was associated with significantly increased hazard of AESIs in MG patients. Steroid-sparing immunotherapies for the underlying disease are needed in this population.

Disclosures:

Sicong Huang - Is or was an employee of Janssen Pharmaceuticals and may own stock in Johnson & Johnson

Sindhu Ramchandren - Is or was an employee of Janssen Pharmaceuticals and may own stock in Johnson & Johnson

Kristin Heerlein - Is or was an employee of Janssen Pharmaceuticals and may own stock in Johnson & Johnson

Lauren Wilson - Is or was an employee of Genesis Research

Xin Zhao - Is or was an employee of Genesis Research

Amanda Howarth - Is or was an employee of Genesis Research

Carlos Flores - Is or was an employee of Genesis Research

Hemanth Kanakamedala - Is or was an employee of Janssen Pharmaceuticals and may own stock in Johnson & Johnson

DESIGN OF A PHASE 2, MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL-GROUP STUDY OF NIPOCALIMAB IN PARTICIPANTS WITH ACTIVE IDIOPATHIC INFLAMMATORY MYOPATHIES (SPIREA)

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INTRODUCTION: Idiopathic inflammatory myopathies (IIM) are a rare group of systemic autoimmune diseases characterized by progressive muscular weakness and internal organ involvement, often leading to physical disability and decreased quality of life. Nipocalimab is designed to address the underlying disease pathology by selectively blocking the neonatal Fc receptor to reduce pathogenic autoantibodies. In a phase 2 study of generalized myasthenia gravis (NCT03772587), nipocalimab lowered pathogenic IgG autoantibody levels with significant clinical benefit, acceptable safety, and a favorable benefit-risk profile.

OBJECTIVE: SPIREA (NCT05379634) aims to evaluate the efficacy and safety of nipocalimab in patients with IIM.

METHODS: SPIREA is a phase 2, double-blind, placebo-controlled, randomized clinical trial enrolling adults (N≈200) with active IIM. The study comprises screening (≤6 weeks), double-blind treatment (52 weeks), long-term extension (48 weeks), and follow-up periods (8 weeks). Randomized participants are treated every 2 weeks with intravenous nipocalimab or placebo through Week 50. Background oral glucocorticoid (GC) doses will be tapered from Weeks 24-44.

RESULTS: The primary endpoint is the proportion of participants who achieve at least minimal improvement (≥20) in the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) Total Improvement Score (TIS) at Week 52 and on ≤5 mg/day of oral GC from Weeks 44-52. Secondary endpoints include the proportion of participants who achieve ≥20-point improvement in TIS at Weeks 24 and 52.

SUMMARY/CONCLUSION: The ongoing SPIREA study evaluating nipocalimab's safety and efficacy in patients with IIM will help to validate the ACR/EULAR-TIS endpoint in IIM and the role of nipocalimab as a steroid-sparing agent in IIM.

Disclosures:

Catherine E. Najem - Employee of Janssen Pharmaceutical Company of Johnson & Johnson and may own stock or stock options in Johnson & Johnson

Jagriti Craig - Employee of Janssen Pharmaceutical Company of Johnson & Johnson and may own stock or stock options in Johnson & Johnson

Lisa Christopher-Stine - Consultant of: Janssen, Boehringer-Ingelheim, Mallinckrodt, EMD-Serono, Allogene, and argenx

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Rohit Aggarwal - Consultant of: AbbVie, Alexion, AstraZeneca, Pfizer, Octapharma, CSL Behring, BMS, argenx, Corbus, EMD, Janssen, Kezar, Kyverna, Roivant, Q32, Corbus, EMD Serono, Jubliant, Scipher, Boehringer Ingelheim and Mallinckrodt; Grant/research support from: Pfizer, BMS, Q32, EMD Serono, Mallinckrodt, Genentech, and Boehringer Ingelheim

WEAK GLUTEUS MAXIMUS AND WEAK ILIOPSOAS WITH NORMAL GLUTEUS MAXIMUS: NEW SIGNS TO DIAGNOSE FUNCTIONAL WEAKNESS OF THE LOWER LIMBS

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INTRODUCTION: Positive signs are essential for the diagnosis of functional neurological disorders (FND). Those for diagnosing bilateral functional leg weakness are scarce.

OBJECTIVE: To describe a new positive sign to diagnose functional weakness of the lower limb, weak gluteus maximus (weak GM), and its complementary sign, weak iliopsoas with normal gluteus maximus (weak Ip with normal GM), and to test their validity.

METHODS: The test comprised MRC examinations of Ip and GM in the supine position. We retrospectively enrolled patients with FND or organic neurological disorders (OND) who presented with weakness of either Ip, GM, or both. Weak GM means that the MRC score of GM is 4 or less. Weak Ip with normal GM means that the MRC score of Ip is 4 or less whereas that of GM is 5.

RESULTS: Enrolled were 34 patients with FND and 73 patients with OND. The weak GM sign was positive in all 34 patients with FND and in 13 patients with OND, i.e., 100% sensitivity and 82% specificity. Therefore, the complementary sign, weak Ip with normal GM, was observed in no patients with FND, and its presence confirmed OND.

SUMMARY/CONCLUSION: These signs are useful for the detection or exclusion of nonorganic paresis. The background theory is that an “active” movement is preferentially affected in FND, and the downward pressing of the whole lower limb to the bed in the supine position is interpreted as a typical example of an active movement by a patient with FND.

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EFFECT OF ZILUCOPLAN ON DISEASE FLUCTUATION IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS IN THE PHASE 3 RAISE STUDY

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INTRODUCTION: RAISE (NCT04115293) was a phase 3, double-blind, placebo-controlled study of the complement component 5 inhibitor, zilucoplan, in patients with acetylcholine receptor autoantibody-positive (AChR+) generalized myasthenia gravis (gMG), which reported statistically significant and clinically meaningful improvements in MG-specific outcomes.

OBJECTIVE: To assess MG worsening (post hoc), MG worsening as a treatment-emergent adverse event (TEAE), and use of rescue therapy in RAISE.

METHODS: Adults with AChR+ gMG (MG Foundation of America Disease Class II–IV) were randomized 1:1 to receive daily subcutaneous zilucoplan 0.3 mg/kg or placebo for 12 weeks. MG worsening (post hoc) was defined as ≥3-point or ≥5-point increase from baseline in MG Activities of Daily Living (MG-ADL) or Quantitative MG (QMG) scores, respectively, at any time during the study. TEAEs reported as MG worsening were additionally assessed. If the investigator deemed escalation of gMG therapy to be necessary, rescue therapy (IVIg or plasma exchange) was administered concomitantly.

RESULTS: Eighty-six patients were randomized to zilucoplan and 88 to placebo. More patients showed MG worsening (≥3/≥5-point increase in MG-ADL/QMG) in the placebo group compared to the zilucoplan group (25.0% vs 10.5%, respectively; nominal $p<0.05$, not multiplicity-controlled). Among 8 patients who experienced TEAE of MG worsening in the placebo group, all (100%) received rescue therapy. Nine zilucoplan patients had this TEAE, of whom only 2 (22.2%) received rescue therapy.

SUMMARY/CONCLUSION: A significantly lower proportion of zilucoplan patients experienced MG worsening and, of those who had TEAE of MG worsening, a lower proportion required rescue therapy at any time during RAISE, compared with placebo. Funding: UCB Pharma.

Disclosures:

Angela Genge - Consultant for Medtronic, Atlantic Research Group, Calico, Apellis, Anexon, ALS Pharmaceuticals, QurAlis, Orion, Sanofi Genzyme, Ionis, Wave Life Therapies, Anelixis, Roche, Cytokinetics, Mitsubishi Tanabe Pharma, Amylyx, Alexion, UCB Pharma, Ra Pharmaceuticals (now UCB Biosciences), Biogen, Eli Lilly, and Amicus Therapeutics

Channa Hewamadduma - Received speaker and consultancy honoraria from argenx and UCB Pharma

Raphaelle Beau Lejdstrom - Employee and shareholder of UCB Pharma

Babak Boroojerdi - Employee and shareholder of UCB Pharma

Fiona Grimson - Employee and shareholder of UCB Pharma

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James F. Howard Jr - Received support from Alexion Pharmaceuticals, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention, F. Hoffmann-La Roche, Horizon Therapeutics, Immunovant Inc, Merck EMD Serono, the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health, PCORI, Regeneron Pharmaceuticals, Sanofi US, Takeda Pharmaceuticals, Toleranzia AB, and UCB Pharma

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TRAUMATIC SCIATIC NEUROMA DEMONSTRATING FASCICULAR ORGANIZATION OF PROXIMAL SCIATIC NERVE

James Dorman (Chicago, IL)

INTRODUCTION: Proximal sciatic neuropathy often preferentially affects fibular nerve fibers. This is thought to be due to the nerve being fixed and relatively taut at its proximal and distal ends, and to its fascicles having less supporting connective tissue around them, thus rendering these fibers more susceptible to compression or stretch injury. This case presents the opposite situation. That is, a sciatic mononeuropathy with disproportionate involvement of tibial nerve fibers. The ultrasound findings in this case emphasize the importance of the cross-sectional anatomy of the proximal sciatic nerve.

CASE REPORT: A 31-year-old man sustained a gunshot wound to the right proximal anterior thigh with an exit wound in the right gluteal region. Examination showed 5/5 power throughout, but mild decreased power on toe flexion and extension. Deep tendon reflexes were absent. Decreased pin sensation was noted in the right lateral foot and medial ankle. Electromyography and nerve conduction showed a mild right femoral mononeuropathy and a right sciatic mononeuropathy with markedly preferential involvement of tibial fibers. Ultrasound revealed a large (5 cm x 1.5 cm) traumatic neuroma in continuity affecting the medial fibers of the proximal sciatic nerve, just below the gluteal cleft. The lateral portion of the nerve at that site had relatively normal fascicular architecture in comparison.

SUMMARY: This case serves as a reminder of the cross-sectional anatomy of the proximal sciatic nerve, consisting of the medial division (tibial nerve) and lateral division (fibular nerve).

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SPINAL EPIDURAL LIPOMATOSIS IN THE SETTING OF CHRONIC, LOW-DOSE STEROIDS - IMPORTANCE OF EARLY UTILIZATION OF STEROID-SPARING AGENTS

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INTRODUCTION/BACKGROUND: Spinal epidural lipomatosis, or pathological extradural lipid overgrowth, is a rare cause of progressive myelopathy. It is generally associated with spinal surgeries and high-dose steroid bursts. Here we present a case of a patient with thoracic spinal epidural lipomatosis in the setting of low-dose, chronic steroid use for an autoimmune condition.

CASE REPORT: A 56-year-old female with rheumatoid arthritis on chronic steroids for at least 15 years and prior lumbar surgery presented initially to the outpatient neurology office for evaluation of gait disturbance described as impaired balance and muscle weakness for 6 months. This was accompanied by worsening paresthesias, ascending numbness, and progressive gait dysfunction eventually requiring implementation of ambulatory aids. Though her progressive symptoms were initially concerning for a peripheral demyelinating disease or other neuromuscular disease, reflexes remained intact making chronic inflammatory demyelinating polyneuropathy (CIDP) less likely and this was confirmed by normal EMG. However, neuroaxial imaging with MRI revealed prominent thoracic spinal epidural lipomatosis and cerebrospinal fluid (CSF) studies showed severe protein elevation to max 660 consistent with lipid blockage of CSF outflow. The patient was found not to be a surgical candidate but prednisone was discontinued in favor of rituximab infusions per rheumatology recommendations. Conservative measures including weight management, physical therapy, and baclofen for her cramping and increased tone were initiated and the patient remained clinically stable.

SUMMARY/CONCLUSION: Though spinal epidural lipomatosis is frequently associated with high-dose steroids, this case demonstrates that the risk exists with chronic lower dose steroids as well and emphasizes the necessity of early implementation of steroid-sparing agents in autoimmune patients.

IMPROVEMENT IN MYASTHENIA GRAVIS ACTIVITIES OF DAILY LIVING SUBDOMAIN SCORES IN PATIENTS TREATED WITH ECULIZUMAB: RESULTS FROM A GENERALIZED MYASTHENIA GRAVIS REGISTRY STUDY

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BACKGROUND: Eculizumab, a complement component C5 inhibitor, has been shown to improve the symptoms of patients with anti-acetylcholine receptor antibody-positive (AChR Ab+) generalized myasthenia gravis (gMG) as assessed by the Myasthenia Gravis Activities of Daily Living (MG-ADL) scale.

OBJECTIVE: This subgroup analysis from a global gMG registry assessed MG-ADL score changes per muscle subdomain in eculizumab-treated patients in the US.

METHODS: Patient demographics and disease characteristics are presented for the entire gMG registry population and analysis subgroup, which consisted of patients from the registry who had MG-ADL scores both before and after eculizumab initiation (including patients who discontinued treatment; data cut-off: October 4, 2022). The distribution and change in MG-ADL scores by subdomain (bulbar [0–9], ocular [0–6], respiratory [0–3], limbs [0–6]) before and after eculizumab initiation are reported.

RESULTS: Demographics and disease characteristics were similar between the overall registry population (N=162) and analysis subgroup (n=92). Mean (standard deviation) duration of treatment was 1.7 years (1.2). Following eculizumab treatment, MG-ADL scores improved across every subdomain (mean percentage improvement: 58.2% [bulbar], 42.3% [ocular], 38.7% [respiratory], 46.7% [limbs]), and 55 patients (60%) had a lower number of subdomains with any symptoms present. The proportions of patients with improvements in MG-ADL scores were: 65% (bulbar), 70% (ocular), 34% (respiratory), and 51% (limbs).

CONCLUSIONS: These gMG registry results show that eculizumab treatment reduces MG-ADL scores and the number of affected subdomains in clinical practice, substantiating the broad benefit of complement C5 inhibition for patients with gMG.

Disclosures:

Vern Juel - Consultant for Accordant; advisory board member for Alexion; Data and Safety Monitoring Board member for Immunovant; site Principal Investigator in myasthenia gravis for Alexion, argenx, and Janssen

Ema Rodrigues - Employee of Alexion, AstraZeneca Rare Disease

Brian Werneburg - Employee of Alexion, AstraZeneca Rare Disease

Rup Tandan - Site Principal Investigator for Apellis, Alexion, Cytokinetics, and Mitsubishi-Tanabe; consultant for Apellis and Biogen; speaker for Amylyx

NEUROMUSCULAR ULTRASOUND AND ELECTRIC IMPEDANCE MYOGRAPHY IN CHARCOT-MARIE-TOOTH DISEASE: A PROSPECTIVE PILOT STUDY

Yohei Harada (Durham, NC), Paul Zwelling (Burlington, NC), Michael Lutz (Durham, NC), Lisa Hobson-Webb (Durham, NC)

INTRODUCTION: Charcot-Marie-Tooth (CMT) disease is a family of inherited peripheral neuropathies, for which there is no disease-modifying therapy. Recent advances in our understanding of pathophysiological and genetic mechanisms have led to multiple promising candidate treatments. As such, there is a critical and urgent need for novel, readily accessible, and sensitive outcome measures.

OBJECTIVE: Evaluate the association of the measures from quantitative neuromuscular ultrasound (NMUS) and hand-held electrical impedance myography (hEIM) with neurological impairment in CMT.

METHODS: The adult patients with genetically confirmed CMT were prospectively enrolled and underwent NMUS, hEIM evaluation, and clinical assessment. Nerve ultrasound was performed in median, ulnar, and sural nerves. Muscle ultrasound and hEIM were both performed in deltoid, forearm, quadriceps, tibialis anterior, and gastrocnemius muscles. First dorsal interosseous was also measured by muscle ultrasound.

RESULTS: Thirty-one patients with CMT were enrolled. Of these, 21 were women and the mean age was 51.9 years (SD= 16.8). CMT1A was the most common subtype (n=18) followed by CMT2A (n=4). The mean echointensity of any individual nerves or muscles, and muscle quality and body fat percentage of any muscles obtained by hEIM had no correlation with CMT Exam Score version 2 (CMTESv2) or Rasch-modified CMTESv2. No correlation was observed with mean echointensity of all nerves or muscles measured by NMUS, or mean hEIM values of all muscles.

SUMMARY/CONCLUSION: Our study suggested no association between neurologic impairment evaluated by CMTESv2 and the values obtained from quantitative NMUS or hEIM. One-year follow-up data is pending.

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A CASE SERIES OF PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS TREATED WITH THE COMPLEMENT COMPONENT C5 INHIBITORS ECULIZUMAB AND RAVULIZUMAB

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INTRODUCTION: Eculizumab and ravulizumab are complement component C5 inhibitor (C5i) therapies that are indicated for treating acetylcholine receptor antibody-positive generalized myasthenia gravis (AChR+ gMG), an autoimmune disease of the neuromuscular junction that causes muscle weakness. This case series reports real-world data for patients treated with eculizumab and ravulizumab or transitioning from eculizumab to ravulizumab.

CASE REPORT: We report efficacy outcomes for 16 patients (median age, 68 years) with AChR+ gMG who received eculizumab or ravulizumab. Efficacy was assessed using patient-reported MG Activities of Daily Living (MG-ADL) scores (max score, 24), as well as physician-performed manual muscle testing (MMT) assessments (max score, 56). On eculizumab, 10 out of 11 patients improved MG-ADL (median change, -6), and 8 out of 11 patients improved MMT score (median change, -9). For C5i naïve patients on ravulizumab, all patients improved MG-ADL score (n=2; median change, -1.5) and MMT score (median change, -10). Two out of 3 patients that transitioned from eculizumab to ravulizumab maintained or improved their MG-ADL score, while MMT score improved in 1 patient (change, -2) and was maintained in 2 patients. For the 9 patients with reported prednisone treatment, 8 patients tapered dose (median end dose on eculizumab: 5 mg/d; ravulizumab 2.5 mg/d) and 1 patient discontinued prednisone while on ravulizumab.

SUMMARY: Eculizumab and ravulizumab may improve perceived and objective symptoms of gMG while allowing for steroid tapering. Efficacy was maintained for patients transitioning from eculizumab to ravulizumab.

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Christopher Scheiner - Consultant for Alexion

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MATCHING-ADJUSTED INDIRECT COMPARISON OF RAVULIZUMAB/EFGARTIGIMOD IN GENERALISED MYASTHENIA GRAVIS: TIMEPOINT CHALLENGES

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INTRODUCTION: Matching-adjusted indirect comparisons (MAICs) can assess treatment benefits for symptom control in patients with generalized myasthenia gravis (gMG).

OBJECTIVE: Building on previous comparisons of ravulizumab and efgartigimod, we performed a MAIC using mean changes from baseline in Myasthenia Gravis Activities of Daily Living (MG-ADL) scores from the CHAMPION-MG and ADAPT trials to assess the effects of these treatments on symptom control at different timepoints in patients with gMG.

METHODS: Individual patient-level data from CHAMPION-MG were weighted to match summary baseline characteristics from the acetylcholine receptor antibody-positive subset of patients in ADAPT at the trial-arm level. Mean changes in MG-ADL scores from baseline to different timepoints were compared, and anchored comparisons were performed at Weeks (Wks) 4 and 10, and at Wk8 (efgartigimod) vs Wk26 (ravulizumab).

RESULTS: Patients from CHAMPION-MG (N=175) and ADAPT (N=129) were included, with baseline characteristics similar across both studies. Improvements in MG-ADL scores varied across timepoints and appeared to favor efgartigimod vs ravulizumab at Wk4 (mean MG-ADL change from baseline: -1.6, 95% confidence interval [CI] –3.0 to –0.3). However, at Wk10 (mean change from baseline: 1.0, 95% CI –0.5 to 2.5), and Wk8 (efgartigimod) vs Wk26 (ravulizumab) (mean change from baseline: 1.2, 95% CI –0.2 to 2.7), the results trended in favor of ravulizumab.

SUMMARY/CONCLUSION: Outcomes from indirect comparisons of symptom control in patients with gMG treated with ravulizumab vs efgartigimod can vary depending on timepoints and matching methodology. Symptom control consistency over a prolonged period should be considered, alongside efficacy and tolerability, when assessing treatments for gMG.

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Christopher Scheiner - Consultant for Alexion and CSL Behring GmbH

Masayuki Masuda - Received speaker honoraria from argenx, Asahi Kasei Medical, UCB Pharma, and Alexion; participated in advisory board meetings for Alexion and argenx

Adrian Kielhorn - Employee of Alexion

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Lauren Powell - Employee of Broadstreet Health Economics & Outcomes Research, which received funding from Alexion to conduct this work

Basia Rogula - Employee of Broadstreet Health Economics & Outcomes Research, which received funding from Alexion to conduct this work

Karissa Johnston - Employee of Broadstreet Health Economics & Outcomes Research, which received funding from Alexion to conduct this work

COMPARISON OF THE RANGE OF SENSORY POTENTIALS PARAMETER VALUES BETWEEN PARTICIPANTS WITH AND WITHOUT DIABETIC NEUROPATHY BASED ON NEUROPATHY SCALE MEASUREMENTS

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INTRODUCTION: The normative value of sensory nerve potentials based on validated neuropathy assessment tools among diabetic neuropathy and healthy participants is not known.

OBJECTIVE: To use Utah Early Neuropathy Scale (UENS) to classify participants into diabetic neuropathy versus no neuropathy and compare sural and superficial peroneal sensory potentials accordingly.

METHODS: The data of UENS and nerve conductions were collected prospectively. We compared the values of sural and superficial peroneal sensory nerves according to different age group. Participants were classified as diabetic neuropathy if UENS > 4, otherwise they fell into no neuropathy group.

RESULTS: We included 75 participants with diabetic neuropathy and 94 without neuropathy, with age median interquartile range (IQR) of 53 (50-60) and 47.5 (43-56) and male n (%) of 38 (50.7%) and 44 (46.8%), respectively. The median IQR for sural nerve amplitude (μV) for diabetic neuropathy versus no neuropathy for age group <40 years was 8.2 (0-16) vs 15.3 (10.1-21.8) p=0.39, for age 40-49 was 2 (0-7.9) vs 11.9 (8.2-15.5) p=0.003, for age 50-59 was 4.4 (0-9.5) vs 10.5 (8.5-14.5) p<0.001, for age 60-75 was 0 (0-8.7) vs 7.55 (7.5-11.6) p=0.09, respectively. Superficial peroneal sensory potential (μV) for age group <40 years was 1.9 (0-3.7) vs 8.7 (4.6-10.6) p=0.08, for age 40-49 was 3.1 (0-4) vs 7.3 (4.5-10) p=0.002, for age 50-59 was 1.5 (0-4.3) vs 7.2 (4.5-9.9) p<0.001, for age 60-75 was 0 (0-5.3) vs 4.9 (2.7-7.2) p=0.09, respectively.

SUMMARY/CONCLUSION: The value of sural and superficial peroneal sensory potentials were determined among patients with and without diabetic neuropathy who were classified based on a validated neuropathy tool. Among elderly patients with no neuropathy these values were higher than previously reported.

PHANTOM RADICULOPATHY: AN ELECTRODIAGNOSTIC CHALLENGE

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INTRODUCTION/BACKGROUND: A 58-year-old patient developed lumbar radiculopathy pain 18 years after a left traumatic transfemoral amputation. The patient ambulated with prostheses for many years, however, ceased for more than a year secondary to pain. Pain radiated through the residual limb to the amputated foot.

CASE REPORT: Lumbar MRI showed lumbar spondylosis, multilevel disc desiccation, bilateral foraminal stenosis, and facet arthropathy. Electrodiagnostic evidence was suggestive of a left L4 lumbar radiculopathy with corresponding activity in left L4 paraspinal, vastus medialis, and lateralis. The patient failed initial conservative management. Transforaminal epidural spinal injection (TFESI) was performed per 2 with good long-lasting relief and the patient was able to start prosthetic retraining.

SUMMARY/CONCLUSION: The goal of any EDX study is to provide a diagnosis of symptoms the patient is experiencing. Patients with amputation pose a challenge where key muscles may be absent. Additionally, experienced patients with amputation depend on their prosthesis to achieve maximal functionality in activities of daily living (ADLs), making diagnosis timing crucial. To date, no standard radiculopathy protocol exists in patients with amputation; furthermore, EDX studies are not routinely performed. In our literature review, no other case of phantom radiculopathy used EDX as a diagnostic tool. This case opens debate on the utility of EMG on patients with amputation and the possibility to establish a new guideline in diagnosis in this population. We suggest that an accurate diagnosis should arrive after all diagnostic modalities and clinical exams have been performed for proper treatment and diagnosis. Early recognition of phantom radiculopathy in patients with amputation is paramount to prevent treatment delay and promote functionality.

RESPONSE RATES WITH ZILUCOPLAN AMONG PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS IN AN INTERIM ANALYSIS OF RAISE-XT, A PHASE 3 OPEN-LABEL EXTENSION STUDY

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INTRODUCTION: Zilucoplan, a complement component 5 inhibitor, demonstrated efficacy in a 12-week, phase 3, randomized, placebo-controlled study (RAISE; NCT04115293) in patients with acetylcholine receptor autoantibody-positive generalized myasthenia gravis (gMG). Long-term data enhances our understanding of the safety and efficacy of zilucoplan in patients with gMG.

OBJECTIVE: To assess responder rates for Myasthenia Gravis Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) up to 60 weeks of treatment.

METHODS: RAISE-XT (NCT04225871) is an ongoing, phase 3 open-label extension study, which enrolled adults who completed a qualifying, double-blind study (NCT03315130/NCT04115293). Patients self-administered daily subcutaneous injections of zilucoplan 0.3 mg/kg. Primary outcome was incidence of treatment emergent adverse events (TEAEs). Exploratory outcomes included responder rates for MG-ADL and QMG (reduction of ≥3 points and ≥5 points without rescue therapy, respectively).

RESULTS: Out of 200 enrolled patients, 105 continued zilucoplan from their qualifying study, and 95 switched to zilucoplan from placebo (placebo-switch). Median (range) exposure at data cutoff was 1.2 (0.11–4.45) years. TEAEs occurred in 188 (94.0%) patients; 64 (32.0%) patients experienced a serious TEAE. At RAISE-XT baseline (Week 12 of double-blind study), MG-ADL and QMG responder rates were 74.2% and 59.8% for zilucoplan (n=93) and 52.2% and 37.1% for placebo-switch (n=90) groups, respectively. At Week 60, both MG-ADL and QMG responder rates had improved to 87.0% and 84.6% for zilucoplan and 85.7% and 77.1% for placebo-switch groups, respectively.

SUMMARY/CONCLUSION: In this interim analysis, zilucoplan demonstrated a favorable safety profile and improved MG-ADL and QMG responder rates, sustained up to 60 weeks of treatment. Funding: UCB Pharma.

Disclosures:

Tuan Vu - USF Site Principal Investigator for MG clinical trials sponsored by Alexion/AstraZeneca Rare Disease, argenx, Ra/UCB Pharma, Horizon/Viela Bio, Janssen/Momenta, Sanofi, Regeneron, and Cartesian Therapeutics; received speaking and/or consulting honoraria from Alexion, argenx, and UCB Pharma

M. Isabel Leite - Funded by NHS and the University of Oxford, UK; awarded research grants from the UK association for patients with myasthenia – Myaware and the University of Oxford; received speaker honoraria or travel grants from Biogen Idec, Novartis, argenx, UCB, and the Guthy-Jackson Charitable Foundation; serves on scientific or educational advisory boards for UCB Pharma, argenx, and Viela/Horizon

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Babak Boroojerdi - Employee and shareholder of UCB Pharma

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James F. Howard Jr - Received research support from Alexion Pharmaceuticals, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention, the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health, PCORI, UCB Pharma, and Takeda Pharmaceuticals; honoraria from Alexion Pharmaceuticals, argenx, F. Hoffmann-La Roche, Immunovant Inc, Merck EMD Serono, UCB Pharma, Regeneron Pharmaceuticals, Sanofi US, and Horizon Therapeutics; and non-financial support from Alexion Pharmaceuticals, argenx, UCB Pharma, and Toleranzia AB

LONG-TERM SAFETY OF REPEATED CYCLES OF ROZANOLIXIZUMAB TREATMENT IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: The MycarinG (MG0003/NCT03971422) phase 3 study demonstrated efficacy and safety of one 6-week cycle of rozanolixizumab in adults with generalized myasthenia gravis (gMG). Patients were enrolled in open-label extension MG0007 to evaluate long-term safety of repeated treatment cycles.

OBJECTIVE: To evaluate consistency of safety of repeated rozanolixizumab treatment cycles.

METHODS: Interim safety data were pooled for patients receiving ≥1 rozanolixizumab treatment cycle across MycarinG and MG0007.

RESULTS: One hundred eighty-eight patients received ≥1 cycle of rozanolixizumab 7 mg/kg (cycle 1, n=94) or 10 mg/kg (cycle 1, n=94). Treatment-emergent adverse events (TEAEs; most mild-to-moderate) occurred in 89.9% (169/188) overall, and 77.4% (103/133) and 91.6% (120/131) receiving rozanolixizumab 7 mg/kg or 10 mg/kg. TEAEs occurred in 78.2% (147/188), 69.9% (100/143), 59.3% (67/113), 57.6% (53/92), 73.0% (46/63), and 65.1% (28/43) of patients in Cycles 1-6, respectively. Incidence of common, severe, and serious TEAEs and TEAEs leading to discontinuation did not increase with additional treatment cycles. The most common TEAEs across all cycles were headache (46.3%), diarrhea (28.7%), pyrexia (18.1%), and nausea (14.9%). Infection (45.2%) and headache incidence did not increase across cycles. Overall, 22.3% (42/188) patients reported serious TEAEs. Serious TEAEs occurring in >1 patient were MG (6.4%), MG crisis (2.1%), and COVID-19 (1.6%). At data cut-off, 4 deaths had occurred during MG0007, all deemed unrelated to rozanolixizumab by investigators. With repeated cycles no clinically meaningful reductions in albumin or lipid levels from baseline were observed.

CONCLUSIONS: Rozanolixizumab was well tolerated in patients with gMG and had an acceptable safety profile that was consistent across repeated treatment cycles.

Funding: UCB Pharma.

Disclosures:

Tuan Vu - USF Site Principal Investigator for MG clinical trials sponsored by Alexion, argenx, Ra/UCB Pharma, Horizon/Viela Bio, Janssen/Momenta, Sanofi, Regeneron, and Cartesian Therapeutics; receives speaking and consulting honoraria from Alexion, argenx, and UCB Pharma

Julian Grosskreutz - Consultant for Biogen, Alexion, and UCB Pharma; his institution received research support from the Boris Canessa Foundation

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DOSE SELECTION AND CLINICAL DEVELOPMENT OF EFGARTIGIMOD PH20 SUBCUTANEOUS IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: Treatment with efgartigimod IV resulted in clinically meaningful improvement in generalized myasthenia gravis (gMG)-specific outcome measures in the ADAPT study. Based on the observed association between total immunoglobulin G (IgG) level reductions and MG-ADL improvements, a population pharmacokinetic (PK)/pharmacodynamic (PD) approach was utilized for dose selection of subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20).

OBJECTIVE: To confirm dose selection using the reduction of total IgG levels as a PD marker of noninferiority for efgartigimod PH20 SC.

METHODS: PK/PD data from a phase 1 study where healthy participants (n=32) received a single injection of efgartigimod PH20 SC at various fixed doses or 10 mg/kg were analyzed. Simulations were performed for a typical participant of 70 kg for a dose range of 750-1750 mg (25-mg increments). The selected dose was subsequently evaluated in healthy participants and patients with gMG (ADAPT-SC study) as treatment cycles of 4 weekly injections.

RESULTS: The 1000-mg dose of efgartigimod PH20 SC was predicted to result in comparable reduction in total IgG on day 29 as with efgartigimod IV. Both in healthy participants and in participants with gMG, the total IgG reduction with efgartigimod PH20 SC at Day 29 (i.e. 1 week after the last administration) was noninferior to efgartigimod IV 10 mg/kg. MG-ADL scores were comparable for PH20 SC and IV administration in ADAPT SC.

SUMMARY/CONCLUSION: The ADAPT-SC study demonstrated that the dose selection was appropriate as treatment with efgartigimod PH20 SC 1000 mg resulted in noninferior reduction in total IgG to efgartigimod IV at day 29.

Disclosures:

Tuan Vu - Speaker for Alexion, argenx BV, CSL Behring, and Allergan/AbbVie; consultant for argenx BV, Alexion/AstraZeneca, and UCB; participated in trials in MG sponsored by Alexion/AstraZeneca, argenx BV, Ra/UCB, Horizon/Viela Bio, Regeneron, Janssen/Momenta, Cartesians Therapeutics, and Sanofi

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Denis Korobko - Received speaker honoraria from Roche, Novartis Russia, Sanofi, Merck, Janssen (Johnson & Johnson company) and research grants from Novartis, UCB, argenx BV, Horizon Therapeutics, Bristol-Mayers-Squib; served on a scientific advisory boards for Novartis Russia, Janssen (Johnson & Johnson company), and BIOCAD

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Kimiaki Utsugisawa - Consultant for UCB Pharma, Janssen Pharma, Horizon Therpeutics (Viela Bio), Chugai Pharma, Hanall BioPharma, Merck, and Mitsubishi Tanabe Pharma; received speaker honoraria from argenx BV, Alexion Pharmaceuticals, UCB Pharma, and the Japan Blood Products Organization

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ANTI-3-HYDROXY-3-METHYLGLUTARYL-COA REDUCTASE MYOPATHY CAN MIMIC TYPE 2 MYOTONIC DYSTROPHY

William Baek (Rancho Cucamonga, CA)

INTRODUCTION/BACKGROUND: 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) myopathy is a rare but treatable immune-mediated myopathy. Myotonic dystrophy type 2 (DM2) presents as a chronic proximal leg myopathy which is hereditary and incurable. We present 2 cases initially thought to be DM2 but genetically ruled out and confirmed to have anti-HMGCR myopathy.

CASE REPORT: Case 1 was a 68-year-old female with a 6-month history of progressive leg weakness who became wheelchair-bound. Creatine phosphokinase (CPK) levels were 3313. Anti-HMGCR Ab was 363. EMG showed myopathic units and myotonic discharges with fibrillations. The patient was treated with prednisone and rituximab with dramatic improvement. Both atorvastatin and pravastatin were discontinued. Case 2 was a 65-year-old female with a 2-year history of progressive leg weakness who became wheelchair-bound. CPK levels were 3276. Ant-HMGCR Ab was over 200. EMG showed myopathic units and myotonic discharges with fibrillations. The patient was treated with prednisone, IVIg, and mycophenolate mofetil with dramatic improvement. Both tested negative for DM2.

SUMMARY/CONCLUSION: Both anti-HMGCR myopathy and DM2 can present as a chronic proximal leg myopathy with elevated CPK levels and myotonic discharges on EMG. Anti-HMGCR myopathy is treatable, whereas DM2 is not. Checking anti-HMGCR antibodies is imperative to confirm the diagnosis.

Disclosures:

William Baek - Speakers Bureau for AbbVie Pharmaceuticals

EVALUATING THE SPECIFICITY OF THE WARM WATER SUBMERSION TEST FOR ERYTHROMELALGIA

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INTRODUCTION: Erythromelalgia is a rare neurovascular disorder that presents with symptoms of burning pain, warmth, and redness in the extremities, often triggered by heat or exertion. A commonly used bedside test involves soaking one hand or foot in warm water to provoke symptoms. Erythema in the soaked foot is considered a positive test. However, there is little information on the sensitivity or specificity of this screening tool.

OBJECTIVE: To investigate the specificity of the warm water submersion test for erythromelalgia.

METHODS: One patient with typical symptoms of erythromelalgia and 11 normal controls soaked their right foot in warm (approximately 40-43°C) water for 60 seconds. Photos of the subjects' feet were taken against a white background before and after soaking. A GitHub average color tool was used to obtain the average decimal red/green/blue (RGB) values of the 24-bit pixel colors from a sample of skin from each foot. The percentage difference between the normalized red components of the foot before compared to after submersion was calculated.

RESULTS: In the baseline group, the submersed feet were on average 1.7% more red after soaking compared to before (range = 97%-105%). For comparison, the submersed foot of the patient with erythromelalgia was 4.1% more red.

SUMMARY/CONCLUSION: In the general population, the warm water submersion test will produce some small amount of erythema. For a submersion test to be considered positive for erythromelalgia, the color change must be significantly higher than this baseline. We plan to continue to gather data to better define the specificity and sensitivity of this test.

POSITIVE RESULTS FROM A FIRST IN-HUMAN STUDY SUPPORTING CONTINUED DEVELOPMENT OF PGN-EDO51 FOR THE TREATMENT OF DUCHENNE MUSCULAR DYSTROPHY

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INTRODUCTION: PepGen's Enhanced Delivery Oligonucleotide (EDO) cell-penetrating peptide technology is engineered to optimize tissue delivery and cellular uptake of therapeutic oligonucleotides. Delivery of oligonucleotides is a major challenge that limits their efficacy. PGN-EDO51 is being evaluated for the treatment of DMD amenable to exon 51 skipping.

OBJECTIVE: To evaluate the safety, tolerability, pharmacokinetics (plasma and muscle), and pharmacodynamics (exon skipping) of single-ascending doses of PGN-EDO51 administered intravenously (IV) to healthy male volunteers (HV).

METHODS: Thirty-two adult HVs were randomized to receive a single dose of PGN-EDO51 (1, 5, 10, or 15 mg/kg; n=6 per cohort) or placebo (n=2 per cohort). Safety and tolerability were monitored over 28 days. Tissue concentrations of PGN-EDO51 and exon skipping were measured in biceps needle biopsies on Days 10 and 28.

RESULTS: All HVs completed the study. The majority of treatment-emergent adverse events were mild and resolved without intervention, including transient, reversible changes in kidney biomarkers (n=9) and hypomagnesemia (n=2) at the highest doses, with no clinical sequelae. Dose-dependent and sustained concentrations of PGN-EDO51 were measured in biceps biopsies: up to 50nM (both days at 15 mg/kg); and dose-dependent increases in mean exon skipping of up to 1.4% (10 mg/kg) and 2.0% (15 mg/kg).

SUMMARY/CONCLUSION: PGN-EDO51 has a generally tolerable profile at clinically relevant doses with evidence of pharmacological activity. PGN-EDO51 concentrations and levels of exon skipped transcripts in muscle at Day 28 indicate potential for accumulation of dystrophin with repeat dosing. A phase 2 program to assess the effects of multiple-ascending doses will be initiated in 2023.

Disclosures:
Michelle Mellion - PepGen employee and holds stock options
Jane Larkindale - PepGen employee and holds stock options; honorarium from NINDS for participation on advisory board
Pallavi Lonkar - PepGen employee and holds stock options
Jaya Goyal - PepGen employee and holds stock options
Ashling Holland - PepGen employee and holds stock options
Jeffrey Foy - PepGen employee and holds stock options
Brijesh Garg - PepGen employee and holds stock options
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Anthony Frank - PepGen employee and holds stock options
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Jennifer Cormier - PepGen employee and holds stock options
Sarah Vacca - PepGen employee and holds stock options
James McArthur - PepGen employee and holds stock options

DESIGN OF A PHASE 1, PLACEBO-CONTROLLED STUDY TO ASSESS SAFETY, TOLERABILITY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF SINGLE-ASCENDING DOSES OF PGN-EDODM1 IN MYOTONIC DYSTROPHY TYPE 1

Michelle Mellion (Boston, MA), Jennifer Shoskes (Boston, MA), Jane Larkindale (Boston, MA), Jennifer Cormier (Boston, MA), Holly Hand (Boston, MA), Sarah Vacca (Boston, MA), Pallavi Lonkar (Boston, MA), Ashling Holland (Boston, MA), Brijesh Garg (Boston, MA), Jeffrey Foy (Boston, MA), James McArthur (Boston, MA)

INTRODUCTION: PepGen's Enhanced Delivery Oligonucleotide (EDO) cell-penetrating peptide technology is engineered to optimize tissue delivery and cellular uptake of therapeutic oligonucleotides. Delivery of oligonucleotides is a major challenge that limits their efficacy. PGN-EDODM1 is being developed as a potential treatment for myotonic dystrophy type 1 (DM1). DM1 is caused by an expansion of a CTG trinucleotide sequence in the DMPK gene. PGN-EDODM1 binds to the pathogenic CUG trinucleotide repeat in DMPK mRNA, thereby liberating Muscleblind Like Splicing Regulator 1 (MBNL1) protein through steric blocking. Release of MBNL1 is hypothesized to correct DM1 spliceopathy, the root cause of DM1 symptoms.

OBJECTIVE: This single-ascending dose (SAD) study will evaluate the safety and tolerability of intravenous PGN-EDODM1 in adults with DM1. Secondary and exploratory endpoints include pharmacokinetics (PK), muscle distribution, pharmacodynamics (changes in splicing of transcripts), and select functional outcome measures.

METHODS: Males and females 18-50 years of age, inclusive, with genetically confirmed diagnosis of DM1 will be randomized (6 PGN-EDODM1: 2 placebo) to 3 dose cohorts. A muscle needle biopsy (tibialis anterior) will be performed at Baseline and at Weeks 4 and 16 for assessment of PGN-EDODM1 muscle concentrations and splicing of selected transcripts. Functional outcome assessments will also be included. An independent data and safety monitoring board will oversee dose escalation.

RESULTS: Doses to be assessed will be based on preclinical data. A detailed clinical plan will be presented.

SUMMARY/CONCLUSION: This phase 1 SAD clinical study, to be initiated in 2023, will support continued development of PGN-EDODM1 for the treatment of DM1.

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Sarah Vacca - PepGen share options and employment
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Ashling Holland - PepGen share options and employment
Brijesh Garg - PepGen share options and employment
Jeffrey Foy - PepGen share options and employment
James McArthur - PepGen share options and employment

CLINICAL AND REAL-WORLD PHARMACOVIGILANCE DATA OF MENINGOCOCCAL INFECTIONS IN ECULIZUMAB- OR RAVULIZUMAB-TREATED PATIENTS

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INTRODUCTION: Terminal complement inhibiting therapies (C5ITs) for rare hematological and neurological disorders are associated with increased Neisseria meningitidis (Nm) infection risk. Robust risk mitigation measures include vaccination, drug safety programs, and patient safety cards. Pharmacovigilance analysis of exposure-adjusted incidence and mortality data for Nm infections continues.

OBJECTIVE: Evaluate Nm infection and mortality rates in eculizumab- or ravulizumab-treated patients using clinical and real-world data.

METHODS: A cumulative search of the Alexion safety database was conducted for eculizumab (Mar 2007–Oct 2022) and ravulizumab (Dec 2018–Jun 2022) across indications, using the MedDRA High Level Term of Neisseria infection. Only cases associated with Nm were included.

RESULTS: For eculizumab- or ravulizumab-treated patients, respectively: cumulative clinical trial Nm infection rates are ~0.30 and 0.21 cases per 100 patient-years (PY), Nm mortality rates are ~0.00 and 0.03 cases per 100 PY; cumulative post-marketing reporting rates for Nm infections are stable at ~0.24 and 0.08 cases per 100 PY, Nm mortality rates are ~0.03 and 0.02 cases per 100 PY. In the real world, Nm infection rates in eculizumab-treated patients decreased over 15 years (0.57 to 0.24 per 100 PY); mortality rates remained stable (0.00 to 0.03 per 100 PY).

SUMMARY/CONCLUSION: Although cumulative exposure to eculizumab increased, including addition of rare neurological indications, Nm infection rates steadily decreased; mortality rates remained stable. Ravulizumab-treated patients have comparable rates. These data suggest that infection awareness, risk mitigation strategies, and availability of additional vaccines effectively reduced the risk of Nm infections in C5IT-treated patients, underlining the importance of adhering to those measures.

Disclosures:
Brian Werneburg - Employed by Alexion
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Guido Sabatella - Employed by Alexion
Arshad Mujeebuddin - Employed by Alexion

SEVERITY OF AUTONOMIC SYMPTOMS AND BLOOD PRESSURE RECOVERY PATTERNS DURING THE HEAD-UP TILT TEST IN PATIENTS WITH ORTHOSTATIC HYPOTENSION

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INTRODUCTION: Orthostatic hypotension (OH), defined as a reduction of at least 20 mmHg in systolic blood pressure (BP) or 10 mmHg in diastolic BP when standing, results from sympathetic adrenergic dysfunction.

OBJECTIVE: Although BP recovery reflects an ability of adrenergic compensation, the relationship between BP recovery and dysautonomia has been rarely evaluated. We aimed to investigate whether the severity of dysautonomia differs according to BP recovery patterns.

METHODS: We assessed dysautonomia using composite autonomic symptom scale 31 (COMPASS 31). Patients were classified into 4 groups according to BP recovery patterns: progressive OH (POH), sustained OH (SOH), OH with partial recovery (OHPR), and transient OH (TOH). We compared clinical findings, head-up tilt test (HUTT) results, and COMPASS 31 scores between OH groups.

RESULTS: A total of 167 patients (mean age 70.1±9.8 years; 62.3% male) were included (POH: 32, SOH: 64, OHPR: 11, and TOH: 60). Early tilt termination due to orthostatic intolerance was more common in the POH (43.8%) than the TOH groups (6.6%) ($p<0.001$). The POH group showed the greatest drop in systolic BP (64.0±20.2 mmHg) after tilting. The mean scores were highest in the POH group and greater in the POH than the TOH group ($p=0.001$).

SUMMARY/CONCLUSION: According to OH groups, patients showed different severity of autonomic symptoms and hemodynamic profiles in HUTT. The POH group exhibited more severe dysautonomia compared with the others. Based on HUTT result, clinicians may anticipate the severity of dysautonomia in OH patients and provide proper management in clinical practice.

CLINICALLY MEANINGFUL REDUCTION IN MYASTHENIA GRAVIS ACTIVITY OF DAILY LIVING SCORES IN 6 PATIENTS OVER 46 EFGARTIGIMOD INFUSION SESSIONS

George Small (Pittsburgh, PA), Sukmani Sandhu (Pittsburgh, PA)

INTRODUCTION: Efgartigimod (Vyvgart) is a recently approved infusion therapy for adult patients with antibody positive generalized myasthenia gravis (gMG).

CASE REPORT METHOD: Significant clinically meaningful improvement in Myasthenia Gravis Activities of Daily Living (MG-ADL) scores resulted in FDA approval of the drug on December 17, 2021.

RESULTS: This type of MG-ADL improvement generally accepted to be a 2-point reduction, we report our positive experience in treating 6 patients with a total infusion number to date of 46, with no reported adverse events except minimal hair loss in 1 several weeks after infusion initiation, and no hospitalizations, musculoskeletal pain, or infections. Five patients have had multiple cycles of infusions, 1 patient having had 6 cycles. All patients reduced their oral corticosteroid doses, 1 ceased immunoglobulin (Ig) therapy in favor of using Vyvgart, and 1 experienced a large deep vein thrombosis while previously on Ig, switching to efgartigimod. Pretreatment ADL scores were 6 through 10, all patients reducing their ADL scores by at least 2, the average ADL score reduction, 3.

CONCLUSIONS: Our favorable therapeutic experience with this neonatal Fc receptor fragment inhibitor over 46 infusions in its first 18 months post-FDA approval for antibody positive gMG adult patients in clinically meaningful recovery bodes well for this difficult-to-control population. The next step in practice in our experience is accelerating insurance approval processes to allow more treatment access and studying the potential for morbidity reduction if long-term corticosteroid exposure can be achieved in treated patients.

PATIENT-REPORTED OUTCOMES WITH HYALURONIDASE-FACILITATED SUBCUTANEOUS IMMUNOGLOBULIN 10% MAINTENANCE THERAPY FOR CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY

Colin Anderson-Smits (Cambridge, MA), James French (Cambridge, MA), Shabbir Hasan (Cambridge, MA), Erin Greco (Cambridge, MA), Hakan Ay (Cambridge, MA)

INTRODUCTION: Facilitated subcutaneous immunoglobulin (fSCIG; human immunoglobulin G 10% with recombinant human hyaluronidase) is under investigation as a potential maintenance therapy for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

OBJECTIVE: To determine the effect of fSCIG on patient-reported outcomes (PROs) in a phase 3, randomized, placebo-controlled, double-blind, multicenter study (ADVANCE-CIDP 1; NCT02549170).

METHODS: Adults with CIDP who had received stable doses of IVIg for ≥12 weeks were randomized to fSCIG or placebo (at same dose/interval as pre-randomization IVIg) for 6 months or until relapse/discontinuation. Rasch-built Overall Disability Scale (R-ODS), EQ-5D-3L, 36-Item Short Form health survey (SF-36), 9-item Treatment Satisfaction Questionnaire for Medication (TSQM-9), and treatment preference were assessed.

RESULTS: Overall, 132 patients received fSCIG (n=62) or placebo (n=70). From baseline to end of therapy (EOT), least-squares mean changes in R-ODS centile score were -0.9 and -6.1 with fSCIG and placebo, respectively (p=0.03). Median EQ-5D-3L and SF-36 scores generally indicated stable/improved health-related quality of life (HRQoL) with fSCIG and stability/deterioration with placebo. Median TSQM-9 global satisfaction/effectiveness scores remained stable with fSCIG and decreased from baseline to EOT with placebo; convenience scores improved in both groups. Overall, 67% of the fSCIG group preferred fSCIG to pre-study IVIg at EOT and 83% stated that they would choose to continue study treatment.

SUMMARY/CONCLUSION: fSCIG maintained the HRQoL that patients with CIDP previously experienced with IVIg and demonstrated favorable treatment satisfaction, preference, and convenience.

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Disclosures:

Colin Anderson-Smits - Employee of Takeda Development Center Americas, Inc and is a Takeda shareholder

James French - Employee of Takeda Development Center Americas, Inc and is a Takeda shareholder

Shabbir Hasan - Employee of Takeda Development Center Americas, Inc and is a Takeda shareholder

Erin Greco - Employee of Takeda Development Center Americas, Inc and is a Takeda shareholder

Hakan Ay - Employee of Takeda Development Center Americas, Inc and is a Takeda shareholder

A COMPARATIVE REAL-WORLD STUDY EVALUATING THE SAFETY OF GAMMAGARD LIQUID AND OTHER INTRAVENOUS IMMUNOGLOBULIN THERAPIES FOR THE TREATMENT OF CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY

J. Bradley Layton (Research Triangle Park, NC), Colin Anderson-Smits (Cambridge, MA), Zhongwen Huang (Cambridge, MA), Hakan Ay (Cambridge, MA), William Spalding (Cambridge, MA), Bilal Khokhar (Cambridge, MA), Jie Zhou (Cambridge, MA), Lee Bennett (Research Triangle Park, NC), Mary S. Anthony (Research Triangle Park, NC)

INTRODUCTION: We evaluated the safety of GAMMAGARD LIQUID (GGL), an IVIg 10% therapy, versus comparator IVIgs with US approval to treat chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

OBJECTIVE: Determine rates of adverse events of special interest (AESIs) in patients with CIDP initiating GGL versus comparator IVIgs by prior treatment status (immunoglobulin-naive and immunoglobulin-experienced) using real-world healthcare insurance databases.

METHODS: This nonrandomized active-comparator new-user cohort study of adults with CIDP used the Optum Clinformatics® and MarketScan® databases (Jan-1-2008–Dec-31-2019; protocol registered a priori [NCT05363358]). Treatment groups comprised GGL and US-approved comparator IVIgs for CIDP: Gammaked, Gamunex-C, and Privigen (all human IVIg 10%). AESI rates (thrombotic/hemolytic events, acute kidney injury) were compared between groups within propensity score-weighted samples using hazard ratios (HR), time-specific risk ratios (RR), and risk differences (RD). Database-specific estimates were pooled with meta-analysis.

RESULTS: Data from eligible patients in Optum (GGL, n=644; comparators, n=1293) and MarketScan (GGL, n=1441; comparators, n=2708) were analyzed, with good between-group comparability after propensity score weighting. AESIs were rare across cohorts and database-pooled estimates were consistent, with no overall differences (e.g., for patients initiating GGL versus comparator IVIgs, pooled thrombosis HR=1.35 [95% confidence interval 0.84, 2.15]; 1-year specific RR=0.86 [0.47, 1.57]; RD=−0.0008 [−0.0138, 0.0122]). Time-specific thrombosis rate estimates showed some differences; overall 1-year risk was lower for GGL versus comparators in Optum and similar in MarketScan.

SUMMARY/CONCLUSION: This large real-world study evaluated risks of rare IVIg-associated AESIs using methods to control for confounding. There were similar AESI risks for different IVIgs.

Study/writing funding: Takeda Development Center Americas, Inc./Takeda Pharmaceuticals International AG.

Disclosures:

J. Bradley Layton - Employee of RTI Health Solutions, an independent, non-profit research organization, that received funding from Takeda for the conduct of this study

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Mary S. Anthony - Employee of RTI Health Solutions, an independent, non-profit research organization, that received funding from Takeda for the conduct of this study

SURVIVAL IN ETEPLIRSEN-TREATED VS DUCHENNE MUSCULAR DYSTROPHY NATURAL HISTORY PATIENTS: AN INDIRECT TREATMENT COMPARISON USING REAL-WORLD DATA

Joel Iff (Cambridge, MA), Nicolae Done (Baltimore, MD), Ed Tuttle (Boston, MA), Yi Zhong (Boston, MA), Fangzhou Wei (Boston, MA), Basil Darras (Boston, MA), Craig McDonald (Sacramento, CA), Eugenio Mercuri (Rome, Italy), Francesco Muntoni (London, United Kingdom)

INTRODUCTION: Eteplirsen results in attenuation of ambulatory and pulmonary decline in patients with Duchenne muscular dystrophy (DMD) vs natural history (NH) controls.

OBJECTIVE: Compare survival of eteplirsen-treated patients vs NH controls.

METHODS: Survival of eteplirsen-treated patients as part of routine care was compared with DMD NH data (2 US-based and 2 European studies). Kaplan-Meier curves were digitized to reproduce individual patient data. Survival age was compared between eteplirsen-treated patients and NH controls using unadjusted Kaplan-Meier curves, log-rank tests, Cox models, and parametric specifications. Time from treatment initiation to death was compared in a simulation randomly matching each eteplirsen-treated patient alive at age of treatment initiation with up to 15 NH controls, adjusted for baseline age and age-treatment interaction.

RESULTS: Among 579 patients, mean age at eteplirsen initiation was 11.9 years (range, 1.0-35.0) and mean exposure was 3.7 years (0.0-8.6). Median age at death was higher for eteplirsen-treated patients vs NH controls (32.8 vs 27.4 years, $p<0.0001$), resulting in prolonged median survival of 5.4 years for eteplirsen-treated patients. Eteplirsen-treated patients appeared to have a 66% higher survival vs NH controls (HR 0.34, 95% CI [0.23, 0.50], $p<0.001$). Mortality rates were lower for eteplirsen-treated patients vs NH controls across all 5-year segments (5-45 years). Younger initiation and longer treatment exposure were independently associated with longer survival. Results were robust to different combinations of NH controls; data limitations prevented adjusted comparison controlling for prognostic factors.

SUMMARY/CONCLUSION: These real-world data suggest that eteplirsen may prolong survival in patients with DMD across a wide age range.

Disclosures:

Joel Iff - Employee of Sarepta Therapeutics, Inc, and may own stock/options in the company

Nicolae Done - Employee of Analysis Group, Inc, which received payment from Sarepta Therapeutics, Inc, for participation in this research

Ed Tuttle - Employee of Analysis Group, Inc, which received payment from Sarepta Therapeutics, Inc, for participation in this research

Yi Zhong - Employee of Analysis Group, Inc, which received payment from Sarepta Therapeutics, Inc, for participation in this research

Fangzhou Wei - Employee of Analysis Group, Inc, which received payment from Sarepta Therapeutics, Inc, for participation in this research

Basil Darras - Received honoraria from Sarepta Therapeutics, Inc, for advisory board participation

Craig McDonald - Reports grants from Capricor, Catabasis, Edgewise, Epirium Bio, Italfarmaco, Pfizer, PTC Therapeutics, Santhera Pharmaceuticals, Sarepta Therapeutics, Inc, and other from Capricor, Catabasis, PTC Therapeutics, Santhera Pharmaceuticals, and Sarepta Therapeutics, Inc

Eugenio Mercuri - Received consultant fees from Sarepta Therapeutics, Inc

Francesco Muntoni - Received Sarepta Therapeutics, Inc, consultancies for advisory board and symposia participation, and consultancies from PTC, Dyne Therapeutics, Roche, Santhera Pharmaceuticals, and Pfizer

HETEROGENEITY FOR DIAGNOSING ULNAR NEUROPATHY AT THE ELBOW: A RETROSPECTIVE STUDY

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INTRODUCTION: Ulnar neuropathy at the elbow (UNE) is the second most common mononeuropathy. In 1999, AANEM published a practice parameter for diagnosis of UNE that includes absolute and relative conduction velocity (CV) slowing of above elbow (AE) and below elbow (BE) segments, decreased compound muscle action potential (CMAP) amplitude, and changes in CMAP configuration between AE and BE. In practice, we appreciate electrodiagnostic evidence of UNE that falls outside of these parameters.

OBJECTIVE: The aim of this study was to characterize clinical and EDX findings describing patterns of focal ulnar neuropathy.

METHODS: This retrospective study included 376 patients diagnosed with ulnar neuropathy. Patients with neuromuscular diseases such as polyneuropathy, C8 radiculopathy, or lower trunk plexopathy were excluded. Classic UNE was defined by slowed CV >10 m/s between AE and BE sites and an absolute CV less than 50 m/s to the abductor digiti minimi. Descriptive statistics were performed.

RESULTS: 76.1% met criteria for classic UNE, 13.3% had atypical findings consistent with UNE, and the remaining 10.6% had a combination that included distal ulnar or non-localizable ulnar lesions. Common atypical UNE findings included involvement to the first dorsal interosseus only, normal nerve conduction studies with abnormal EMG, and normal EDX studies with abnormal ultrasound images.

SUMMARY/CONCLUSION: While established parameters for UNE diagnose most patients, a subset with ulnar distribution symptoms may benefit from an expanded EDX evaluation when routine studies are normal or inconclusive.

INTERIM ANALYSIS OF EVOLVE: A LONG-TERM OBSERVATIONAL STUDY EVALUATING ETEPLIRSEN, GOLODIRSEN, OR CASIMERSEN IN ROUTINE CLINICAL PRACTICE

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INTRODUCTION: Eteplirsen, golodirsen, and casimersen are exon-skipping therapies approved for patients with Duchenne muscular dystrophy (DMD) with mutations amenable to 51, 53, and 45 exon skipping, respectively.

OBJECTIVE: Assess the usage, safety, and clinical outcomes of long-term use of eteplirsen, golodirsen, or casimersen in routine clinical practice from EVOLVE, an ongoing 5-year, phase 4, multicenter, observational study.

METHODS: This interim analysis includes data on serious adverse events (SAEs), adverse events of special interest, and loss of ambulation (LOA).

RESULTS: As of December 2021, 144 patients were enrolled with a mean (SD) age (years) of: eteplirsen (n=123), 13.7 (5.50); golodirsen (n=17), 13.5 (4.27); casimersen (n=4), 16.3 (11.67). Mean (SD) duration of treatment (years) was: eteplirsen, 4.7 (1.88); golodirsen, 1.3 (0.45); casimersen, 0.3 (0.22). Mean time (years) from DMD diagnosis to treatment initiation was: eteplirsen, 6.0 (4.74); golodirsen, 8.2 (3.76); casimersen, 13.5 (14.04). At treatment initiation, 82/123 (66.7%) eteplirsen-treated, 7/17 (41.2%) golodirsen-treated, and 2/4 (50%) casimersen-treated patients were ambulatory. To date, favorable safety profiles have been observed for all 3 therapies. During EVOLVE, SAEs occurred in 14 (11.4%) eteplirsen-treated patients; none were treatment related. No SAEs were reported for golodirsen or casimersen. Median age at LOA for eteplirsen-treated patients was 15.3 years, consistent with prior clinical trial post hoc results; small sample size to date precludes analysis of age at LOA for golodirsen and casimersen.

SUMMARY/CONCLUSION: These real-world data from the interim analysis of EVOLVE support the safety profiles and will continue to describe long-term clinical outcomes of eteplirsen, golodirsen, and casimersen.

Disclosures:

Kristen Ricchetti-Masterson - Employee of Sarepta Therapeutics, Inc

Sourav Santra - Employee of Sarepta Therapeutics, Inc
Shane Hornibrook - Employee of Sarepta Therapeutics, Inc

Ashutosh Kumar - Received research support from Sarepta Therapeutics, Inc, PTC Therapeutics, Avexis/Novartis, Fibrogen, PPMD, MDA, NIH, NINDS – U01 NS061799-01A2; served as consultant/advisory board member for PTC Therapeutics, Audentes, Sarepta Therapeutics, Inc, Avexis/Novartis, Roche, and Biogen; served on the speakers' bureau for PTC Therapeutics

Katherine Mathews - Received research support as site Principal Investigator from Sarepta Therapeutics, Inc, Italfarmaco, Retrotope, Reata, Catabasis, and Santhera; received research support from NIH, CDC, and FARA

Leigh Maria Ramos-Platt - Served on advisory boards for NS Pharma, PTC Therapeutics, Santhera Pharmaceuticals, Mallinckrodt, and Sarepta Therapeutics, Inc; received research support as Principal Investigator from Capricor, PTC Therapeutics, Catabasis, Fibrogen, Santhera Pharmaceuticals, and Sarepta Therapeutics, Inc

Megan Waldrop - Received research funding as site or study Principal Investigator from Sarepta Therapeutics, Inc, Novartis Gene Therapies, and Alcyone Therapeutics, Inc; serves as consultant for Sarepta Therapeutics, Inc

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Ihor Sehinovych - Employee of Sarepta Therapeutics, Inc

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Craig McDonald - Serves as consultant for Astellas/Mitobridge, Bristol Myers Squibb, Capricor, Catabasis Pharmaceuticals, Edgewise Therapeutics, Eli Lilly, Epirium Bio, Gilead, Halo Therapeutics, Italfarmaco, Novartis, Pfizer, Prosensa, PTC Therapeutics, Santhera Pharmaceuticals, and Sarepta Therapeutics, Inc; receives research funding and speaking fees from Sarepta Therapeutics, Inc

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INTERIM ANALYSIS OF EVOLVE: EVALUATING ETEPLIRSEN, GOLODIRSEN, OR CASIMERSEN TREATMENT IN PATIENTS <7 YEARS OLD IN ROUTINE CLINICAL PRACTICE

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INTRODUCTION: Current clinical recommendations for Duchenne muscular dystrophy (DMD) emphasize the importance of early diagnosis and treatment. Clinical trial 4658-102 (NCT03218995) demonstrated the safety and tolerability of eteplirsen in young patients (6–48 months old) with DMD.

OBJECTIVE: Describe patients' (<84 months) experience with phosphorodiamidate morpholino oligomer (PMO) treatment (eteplirsen, golodirsen, or casimersen) in routine clinical practice from the ongoing phase 4 observational EVOLVE study.

METHODS: Patients were stratified by age at PMO treatment initiation: <24, 24 to <48, and 48 to <84 months. The interim analysis included treatment patterns, safety, and functional assessments.

RESULTS: As of December 2021, 32 patients <84 months were enrolled; eteplirsen-treated (n=30): mean (SD) age (years) at treatment initiation was 1.8 (0.05), 3.3 (0.42), and 5.7 (0.74), and mean (SD) treatment duration (years) was 2.5 (1.45), 2.8 (1.66), and 4.6 (1.54) for the <24-, 24- to <48-, and 48- to <84-month-old groups, respectively. Steroid usage before eteplirsen initiation was 0/3 (0%), 1/7 (14.3%), and 12/20 (60.0%) for the 3 age groups. Three serious adverse events (SAEs) occurred in 2/30 (6.7%) eteplirsen-treated patients; none were deemed treatment related. Eteplirsen was well tolerated with no treatment-related discontinuations/interruptions. One golodirsen-treated and 1 casimersen-treated patient was enrolled (ages 6.4 and 6.2 at treatment initiation, respectively; treatment duration was 0.7 years for each). Neither had prior steroid use or reported SAEs.

SUMMARY/CONCLUSION: These real-world data are consistent with the safety of previous clinical studies and add to the body of evidence supporting early initiation of PMO treatment in young patients.

Disclosures:

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Rebecca Scharf - Received research funding from Genentech, Sarepta Therapeutics, Inc, Novartis, Fibrogen, Capricor, argenx BVBA, and Biohaven

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Ihor Sehinovych - Employee of Sarepta Therapeutics, Inc

Craig McDonald - Consultant for Astellas/Mitobridge, Bristol Myers Squibb, Capricor, Catabasis Pharmaceuticals, Edgewise Therapeutics, Eli Lilly, Epirium Bio, Gilead, Halo Therapeutics, Italfarmaco, Novartis, Pfizer, Prosensa, PTC Therapeutics, Santhera Pharmaceuticals, and Sarepta Therapeutics, Inc; receives research funding and speaking fees from Sarepta Therapeutics, Inc

EFFECT OF ZILUCOPLAN ON FATIGUE IN GENERALIZED MYASTHENIA GRAVIS IN THE PHASE 3 RAISE AND RAISE-XT STUDIES

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INTRODUCTION: Myasthenic fatigue has a marked negative impact on quality of life in patients with generalized myasthenia gravis (gMG). Zilucoplan demonstrated sustained efficacy in patients with gMG in RAISE (NCT04115293), a double-blind, placebo-controlled phase 3 study.

OBJECTIVE: This post-hoc analysis evaluated long-term effects on fatigue in RAISE patients who entered RAISE-XT (NCT04225871), an ongoing, open-label extension study of zilucoplan.

METHODS: In RAISE, adults with acetylcholine receptor autoantibody-positive MG Foundation of America Disease Class II–IV gMG were randomized 1:1 to daily subcutaneous zilucoplan 0.3 mg/kg or placebo for 12 weeks. Patients completing RAISE could enter RAISE-XT to receive zilucoplan 0.3 mg/kg. We report change in Quality of Life in Neurological Disorders (Neuro QoL) Short Form fatigue T-score from RAISE baseline to Week 60.

RESULTS: At the end of RAISE (Week 12), least squares mean (LSM) change from baseline in Neuro-QoL T-score was −6.26 for zilucoplan (n=86) vs -2.65 for placebo (n=88) (LSM difference: -3.61 [95% CI: −6.18, −1.05]; nominal p=0.0060, not multiplicity-controlled). After Week 12, 166 (95.4%) patients entered RAISE-XT to receive zilucoplan. T-scores improved within 1 week for patients who switched from placebo to zilucoplan (placebo-switch group). T-scores improved further to Week 16 for placebo-switch and zilucoplan groups and were sustained through Week 60 (mean [SD] change from RAISE baseline: -10.71 [11.71; n=42] and -9.15 [11.65; n=42], respectively).

SUMMARY/CONCLUSION: Fatigue is a challenge for patients with gMG. Zilucoplan significantly and clinically meaningfully improved myasthenic fatigue vs placebo during RAISE. Further improvements were observed during RAISE-XT and were sustained up to 60 weeks of treatment. Funding: UCB Pharma.

Disclosures:

Michael D. Weiss - Received honoraria for serving on scientific advisory boards for Alexion, Ra Pharmaceuticals (now UCB Biosciences), argenx, Biogen, Mitsubishi Tanabe Pharma, and Amylyx, consulting honoraria from Cytokinetics and CSL Behring, and speaker honoraria from Soleo Health; serves as a special government employee for the Food and Drug Administration

Miriam Freimer - Consultant for argenx, UCB Pharma, and Alexion; receives research support from the NIH, UCB Pharma, Janssen, Alnylam, Avidity, and Fulcrum

Angelina Maniaol - Received funding for travel, meeting attendance, consulting honoraria, or advisory board participation from argenx, CSL Behring, and UCB Pharma

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James F. Howard Jr - Received research support from Alexion Pharmaceuticals, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention, the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health, PCORI, UCB Pharma, and Takeda Pharmaceuticals; honoraria from Alexion Pharmaceuticals, argenx, F. Hoffmann-La Roche, Immunovant Inc, Merck EMD Serono, UCB Pharma, Regeneron Pharmaceuticals, Sanofi US, and Horizon Therapeutics; and non-financial support from Alexion Pharmaceuticals, argenx, UCB Pharma, and Toleranzia AB

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ASSESSING THE INCIDENCE AND PREVALENCE OF CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY IN THE UNITED STATES: RETROSPECTIVE CLAIMS DATA ANALYSIS

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INTRODUCTION: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an immune-mediated neuropathy disorder predominantly affecting the peripheral nervous system. While global incidence and prevalence of CIDP has been reported, no recent, large studies of the United States (US) incidence and prevalence are available.

OBJECTIVE: To estimate the prevalence and incidence of CIDP in the US.

METHODS: This retrospective study used Inovalon data from 2016 through 2020, covering nearly 170 million lives and containing professional and institutional medical claims from Commercial, Medicare Advantage, and Medicaid payors. CIDP diagnosis was defined by a patient having 2 diagnoses ≥30 days apart. We conducted a prevalence estimation of CIDP in 2019 and an incidence estimation across 2018 and 2019. Data collected included CIDP diagnoses, age at initial diagnosis, gender, comorbidities, and race.

RESULTS: For the prevalence estimation, 7,482 patients with CIDP were identified and stratified by age groups and gender. Extrapolating this to the US population using census data gave an estimate of 58,405 patients living in the US with CIDP. A raw incidence rate of 3.58 patients per 100,000 patient-years was found which, extrapolated to the US population, gave an adjusted the rate of 3.64 per 100,000 patient-years.

SUMMARY/CONCLUSION: We observed CIDP prevalence and incidence rates higher than previously reported. This was a relatively short observational study and CIDP identification relied on billing diagnoses and was limited primarily to Medicaid and commercially insured patients, therefore older patients are likely underrepresented. Additional research to confirm the methodology employed to identify CIDP patients seems warranted.

Disclosures:
Brett Venker - Employee of Roivant Sciences, Ltd
Jingyu Wang - Employee of Roivant Sciences, Ltd
Jennifer Schwinn - Employee of Immunovant, Inc
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INCIDENCE AND PREVALENCE OF MYASTHENIA GRAVIS: ANALYSIS OF A US COMMERCIAL INSURANCE CLAIMS DATABASE

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INTRODUCTION: Myasthenia gravis (MG) is an autoimmune disease mediated by antibodies disrupting various postsynaptic components at the neuromuscular junction. Estimates of the prevalence and incidence of MG in the United States (US) vary and robust studies describing this population are lacking.

OBJECTIVE: To estimate the prevalence and incidence of MG in the US and describe patient demographics.

METHODS: This retrospective study used Inovalon data from 2016 through 2020, covering nearly 170 million lives and containing professional and institutional medical claims from Commercial, Medicare Advantage, and Medicaid payors. Confirmation of MG diagnosis was made using a previously validated, peer-reviewed methodology. We conducted a prevalence estimation in 2019 and an incidence estimation across 2018 and 2019. MG diagnoses, age at initial diagnosis, gender, comorbidities, race, and ethnicity were analyzed.

RESULTS: For the prevalence estimation, 14,373 patients with MG were identified. Extrapolating this to the US population using census data gives an estimate of 116,255 patients living with MG in the US. For patients 18 and over, a raw incidence rate of 4.86 patients per 100,000 patient-years was found with an adjusted rate of 5.20 per 100,000 patient-years.

SUMMARY/CONCLUSION: This was a relatively short observational study (1-2 years). MG identification relied on billing diagnoses and was limited primarily to Medicaid and commercially insured patients, therefore older patients are likely underrepresented. However, the validity of the datasets used in this analysis give particular strength to the prevalence, incidence, and demographics observed in this study, which support the need for continued research in MG.

Disclosures:
Paola Mina-Osorio - Employee of Immunovant, Inc
Jingyu Wang - Employee of Roivant Sciences, Ltd
Jennifer Schwinn - Employee of Immunovant, Inc
Brett Venker - Employee of Roivant Sciences, Ltd

SUBSYNOVIAL CONNECTIVE TISSUE THICKNESS IS CORRELATED WITH DISEASE STATUS AND SEVERITY IN CARPAL TUNNEL SYNDROME

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INTRODUCTION: Non-inflammatory thickening of the subsynovial connective tissue (SSCT) is commonly found in carpal tunnel syndrome (CTS). As this thickening may happen early in the pathogenesis of CTS, sonographic evaluation of this structure might be useful.

OBJECTIVE: The aim of this study was to correlate SSCT thickness with disease status and severity in subjects with and without CTS.

METHODS: One hundred and forty-nine wrists of 82 subjects (mean age 51.4±17.8; 32 men, 50 women) were assessed for the absence/presence of CTS, based on NCS of the mixed median nerve. Subjects also completed the Katz hand diagram, Boston Carpal Tunnel Questionnaire (BCTQ), Disability of Arm, Shoulder, and Hand (DASH) and visual analogue scale (VAS). Sonographic evaluation of SSCT thickness and cross-sectional area (CSA) of the median nerve were obtained. Several linear mixed-effects models were fitted to assess the effect of disease status or severity on SSCT thickness. Age, sex, body length, and side of testing were set as covariates in each model.

RESULTS: Disease status based on NCS (ß=0.121; $p<0.0001$) and Katz hand diagram ($p= 0.003$), as well as disease severity based on VAS (ß= 0.001; $p=0.01$), BCTQ (ß=0.030; $p= 0.03$), and CSA (0.010; $p=0.001$) are significantly correlated with SSCT thickness. The DASH score is not ($p>0.05$).

SUMMARY/CONCLUSION: SSCT thickness is a predictor for disease status based on NCS. SSCT thickness also correlates with disease severity. Assessment of SSCT thickness may thus support the diagnosis of CTS, as well help to estimate the severity.

EFFECT OF RAVULIZUMAB ON MYASTHENIA GRAVIS–ACTIVITIES OF DAILY LIVING ITEM SCORES IN ADULTS WITH GENERALIZED MYASTHENIA GRAVIS: POST HOC ANALYSIS OF DATA FROM THE PHASE 3 CHAMPION MG STUDY

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INTRODUCTION: In the 26-week, randomized placebo-controlled period of CHAMPION MG (NCT03920293) in adults with anti-acetylcholine receptor antibody-positive (AChR Ab+) generalized myasthenia gravis (gMG), ravulizumab was associated with improved Myasthenia Gravis–Activities of Daily Living (MG-ADL) total score versus placebo.

OBJECTIVE: This post hoc analysis evaluated changes in the 8 MG-ADL item scores.

METHODS: Patients scored MG-ADL item impairment as 0–3 (higher scores, more severe impairment) at baseline and Week 26. Proportions of patients with improved MG-ADL item scores were calculated.

RESULTS: In patients with data available at baseline and Week 26 (160/175), greater proportions of ravulizumab-treated patients than patients receiving placebo achieved improved scores in 7 of the 8 MG-ADL items (ravulizumab/placebo: breathing, 33.3%/24.4%; chewing, 44.9%/28.0%; talking, 42.3%/37.8%; double vision, 37.2%/22.0%; eyelid droop, 50.0%/28.0%; brushing teeth/combing hair, 43.6%/41.5%; rising from chair, 30.8%/24.4%), and achieved complete resolution (score 0) for all 8 items. The ocular items had the highest proportions of patients with severe impairment (score 3) at baseline. Proportions of patients with a score of 3 in the ravulizumab-treated group were reduced from baseline to Week 26 for eyelid droop (23.1% to 14.1%) and were similar at baseline and Week 26 for double vision (11.5% and 10.3%). With placebo, increases from baseline to Week 26 were observed for both eyelid droop (20.7% to 24.4%) and double vision (6.1% to 12.2%).

SUMMARY/CONCLUSION: In patients with AChR Ab+ gMG, ravulizumab provided greater benefit in reducing symptom severity than placebo in 7/8 MG-ADL items, including ocular items, which had the highest proportions of patients with severe impairment at baseline.

Disclosures:

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Renato Mantegazza - Serves on advisory boards for Alexion, AstraZeneca Rare Disease, UCB, argenx, Catalyst, and Sanofi; received speaker's honoraria from Alexion, AstraZeneca Rare Disease, UCB, and argenx, and consultancy fees from Catalyst

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LONG-TERM EFFICACY AND SAFETY OF CIPAGLUCOSIDASE ALFA/MIGLUSTAT IN AMBULATORY PATIENTS WITH POMPE DISEASE: A PHASE III OPEN-LABEL EXTENSION STUDY (ATB200-07)

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INTRODUCTION: The phase 3 double-blind PROPEL study (NCT03729362) compared the investigational two-component enzyme replacement therapy (ERT) cipaglucosidase alfa/miglustat (cipa/mig) with alglucosidase alfa/placebo (alg/pbo) in ambulatory adults with late-onset Pompe disease (LOPD).

OBJECTIVE: This ongoing open-label extension (OLE) (NCT04138277) evaluates the long-term efficacy and safety of cipa/mig.

METHODS: Outcomes include 6-minute walk distance (6MWD), forced vital capacity (FVC), creatine kinase (CK) and hexose tetrasaccharide (Hex4) levels, and safety. Data are reported as change from the PROPEL baseline to OLE week 52 (104 weeks after the PROPEL baseline).

RESULTS: Of 119 patients from PROPEL who enrolled to the OLE (91 ERT-experienced; 28 ERT-naïve), 82 continued cipa/mig (cipa/mig group) and 37 switched from alg/pbo to cipa/mig (switch group). Mean (standard deviation [SD]) change in % predicted 6MWD was +3.1 (8.07) for the cipa/mig group and −0.5 (7.76) for the switch group in ERT-experienced patients, and +8.6 (8.57) and +8.9 (11.65) in ERT-naïve patients, respectively. Mean (SD) change in % predicted FVC was −0.6 (7.50) for the cipa/mig group and −3.8 (6.23) for the switch group in ERT-experienced patients, and −4.8 (6.48) and −3.1 (6.66) in ERT-naïve patients, respectively. Biomarker levels (CK and Hex4) improved with cipa/mig treatment; both groups reached similar levels by OLE week 52. Three patients discontinued the OLE due to infusion-associated reactions (urticaria, urticaria and hypotension, and anaphylaxis). No new safety signals were identified.

SUMMARY/CONCLUSION: Data demonstrate treatment with cipa/mig up to 104 weeks was associated with a durable effect and was well tolerated, supporting long-term benefits of cipa/mig treatment for patients with LOPD.

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Disclosures:

Tahseen Mozaffar - Advisory capacity: AbbVie, Alexion, Amicus Therapeutics, Inc, argenx, Audentes, Maze Therapeutics, Modis, Momenta, Ra Pharmaceuticals, Sanofi Genzyme, Sarepta, Spark Therapeutics, UCB, and Ultragenyx. Speaker's bureau: Sanofi Genzyme. Research funding: Myositis Association, the Muscular Dystrophy Association, the NIH and from the following sponsors: Alexion, Amicus Therapeutics, Inc, argenx, Audentes, Bristol-Myers Squibb, Cartesian Therapeutics, Grifols, Momenta, Ra Pharmaceuticals, Sanofi Genzyme, Spark Therapeutics, UCB, and Valerion. Data safety monitoring board: Acceleron, Avexis, Sarepta, and the NIH

Barry J. Byrne - Consultant/advisory board member: Pfizer, Amicus Therapeutics, Inc., and Sanofi. Stocks ownership: Lacerta Therapeutics

Jordi Díaz-Manera - Consulting fees/honorarium: Sarepta, Sanofi Genzyme, and Audentes; grants: Sanofi, Boehringer; payment for speaking: Sanofi Genzyme, Sarepta, and Lupin

Pascal Laforêt - Consultant/advisory board member: Amicus Therapeutics, Inc, Sanofi Genzyme, and Spark Therapeutics; travel expenses: Sanofi Genzyme and Spark Therapeutics

Priya Kishnani - Member: Pompe and Gaucher Disease Registry Advisory Board for Sanofi Genzyme, Amicus Therapeutics, Inc, and Baebies; consulting fees and honoraria: Sanofi Genzyme, Amicus Therapeutics, Inc, Maze Therapeutics, and Asklepios BioPharmaceutical, Inc; research/grant support: Sanofi Genzyme and Amicus Therapeutics, Inc; equity: Asklepios Biopharmaceutical, Inc and Maze Therapeutics

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Ans T. van der Ploeg - Advisory board member: Amicus Therapeutics, Inc, BioMarin, Sanofi Genzyme, and Spark Therapeutics; consultant: Amicus Therapeutics, Inc, BioMarin, Sanofi Genzyme, and Spark Therapeutics; contracted research: Amicus Therapeutics, Inc, BioMarin, Sanofi Genzyme, and Spark Therapeutics; all collaborations are done under an agreement between Erasmus MC and these industries

Jeff Castelli - Employee and stockholder: Amicus Therapeutics Inc

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THERAPEUTIC ELECTRICAL STIMULATION ACCELERATES DIAPHRAGM MUSCLE REINNERVATION IN A RAT MODEL OF SPINAL ACCESSORY TO PHRENIC NERVE TRANSFER REPAIR

Hongkai Wang (Chicago, IL), Colin K. Franz (Chicago, IL)

INTRODUCTION: Diaphragm muscle paralysis is a life-altering condition in which the primary muscle of respiration is rendered non-functional. It can occur due to a variety of causes, including spinal cord injury and phrenic neuropathy.

OBJECTIVE: We hypothesized that: (i) spinal accessory nerve to phrenic nerve transfer would restore diaphragm paralysis; and (ii) diaphragm muscle reinnervation would be accelerated by therapeutic electrical stimulation.

METHODS: Our therapeutic electrical stimulation protocol consisted of 1 hour of 20 Hz stimulation at 2-4 mA intensity delivered immediately after nerve repair. Rats with phrenic nerve transection and repair were randomly separated into 4 groups: phrenic-to-phrenic repair with or without electrical stimulation, and spinal-accessory-to-phrenic transfer repair with or without electrical stimulation. Our primary outcome measurement was M-Mode ultrasound of diaphragmatic excursion. Other outcome measurements included phrenic NCS and concentric needle EMG.

RESULTS: Therapeutic electrical stimulation did not improve phrenic axon regeneration and it took 10 weeks to recover normal diaphragm excursion on ultrasound. However, therapeutic electrical stimulation did improve spinal accessory axon regeneration and significantly decreased the time for diaphragm muscle recovery compared to all other groups by approximately 50% (5 weeks vs 10 weeks). In addition, spinal accessory electrical stimulation increased the compound muscle action potential amplitude compared to sham group (17.4% vs 9.3%).

SUMMARY/CONCLUSION: Brief therapeutic electrical stimulation selectively improves regeneration of spinal accessory axons, but not phrenic axons, for restoration of the paralyzed diaphragm. CKF acknowledges the support of the American Neuromuscular Foundation Development grant.

PREVALENCE OF TRANSTHYRETIN GENE VARIANTS IN THE ROCKY MOUNTAIN WEST REGION

Ellie Jacoby (Aurora, CO), Dianna Quan (Aurora, CO), Emily Todd (Aurora, CO), Brooke Hawkes (Aurora, CO), Nicholas Rafaels (Aurora, CO), Harry Smith (Aurora, CO), Kristy Crooks (Aurora, CO)

INTRODUCTION: Hereditary transthyretin (hATTR) amyloidosis is a genetic condition caused by pathogenic variants in the transthyretin (TTR) gene resulting in multisystem amyloid deposition, especially in peripheral nerve and heart. Strong founder effect and genotype/phenotype correlations exist among several populations despite the condition's heterogeneity. Information on prevalence of hATTR in the US is limited.

OBJECTIVE: To understand prevalence of TTR variants in our regional population and the most common variants.

METHODS: Colorado Center for Personalized Medicine (CCPM) BioBank collects specimens from consenting adults seen throughout the University of Colorado Health System, a catchment encompassing a large region within the Rocky Mountain West. Single nucleotide polymorphism (SNP) array genotyping is performed for genetic research. Participants have the option to learn about actionable variants including pathogenic TTR mutations. Prevalence of TTR variants was studied.

RESULTS: 33,664 participants had SNP array genotyping. 94-126 (0.2-0.3%) individuals had a pathogenic or likely pathogenic variant in TTR in the analyzed population. The most common TTR variant was Val142Ile with a frequency of 61, making up 48-65% of TTR variants found.

SUMMARY/CONCLUSION: The prevalence of TTR variants in the US population is not well studied. The most common variant reported worldwide is Val50Met while the most common in the US is Val142Ile followed by Thr80Ala. This project describes the prevalence of TTR variants in a large North American biobank population. The availability of treatments for symptomatic hATTR patients raises opportunities and challenges for biobanks as identification of at-risk individuals places pressure on highly specialized providers to see patients for screening and follow up.

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FEASIBILITY AND ACCEPTABILITY OF TELEMEDICINE IN NEUROMUSCULAR CLINIC DURING COVID-19 PANDEMIC

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INTRODUCTION/OBJECTIVE: The aim of the present study was to evaluate the feasibility and acceptability of telehealth for the care of neuromuscular patients during the COVID-19 pandemic.

METHODS: Neuromuscular patients or their caregivers, as well as health care providers (HCPs), who completed a televisit during the pandemic received an online survey, assessing satisfaction with the visit, quality of care, and experience with the televisit interference.

RESULTS: Surveys from 46 neuromuscular patients (including 18 with motor neuron disease [MND])/caregivers and 7 HCPs were completed. Several aspects of televisits, including good communication, adequate time to discuss concern, provision of equal care, and telemedicine interference, were rated favorably among participants. Telehealth was strongly satisfactory in 30 (65.22%) and satisfactory in 15 (32.61%) neuromuscular patients/caregivers. In 18 MND patients, this was 10 (55.56%) and 7 (38.89%), respectively. Moreover, 24 (52.17%) neuromuscular patients/caregivers would strongly agree and 18 (39.13%) would agree to participate again in televisits. This was 10 (55.56%) and 4 (33.33%) for MND cases, respectively. Various medical issues were addressed during the televisits including medication management, ordering tests/referrals, discussion of goals of care, and research. The predictive stepwise logistic model found younger age as a predicting factor for higher satisfaction from, or participation again in, televisits in neuromuscular patients. Limb onset location was also a predicting factor for strong satisfaction from televisits in MND cases.

SUMMARY/CONCLUSION: Telemedicine is feasible and highly effective at achieving personalized care that was rated satisfactory by the majority of neuromuscular patients/caregivers and HCPs during the COVID-19 pandemic.

SCIENTIFIC SESSION OF THE MYASTHENIA GRAVIS FOUNDATION OF AMERICA, INC. (MGFA)

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TREATMENT-RELATED INEQUITIES IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS FACING SOCIAL DETERMINANTS OF HEALTH CHALLENGES: A SURVEY OF NEUROLOGISTS IN THE UNITED STATES

Nicole Wright (Birmingham, AL), Deborah Gelinas (Durham, NC), Paul Nisbet (Mt Pleasant, SC), Tom Hughes (Phoenix, AZ), Elizabeth Ashcraft (Pfafftown, NC), A. Gordon Smith (Richmond, VA)

INTRODUCTION: Social determinants of health (SDOH) contribute to inequities in outcomes for patients with generalized myasthenia gravis (gMG).

OBJECTIVE: US neurologists were surveyed to better understand impact of SDOH on treatment access and utilization.

METHODS: The 42-item online survey on healthcare access was deployed using email. Questions focused on demographics, diagnosis, treatment, and continuity of care in patients with gMG they considered to be facing SDOH challenges (racial/ethnic minority or financial limitations).

RESULTS: The survey was completed by 150 neurologists in October 2022. Respondents estimated that 33% of their patients with gMG face care inequities. 74.7% (112/150) reported it is more difficult for these patients to afford prescribed gMG therapies. Compared to other patients with gMG, they view patients facing inequities as less receptive to infusion therapies and thymectomy; less likely to be presented with newer therapies; less likely to receive payor approval for antibody-based biologics, IVIg, and plasmapheresis; and more likely to experience difficulty traveling to infusion centers. 67.3% (101/150) of respondents reported these patients experience greater difficulty in continuing gMG treatment, and 60.0% (90/150) said these patients have a greater likelihood of experiencing exacerbation or crisis-related hospitalization. Respondents identified cost of treatment/insurance and transportation issues as the biggest contributors to difficulties in obtaining and continuing gMG treatment.

SUMMARY/CONCLUSION: Patients with gMG facing SDOH challenges experience healthcare access inequities when initiating and continuing treatment. Assistance with drug costs, transportation, and in-home infusions, as well as increased awareness and patient advocacy, could mitigate treatment-related disparities in gMG treatment.

Disclosures:

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Deborah Gelinas - Employee of argenx

Paul Nisbet - Employee of One Research; One Research received payment for the conduct of this study and for the initial data analysis; Dr. Nisbet was not compensated for development of this publication

Tom Hughes - Employee of argenx

Elizabeth Ashcraft - Employee of argenx

A. Gordon Smith - Consultant to Alexion, argenx, Eidos, Lexicon, Merz, and Sangamo

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DIAGNOSIS INEQUITIES IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS FACING SOCIAL DETERMINANTS OF HEALTH CHALLENGES: A SURVEY OF NEUROLOGISTS IN THE UNITED STATES

Nicole Wright (Birmingham, AL), Deborah Gelinas (Durham, NC), Paul Nisbet (Mt Pleasant, SC), Tom Hughes (Phoenix, AZ), Elizabeth Ashcraft (Pfafftown, NC), A. Gordon Smith (Richmond, VA)

INTRODUCTION: Social determinants of health (SDOH) challenges may contribute to care inequities in generalized myasthenia gravis (gMG).

OBJECTIVE: We surveyed US neurologists to better understand the impact of SDOH on patients receiving a diagnosis of gMG.

METHODS: The 42-item online healthcare access survey was deployed using email. Questions addressed demographics, diagnosis, treatment, and continuity of care for patients with gMG whom respondents considered to be facing SDOH challenges (racial/ethnic minority or financial limitations).

RESULTS: The survey, launched in October 2022, was completed by 150 neurologists. The majority (84% [126/150]) are board certified in neurology; the remainder, in neuromuscular or electrodiagnostic medicine. Roughly half of respondents are university affiliated. Respondents reported that 33% of their patients with gMG face inequities in healthcare access. More than half of respondents (55% [82/150]) indicated these patients experience longer duration between symptom onset and gMG diagnosis and a higher likelihood of diagnosis in an inpatient setting (56% [84/150]). Similarly, 55.3% (83/150) reported these patients have more difficulty scheduling appointments; 76.7% (115/150) reported these patients have more difficulty attending appointments; and 72.7% (109/150) reported these patients miss more appointments. Respondents suggested these disparities stem from cost, challenges with appointments, transportation difficulties, being less likely to seek care, and more likely to visit an emergency room as disease progresses.

SUMMARY/CONCLUSION: Patients with gMG facing SDOH challenges are more likely to experience healthcare inequities when receiving diagnosis. Flexible scheduling, improved transportation options, and increased primary care education could shorten time between symptom onset and diagnosis.

Disclosures:

Nicole Wright - Consultant for argenx and Radius Pharmaceuticals

Deborah Gelinas - Employee of argenx

Paul Nisbet - Employee of One Research; One Research received payment for the conduct of this study and for initial data analysis; Dr. Nisbet was not compensated for development of this publication

Tom Hughes - Employee of argenx

Elizabeth Ashcraft - Employee of argenx

A. Gordon Smith - Consultant to Alexion, argenx, Eidos, Lexicon, Merz, and Sangamo

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INDIVIDUALIZING THERAPY FOR GENERALIZED MYASTHENIA GRAVIS: CAN CONTINUING MEDICAL EDUCATION HELP GUIDE TREATING CLINICIANS?

Carole Drexel (Needham, MA), Katie Kowalski (Washington, DC), James Howard (Chapel Hill, NC)

INTRODUCTION: With the recent approvals of efgartigimod and C5 inhibitors, and the development of other pipeline agents, the treatment landscape for general myasthenia gravis (gMG) is helping clinicians (HCPs) more effectively individualize therapy.

OBJECTIVE: To assess the impacts of CME on the ability of treating HCPs [T-HCPs] who manage gMG to account for comorbidities, disease presentation, and patient preferences when making individualized treatment recommendations.

METHODS: A 60-minute activity and four 15-minute case discussions were launched live-online on 09/09/22 and will remain on-demand for 1 year. Test questions were administered before and immediately after each activity. A follow-up survey on behavior change was sent to post-test respondents 2 months after activity completion. Chi-square tests compared paired responses (P<0.05; pre/post).

RESULTS: As of 4/05/23, 642 HCPs had engaged in the education (64% T-HCPs). Baseline performance showed most T-HCPs were comfortable recommending rituximab for a patient with MuSK+ MG (92%) and recognized bulbar involvement justified an aggressive therapeutic approach (89%). In contrast, many undervalued the importance of patients' ability to attend appointments (30%) or for comorbidities (52%) or acute infection (11%) in treatment decisions. After the education, T-HCPs' performance in each area ranged from 88% to 92%. Cost-related issues were the greatest barrier to initiating novel therapies.

SUMMARY/CONCLUSION: Live and on-demand education positively impacted T-HCPs' ability to personalize therapy for gMG. Overall low baseline performance related to newer concepts in therapy selection emphasizes that future education should continue to enhance T-HCPs' ability to identify patient and disease factors that drive therapy selection.

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NATIONAL TRENDS IN THE UTILIZATION OF THYMECTOMY FOR MYASTHENIA GRAVIS

Jennifer Morganroth (Philadelphia, PA), Leah Zuroff (Philadelphia, PA), Ali Hamedani (Philadelphia, PA)

INTRODUCTION: Thymectomy is a well-established treatment for non-thymomatous myasthenia gravis (MG), but only in 2016 was the transsternal approach proven to improve outcomes.

OBJECTIVE: Our study aims to investigate changes in thymectomy types and utilization for non-thymomatous MG over time and assess for disparities.

METHODS: We used the National Inpatient Sample (NIS) database from 2012-2019, including patients aged 18+ with MG (excluding those with thymoma). Our primary objective was to evaluate the number of thymectomies performed over time, including both transsternal and transcervical approaches. We also examined several predictive factors, such as age, gender, race, insurance payor, hospital size and teaching location, and elixhauser comorbidity index.

RESULTS: Total thymectomy utilization for MG increased by 8.43% per year from 2014-2019 (p<.002). The transsternal approach increased by 6.88% per year (p<0.001), and the transcervical approach increased by 5.58% per year (p<0.043) from 2012-2019. In a multi-variate regression, several factors increased the odds of a having a thymectomy: private insurance (OR 2.28, 95% CI 2.09 to 2.48), 76th-100th income zip code (OR 1.15, CI 1.04 to 1.28), medium (OR 1.57, CI 1.35 to1.83) and large bed size (OR 2.34, CI 2.04 to 2.69). Other factors decreased the odds of having a thymectomy: age (OR 0.98, CI 0.97 to 0.98), female (OR 0.77, CI 0.72 to 0.83), southern region (OR 0.88, CI 0.79 to 0.98), and elixhauser comorbidity index (OR 0.83, CI 0.81 to 0.84).

SUMMARY/CONCLUSION: Thymectomy is being performed more frequently for non-thymomatous myasthenia gravis. There are several disparities in thymectomy utilization that warrant further investigation.

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EFFICACY OF RITUXIMAB FOR REFRACTORY LRP4+ MYASTHENIA GRAVIS, A CASE REPORT.

Huang He Ding (Glen Allen, VA), Xinli Du (Glen Allen, VA)

INTRODUCTION: About 2-3% myasthenia gravis (MG) patients have antibodies recognizing lipoprotein-related protein 4 (LRP4). This subgroup tends to have more severe disease with increased bulbar involvement and is oftentimes managed with standard therapy used in AChR+ MG.

OBJECTIVES: To report the efficacy of rituximab in a LRP4+ MG patient who had severe disease and was refractory to standard treatment.

METHODS: A LRP4+ MG patient was identified and followed. Patient has a refractory course with severe MG symptoms. Rituximab was started due to treatment failure with standard therapy. At the time of initiation of rituximab, patient was on plasmapheresis every 1-2 weeks. Her work and quality of time were greatly compromised.

RESULTS: Six weeks following rituximab infusion, patient noted remarkable improvement in dyspnea, dysphagia, and limb muscle strength. She stopped plasmapheresis completely due to sufficient control of MG symptoms. Improvement on MG activities of daily living (MG-ADL), MG quality of life 15 (MG-QoL15r), and MG composite (MGC) score were recorded 11 weeks following Rituximab infusion. No side effects have been reported.

CONCLUSION: LRP4 autoantibody is the newest antibody identified in MG. The clinical features have been recently reported where this subgroup tends to have more severe diseases and bulbar involvement. There is no specific treatment guideline for this subtype. Our case raises a possibility that LRP4+ MG may act similarly to MuSK+ MG and benefit from rituximab. More research in this direction is needed as the availability of LRP4 testing increases and more patients are being identified with this subtype.

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IMPROVING SEROLOGICAL DIAGNOSIS OF MYASTHENIA GRAVIS BY A COMPREHENSIVE REFLEX TESTING ALGORITHM: A REAL WORD EXPERIENCE WITH MORE THAN TWELVE THOUSAND PATIENT SAMPLES

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INTRODUCTION: Serological testing plays an essential role in the diagnosis of myasthenia gravis (MG) and with the development of novel methods, their algorithms have changed. We, at BC Neuroimmunology Lab, in a full reflex testing algorithm first assay acetylcholine receptor (AChR) Abs by Radio Immuno Precipitation of Antibodies (RIPA), if AChR Ab is absent, then reflex to Muscle-specific tyrosine kinase (MuSK) Abs by RIPA. If samples are double seronegative, they are tested with clustered AChR Abs live Cell-Based assay (L-CBA). Further negative samples are tested for low-density lipoprotein receptor-related protein 4 (LRP4) Ab by CBA.

OBJECTIVE: This study reports the results of the improvement of the serological diagnosis of MG by a reflex testing algorithm.

METHODS: Between August 2021 and February 2023, we assayed 7418 samples for AChR Ab and 3640 samples for MuSK Ab by RIPA, and 744 for AChR Ab and 379 for LRP4 by CBA.

RESULTS: We found 681 AChR Ab-positive samples by RIPA. Among the 3640 AChR Ab negative samples we found 57 positives for MuSK Ab by RIPA. Among double seronegative samples, L- CBA found 47 positive AChR Ab. Among seronegative samples for AChR Ab by both RIPA and CBA and MuSK by RIPA, we found 6 positive LRP4 Ab.

SUMMARY/CONCLUSION: While we found 9% AChR Ab positive by RIPA, we added another 10% to the seropositivity of clinically suspected MG by proposing a full reflex testing algorithm. This increment includes 2% MuSK Ab by RIPA, 6% AChR Ab, and about 2% LRP4 Ab seropositivity by CBA.

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MEASURING ADVERSE EVENT BURDEN IN MYASTHENIA GRAVIS: RETROSPECTIVE VALIDATION OF THE ADVERSE EVENT UNIT WITH MGTX TRIAL DATA

Michael Hehir (South Burlington, VT), Inmaculada Aban (Birmingham, AL), Henry Kaminski (Washington, DC)

INTRODUCTION: The adverse event unit (AEU) is a patient and physician weighted consensus unit that quantifies and compares adverse event (AE) burden among any group of medications in neurologic patients. A recent single-center, prospective, study demonstrated feasibility and preliminary validity of utilizing the AEU to measure AE burden in myasthenia gravis (MG).

OBJECTIVES: Evaluate feasibility of assigning AEU scores retrospectively from AE data recorded in the MGTX randomized trial of thymectomy in MG. Quantify differences in AE burden utilizing the AEU in MGTX trial participants treated with different dosages of prednisone.

METHODS: Serious and non-serious AE were recorded at all MGTX visits. AEU scores were assigned by matching each MGTX AE to the best matched category in the AEU scale; death and MG worsening were not coded as side effects. AEU scores will be compared among participants receiving varied doses of prednisone and for participants receiving prednisone for different durations.

RESULTS: The MGTX trial randomized 126 patients at 36 sites. All patients received prednisone; prednisone dosage was adjusted during the trial. Non-severe AE were reported at 747/2187 (34%) of study visits (Median AEU score 3 IQR 3-7). Severe AE were reported at 46 study visits (2%) (Median AEU score 7.5 IQR 7-12).

SUMMARY/CONCLUSION: This study demonstrates feasibility of assigning AEU scores retrospectively from clinical trial data. MGTX Median AEU scores are similar to UVM prospective study MG median AEU score (5 IQR 0-8). AEU scores in relation to prednisone dose and thymectomy status will be presented.

Disclosures:

Michael Hehir - Consultant for Alexion, argenx, UCB Pharma, Janssen, and Immunovant

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REMOTE MONITORING AND MANAGEMENT OF MYASTHENIA GRAVIS (REMOTE-MG): A PILOT FEASIBILITY STUDY

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INTRODUCTION: Time while myasthenia gravis (MG) patients are symptomatic is critical due to inability to work, perform activities of daily living, or care for families. MG patients are often evaluated every 3-6 months. Physicians are blind to fluctuations in patient function between visits unless patients call to report changes. Given the national shortage of neurologists, more frequent follow-up is not feasible.

OBJECTIVES: Evaluate the feasibility and utility of measuring MG patient symptoms using a web-based or app-based MG monitoring system.

METHODS: We designed a prototype remote monitoring tool in REDCap; the tool measures MG-ADL, MG-QOL15r, global visual analogue scale, patient acceptable symptom state, and presence/absence of side effects. Enrolled MG patients (target N=50) in the Northern New England Clinical and Translational Research Network (Vermont, Northern New York, and Maine) will remotely report MG symptoms weekly for 8 weeks. The primary outcome is >= 75% patient completion rate and >= 75% secure transfer of data to treating physicians. Change in treatment plan based on data is an exploratory outcome.

RESULTS: 10 patients are currently enrolled. Preliminary study results and study design will be presented.

SUMMARY/CONCLUSION: Given the fluctuating nature of MG, prolonged periods of treatment adjustments, shortage of neuromuscular physicians, now is the time to revolutionize MG care and pivot to a care model adapted for the current times and technology. If this study is successful, a future protocol to act on remotely collected data will be designed with an ultimate goal of reducing time with symptoms for MG patients.

Disclosures:

Michael Hehir - Consultant for Alexion, argenx, UCB Pharma, Janssen, and Immunovant

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EVALUATION OF COMPLEMENT BIOMARKERS AFTER TREATMENT WITH NIPOCALIMAB IN GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: Anti-AChR autoantibodies activate the classical complement pathway, causing postsynaptic membrane damage at the neuromuscular junction (NMJ). Nipocalimab can lower anti-AChR autoantibody titers, which may impact complement activation in gMG patients.

OBJECTIVE: To explore whether nipocalimab treatment reduces complement activation in the Vivacity MG phase 2 study.

METHODS: Serum samples were collected at baseline and longitudinally. C3, C4, CH50, and C3D were measured. The median percent change (MPC) from baseline was used to evaluate changes in complement biomarkers over time. Changes on Day 57 in the treatment arms were compared to placebo using the Mann-Whitney U test.

RESULTS: In the lower dose group (5mpk q4w), the MPC in C3, C4, and CH50 were similar to placebo. However, in the higher dosing groups (30 mpk q4w and 60 mpk q2w), the MPC in C3 increased 4.1% and 10.4%, respectively, at Day57. Increases of 4.4% (30mpk q4w) and 17.9% (60mpk q2w) in C4 were observed. The MPC in CH50 increased 2.5% with 30mpk q4w, but decreased 17.9% with 60mpk q2w. Changes in C3 and C4 with 60mpk q2w showed statistically significant differences ($p<0.05$) compared to placebo. Treatment with nipocalimab resulted in decreasing MPC in C3D but this finding was based on limited data (2-7 per treatment arm).

SUMMARY/CONCLUSION: Nipocalimab appears to have an effect on lowering but not completely suppressing complement activation, and may thus potentially reduce NMJ damage, while still allowing the complement pathway to be functional. Further evaluation in the ongoing phase 3 gMG trial with higher sample size is needed to test this finding.

Disclosures:

Nancy Zhang - Employee or contractor of Janssen Pharmaceuticals and may own stock or stock options in Johnson & Johnson

Sindhu Ramchandren - Employee or contractor of Janssen Pharmaceuticals and may own stock or stock options in Johnson & Johnson

Leona Ling - Employee or contractor of Janssen Pharmaceuticals and may own stock or stock options in Johnson & Johnson

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RETROSPECTIVE STUDY OF SELECT ADVERSE EVENTS OF SPECIAL INTEREST ASSOCIATED WITH CORTICOSTEROID USE IN MYASTHENIA GRAVIS

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INTRODUCTION: Myasthenia gravis (MG) is an autoantibody-driven disease. Oral corticosteroids (OCS) remain the initial medication for patients requiring immunotherapy despite known toxicities.

OBJECTIVE: To assess the risk of select adverse events of special interest (AESIs) during real-world OCS use in MG patients.

METHODS: US adults with newly diagnosed MG between 01/2015 and 06/2022 were identified from the Optum Clinformatics database. Periods of OCS exposure and non-exposure were defined for each patient. AESIs were identified based on the Glucocorticoid Toxicity Index using International Classification of Diseases (ICD) codes. Frailty models were fitted to assess risks of recurrent AESIs during OCS-exposed periods versus non-exposed periods as hazard ratios (HR). OCS dose and concomitant medications were included as time-variating covariates along with time-fixed baseline characteristics.

RESULTS: Among the 3,839 newly diagnosed MG patients identified, 1,781 (46%) were treated with OCS after diagnosis. The patients had median 1 episode (interquartile range [IQR] 1–3) of OCS exposure with median duration of 45 days (IQR 14–142). The crude incidence rate of any AESI was 1.57 (95%CI: 1.5–1.65) per patient-year during OCS exposure and 0.57 (0.56–0.59) during non-exposure. Adjusted frailty models identified significantly increased hazard of any AESI during OCS exposure for all OCS dosages, low: 2.45 (2.24–2.67), medium: 2.24 (2.03–2.46), high: 2.56 (2.32–2.82). Increased hazards were also observed for each of the AESIs evaluated including cardiac and bone events.

SUMMARY/CONCLUSION: OCS exposure was associated with significantly increased hazard of AESIs in MG patients. Steroid-sparing immunotherapies for the underlying disease are needed in this population.

Disclosures:

Sicong Huang - Employee of Janssen Pharmaceuticals and may own stock in Johnson & Johnson

Sindhu Ramchandren - Employee of Janssen Pharmaceuticals and may own stock in Johnson & Johnson

Kristin Heerlein - Employee of Janssen Pharmaceuticals and may own stock in Johnson & Johnson

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COULD LIVE CELL-BASED ASSAY INCREASE THE ACETYLCHOLINE RECEPTOR AUTOANTIBODIES SEROPOSITIVITY IN PATIENTS WITH CLINICAL SUSPICION OF MYASTHENIA GRAVIS?

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INTRODUCTION: AChR antibodies (Abs) in myasthenia gravis (MG) are detected in approximately 50% of ocular and 85% of generalized MG by the current gold standard radioimmunoprecipitation assay (RIPA). Recently, fixed and live cell-based assays (L-CBA) are developed.

OBJECTIVE: We clinically validated our in-house L-CBA in detecting AChR Ab in clinically suspected MG patients.

METHODS: Between January 2020 and April 2022, we assayed 10167 sera for AChR Ab by RIPA. We also assayed 4349 of AChR Ab seronegative sera of the above suspected MG samples for anti-MuSK Ab by RIPA. Then 1228 sera of double seronegative and/or borderline AChR Ab were assessed by L-CBA for AChR Ab. For clinical validation, we obtained clinical information on 36 seropositive cases for AChR Ab by L-CBA.

RESULTS: We found additional 84 cases of seropositive for AChR Ab by L-CBA. The clinical information was obtained for 36 cases and based on their final diagnosis, 20 had generalized MG, 13 had ocular MG, 2 were not yet diagnosed, and 1 case was of not-MG.

SUMMARY/CONCLUSION: The L-CBA has demonstrated improved sensitivity and higher diagnostics performance than RIPA. The L-CBA allowed improved clinical diagnosis and increased seropositivity (by 7%) in clinically suspected MG patients who were earlier seronegative/borderline for AChR Ab by RIPA.

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THE PROVIDER'S PERSPECTIVE ON NEWER THERAPEUTICS FOR THE TREATMENT OF GENERALIZED MYASTHENIA GRAVIS: A CROSS-SECTIONAL SURVEY

Kelly Gwathmey (Charlottesville, VA), Huang He Ding (Glen Allen, VA)

INTRODUCTION: Generalized myasthenia gravis (gMG) is an autoimmune disease that results in impaired neuromuscular junction transmission resulting in muscle weakness. Recently, newer, more-targeted therapeutics, such as complement inhibitors and neonatal Fc Receptor (FcRn) inhibitors, have been approved by the FDA for the treatment of gMG. It is unclear where these novel therapies fit in our current treatment paradigm.

OBJECTIVE: To study neuromuscular specialists' opinions on the role of newer therapeutics in gMG.

METHODS: Neuromuscular specialists were recruited from 3 neuromuscular websites to complete a 9-question survey sharing their perspectives regarding the current gMG treatment algorithm.

RESULTS: Eighty-one physicians completed the survey. Azathioprine and mycophenolate mofetil were first-line immunosuppressant therapies, while IVIg was considered the optimal "bridge" therapy to oral immunosuppressants in unstable patients where high-dose corticosteroids are contraindicated. Rituximab was mostly used in refractory cases. FcRn inhibitors and complement inhibitors were typically reserved for refractory cases and as bridge therapy. Cost and lack of experience with these medications were the biggest drawbacks to using newer therapeutics. When considering starting a novel treatment, affordability and safety profile were major concerns, with the route of administration, time to symptom onset, and medication track record cited as lesser concerns.

SUMMARY/CONCLUSION: Despite recent advances in gMG treatment, usage of the newer therapeutics appears to be low and reserved primarily for the treatment-refractory population. These survey results reflect the continued uncertainty about the role of novel gMG therapies. With numerous additional therapeutics on the horizon, navigating the evolving landscape will become increasingly challenging.

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IMMUNE CHECKPOINT INHIBITOR INDUCED MYASTHENIC CRISIS TREATED WITH COMPLEMENT INHIBITOR THERAPY

Sean Zadeh (Boston, MA), Pushpa Narayanaswami (Boston, MA)

INTRODUCTION: Immune checkpoint inhibitors (ICIs) cause autoimmune off-target effects including myasthenia gravis (MG). ICI-associated MG can be severe and difficult to treat.

OBJECTIVE: To describe a patient with ICI-related MG, myositis, and myocarditis requiring prolonged ventilator support, with response to complement inhibitor therapy.

METHODS: Case report.

RESULTS: An 80-year-old male was diagnosed with non-muscle-invasive bladder cancer 6 years previously. He had failed several treatments: Bacillus Calmette-Guerin, interferon-α, gemcitabine, docetaxel, and mitomyocin. Pembrolizumab was initiated in November 2022. Four weeks later he was admitted with dyspnea on exertion, orthopnea, diplopia, myalgias, and generalized weakness. Neurologic examination demonstrated hoarse voice, dysarthria, restricted bilateral lateral gaze, weakness of orbicularis oculi, buccinators, tongue, neck flexion, and extension. He had MRC grade 4/4- weakness of proximal muscles. Serum CK was 9356, CK-MB 221. He was started on prednisone 60 mg/ day for myositis and myocarditis. He required intubation. Acetylcholine-receptor antibodies returned positive. Serum CK normalized, CK-MB improved. Facial weakness, diplopia, and respiratory failure persisted. Plasma exchange was ineffective. Proximal muscle weakness worsened despite normal CK, attributed to steroid myopathy/deconditioning. He was started on eculizumab, with improvement in respiratory status 2 weeks after loading. He was continued on ravulizumab and aggressive rehabilitation. By 2 doses of ravulizumab he was weaned off the ventilator and tracheostomy was closed. Upper extremity function improved to independence; he required assistance to ambulate at follow-up in May 2023.

SUMMARY/CONCLUSION: The role of complement inhibitors in the treatment of ICI-related MG should be evaluated given their quick onset of action and favorable side effect profile.

Disclosures:

Pushpa Narayanaswami - Receives research support from AstraZeneca Rare Diseases-Alexion; has served on advisory boards or performed consulting work for argenx, AstraZeneca Rare Diseases-Alexion, UCB, and Janssen; and consulted for Dianthus, Novartis, and GSK; chaired the data safety monitoring board of a research study by Sanofi

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IGG REDUCTION EXPLAINS A LARGE PROPORTION OF CLINICAL EFFICACY IN GENERALIZED MYASTHENIA GRAVIS – A MODEL-BASED META-ANALYSIS OF FCRN INHIBITORS

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INTRODUCTION: Generalized myasthenia gravis (gMG) is a rare chronic autoimmune neuromuscular disease. Anti-FcRn antibodies (e.g. nipocalimab [in evaluation]/ efgartigimod [approved]) inhibit FcRn-mediated IgG recycling thus lower circulating serum IgG, including anti-AChR pathogenic autoantibodies, in the treatment of gMG.

OBJECTIVE: Model-based meta-analysis of clinical data from 4 anti-FcRn treatments were used to explore IgG as a potential biomarker for the clinical endpoint, MG-ADL score.

METHODS: The proportion of treatment effect (PTE) method was used, wherein the contribution of a biomarker (e.g. IgG) to the overall treatment-related change in clinical endpoint is calculated as the ratio of an estimated surrogate-contribution (if statistically significant) versus an estimated treatment-effect. Clinical data for nipocalimab (NCT03772587), efgartigimod (NCT02965573, NCT03669588, NCT04735432), rozanolixizumab (NCT03052751, NCT03971422), and batoclimab (NCT03863080, NCT04346888) were combined from 8 studies. PTE was calculated using weighted regression on steady-state, aggregate values of placebo-corrected change from baseline MG-ADL (ΔΔMG-ADL), and percent change of IgG from baseline (ΔIgG) from all studies. No covariates or random effects were included due to limited data (18 datapoints).

RESULTS: The estimated IgG coefficient was statistically significant (0.03±0.005 [SE]), suggesting 10% ΔIgG translates to ΔΔMG-ADL of ~0.3. The PTE(%CV) from all aggregate-level FcRn data was 0.82(15%) indicating that a majority of the anti-FcRn effect on ΔΔMG-ADL could be explained by ΔIgG.

SUMMARY/CONCLUSION: Since ΔIgG explains a large proportion of anti-FcRn effect on ΔΔMG-ADL, IgG could be used as a potential biomarker for clinical efficacy. This would increase the efficiency of clinical trials (size and duration) to reduce burden for patients with gMG.

Disclosures:

Mehrdad Javidi - Johnson & Johnson employee and might hold Johnson & Johnson stock

Anne-Gaëlle Dosne - Johnson & Johnson employee and might hold Johnson & Johnson stock

Mahesh N. Samtani - Johnson & Johnson employee and might hold Johnson & Johnson stock

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NIPOCALIMAB DOSE SELECTION FOR A PHASE 3 STUDY IN ADULT PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: Nipocalimab, a fully human Immunoglobulin G1 (IgG1) monoclonal-antibody, blocks neonatal Fc receptors (FcRn) inhibiting IgG recycling and lowering systemic IgG, including pathogenic IgG autoantibodies.

OBJECTIVE: To determine the optimal nipocalimab dose and dosing-regimen for the phase 3 study in patients with generalized myasthenia gravis (gMG) using modeling and simulation.

METHODS: Mathematical models linking nipocalimab intravenous dosing with its pharmacokinetics, FcRn occupancy, total IgG reduction, and efficacy (MG-Activities of Daily Living [MG-ADL]) were developed based on phase 1 data in healthy participants and a phase 2 study in gMG patients. Model-based simulations were conducted to identify optimal nipocalimab dose, schedule, and loading-dose for phase 3 study.

RESULTS: Nipocalimab exhibited nonlinear FcRn-mediated disposition and rapid, dose-dependent IgG lowering in phase 1 and phase 2 studies. Phase 2 study dosing ranged from 5mg/kg every 4 weeks to 60mg/kg every 2 weeks (Q2W). Dose-dependent improvements in MG-ADL associated with 70% IgG reduction accounted for ~90% of maximum MG-ADL reduction. Model-based simulations indicated 15mg/kg Q2W maintenance dose achieved >70% target IgG lowering with minimal gains at higher doses. A 30mg/kg loading-dose was incorporated to lower IgG and MG-ADL scores by 2-weeks. This dosing regimen is predicted to have an average steady-state albumin lowering of 12% and total cholesterol and low-density lipoprotein increase of 6% and 8%, respectively, with limited clinical impact expected.

SUMMARY/CONCLUSION: A 30mg/kg loading-dose followed by 15mg/kg Q2W maintenance dose was identified as optimal for the phase 3 study. Predicted exposure is well below the exposure from 60mg/kg Q2W dosing regimen in phase 2 study, which was generally safe and well-tolerated.

Disclosures:

Juan-José Pérez-Ruixo - Employee of Janssen Research & Development, LLC and may hold stocks/stock options in Johnson & Johnson

Belén Valenzuela - Employee of Janssen Research & Development, LLC and may hold stocks/stock options in Johnson & Johnson

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REAL-WORLD BURDEN ASSOCIATED WITH SOCIAL DETERMINANTS OF HEALTH CHALLENGES FOR INDIVIDUALS LIVING WITH GENERALIZED MYASTHENIA GRAVIS IN THE UNITED STATES

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OBJECTIVE: To evaluate the real-world burden of individuals living with generalized myasthenia gravis (gMG) in the United States (US) who are facing social determinants of health (SDOH) challenges based on their race/ethnic background, employment status, and/or insurance type.

METHODS: US adults (18−75 years) living with gMG and SDOH challenges were recruited to complete a web-based quantitative survey. Quotas were used to capture a diversity of baseline demographics including race/ethnic background, employment status, and insurance type. Respondents were presented with 10 potential challenges encountered while living with gMG and SDOH challenges in randomized order and requested to select all statements that were relevant to their experience during the last 6 months.

RESULTS: The survey was completed by 38 individuals living with gMG. The majority of respondents were non-White/Caucasian (61%), unemployed (74%), and using public health insurance (79%). Three major concerns were identified for which pronounced burden associated with SDOH challenges was observed: 1 – Making ends meet at the end of the month (total [76%] vs. non-White/Caucasian [83%], not employed [82%], Medicaid [92%]); 2 – Maintaining stable housing (total [50%] vs. non-White/Caucasian [52%], not employed [61%], Medicaid [77%]); 3 – Concern that the place they were living is making them sick or unsafe (total [21%] vs. not employed [25%], Medicaid [38%]).

SUMMARY/CONCLUSION: Challenges related to managing finances and securing safe and stable housing were commonly expressed among individuals living with gMG and facing SDOH challenges. Pronounced burden was observed among people of color, not employed, or using Medicaid.

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Tom Hughes - Employee of argenx

James Howard - Received research support from Alexion Pharmaceuticals, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention, the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health, PCORI, UCB Biosciences, and Takeda Pharmaceuticals; honoraria from Alexion Pharmaceuticals, argenx, F. Hoffman-LaRoche Ltd., Immunovant Inc., Merck EMD Serono, NMD Pharma, Novartis Pharmaceuticals, UCB Biosciences, Regeneron Pharmaceuticals, and Sanofi US; and non-financial support from Alexion Pharmaceuticals, argenx, UCB Biosciences, and Toleranzia AB

Nicholas Silvestri - Consultant for argenx, Alexion Pharmaceuticals, UCB Biosciences, and Immunovant Inc. and is a speaker for argenx, Alexion Pharmaceuticals, and UCB Biosciences

Ashley Anderson - Speaker for argenx and a member of the Alexion Speaker Bureau

Sharon Suchotliff - Employee of ZS Associates and serves as a paid consultant for argenx

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REAL-WORLD OUTCOMES OF PATIENTS LIVING WITH GENERALIZED MYASTHENIA GRAVIS INITIATING EFGARTIGIMOD TREATMENT IN THE UNITED STATES

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OBJECTIVE: To evaluate Myasthenia Gravis Activities of Daily Living (MG-ADL) responses following efgartigimod initiation among patients with generalized myasthenia gravis (gMG) in the United States (US).

METHODS: US adults (aged ≥18 years) with gMG who initiated efgartigimod treatment by February 6, 2023 and enrolled in the My VYVGART® Path patient support program (PSP) were screened for inclusion. Patient-reported MG-ADL scores were captured at variable timepoints during efgartigimod treatment. Patients who had both: (1) pre-efgartigimod treatment MG-ADL-scores and (2) at least 4 MG-ADL scores post-efgartigimod initiation were included. Lowest MG-ADL scores and patient-averaged scores post-efgartigimod initiation were compared with baseline scores for each patient, then averaged at the population level. The distribution of patients by magnitude of change in MG-ADL between pre- and post-efgartigimod initiation was evaluated.

RESULTS: In total, 209 individuals who initiated efgartigimod treatment were included. Mean baseline MG-ADL score was 8.9 (SD: 3.5; range: 2-19), and the average number of treatment cycles was 2.8 (range: 1-7). At the population level, the mean largest improvement in MD-ADL compared with baseline was 5.4 points, with 91% of patients experiencing at least a 2-point improvement over baseline. The mean patient-averaged improvement in MG-ADL was 3.2 points, with 69% of patients experiencing at least an averaged 2-point improvement over baseline post-efgartigimod initiation.

SUMMARY/CONCLUSION: A substantial proportion of individuals with gMG enrolled in the PSP receiving efgartigimod treatment in clinical practice experienced ≥2-point improvements in MG-ADL, consistent with clinical trial results.

Disclosures:

Cynthia Qi - Employee of argenx

Mai Sato - Employee of ZS Associates, serves as a paid consultant for argenx

Glenn Phillips - Employee of argenx

Pushpa Narayanaswami - Receives support from AstraZeneca Rare Diseases-Alexion; has served on advisory boards or performed consulting work for argenx, AstraZeneca Rare Diseases-Alexion, UCB, and Janssen; consultant for Dianthus and GSK; chaired data safety monitoring board of a research study by Sanofi

Gil Wolfe - Consultant or speaker for Grifols, Alexion, argenx, Takeda, BPL, and UCB; received grant/research support from argenx, Ra/UCB, Immunovant, Roche, Alexion, Sanofi, NINDS/NIH, and MGFA

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EARLY REAL WORLD EXPERIENCE OF RAVULIZUMAB IN ADULT PATIENTS WITH ACETYLCHOLINE RECEPTOR-POSITIVE GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: Ravulizumab, a long acting complement inhibitor has been approved by FDA for acetylcholine receptor antibody-positive generalized myasthenia gravis (AChR+ve gMG).

OBJECTIVE: To describe the early experience of ravulizumab use in AChR+ve gMG.

METHODS: This multicenter retrospective study included AChR+ve gMG patients who were treated with ravulizumab and had both pre- and at least 3 months post-ravulizumab myasthenia gravis activities of daily living (MG-ADL) scores. Clinical information regarding MG history, concomitant treatment(s), MG-ADL, and adverse events were recorded.

RESULTS: A total of 17 patients with mean age of 60.70 (+15.84) years were included in this cohort. The mean time from loading dose to post ravulizumab MG-ADL assessment was 4.83 (+0.98) months. In 12 patients with active symptoms, a clinically meaningful reduction in mean Mg-ADL (baseline: 7.5 (+2.21) vs 3.91 (+2.21) post ravulizumab) was seen. Eight out of 12 (67%) patients had clinically meaningful reduction (>2 point change in MG-ADL) post ravulizumab and 3 (25%) patients achieved minimum symptom expression. Patients switched from eculizumab to ravulizumab noted significant reduction in post ravulizumab mean Mg-ADL (Baseline: 4.5 (+2.98, n=6) vs 1.83 (+2.6, n=6) post ravulizumab). None of the patients switched from eculizumab to ravulizumab experienced worsening of symptoms. Eight out of 10 (80%) patients were able to reduce their prednisone dose post-ravulizumab. None of the patients experienced any major side effects.

SUMMARY/CONCLUSION: In this clinical cohort, two-thirds of AChR+ve gMG patients experienced clinically meaningful improvement in MG-ADL scores with ravulizumab and 80% patients were able to reduce their prednisone dosage.

Disclosures:

Raghav Govindarajan - On advisory board for argenx, UCB, Janssen, Roche; speaker for argenx and Alexion

Neelam Goyal - On advisory board for argenx, Alexion, and UCB Pharma

Suraj Muley - Speaker for Takeda, CSL Behring, Grifols, Catalyst, Alexion, argenx; consultant for UCB, Alexion, argenx; on advisory board for Horizon, argenx, Alexion, Grifols

Srikanth Muppidi - On advisory board for argenx, Alexion/AstraZeneca, ra/UCB, Horizon Pharma

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IS REPETITIVE NERVE STIMULATION LESS SENSITIVE IN ACUTE ONSET MYASTHENIA GRAVIS?

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INTRODUCTION: Repetitive nerve stimulation (RNS) is a valuable tool in the diagnostic evaluation for myasthenia gravis (MG), especially in seronegative patients. Recent reports give conflicting findings regarding the sensitivity of RNS in acute onset MG.

OBJECTIVE: To compare the sensitivity of RNS in acute onset (≤ 30 days from symptom onset) and later onset MG.

METHODS: Medical records were reviewed of patients with MG who underwent RNS from 2017 to 2021 at Cleveland Clinic and from 1975 to 2001 at Duke University Medical Center. Data including patient demographics, disease duration, Myasthenia Gravis Foundation of America (MGFA) classification, antibody results, and thymus histology were collected.

RESULTS: We identified 525 patients with MG who had undergone RNS testing; 265 were male and 260 were female, median age of 58 years at RNS testing. An average of 2 nerves were tested per RNS session. RNS was performed on 31 patients with acute onset MG (median symptom duration of 21 days) and 494 patients with later onset (median duration of 12.5 months). RNS was abnormal in 54.8% of patients with acute onset and 59.5% of those with later onset disease (p=0.61). RNS positivity rates were nearly identical in acute and later onset groups at both institutions.

SUMMARY/CONCLUSION: We found no significant difference in the sensitivity of RNS between patients with acute and later onset MG. Our findings support the use of RNS in the diagnostic evaluation of MG in those presenting acutely.

Disclosures:

Yuebing Li - Received grant support from argenx; served as a consultant for advisory board meeting by argenx, Catalyst, Immunovant, and UCB Pharma

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MANAGEMENT OF MYASTHENIA GRAVIS AROUND THE GLOBE: CONSENSUS GUIDELINES VS REALITIES OF PRACTICE

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INTRODUCTION: There is great heterogeneity in the underlying pathophysiology of myasthenia gravis (MG), its clinical presentation, and response to treatment. International consensus guidelines were developed in 2016 and 2020 in an effort to standardize the approach to management of MG, however there remains uncertainty as to whether these efforts have been successful.

OBJECTIVE: To explore practices surrounding MG management across the globe with regard to alignment with the 2016 and 2020 international consensus guidelines.

METHODS: We administered an online, cross-sectional, case-based survey regarding MG management via Neurology's: Practice Current section between 2020-2021 to neurologists and advanced practitioners. Preliminary analysis was purely descriptive. Responses were compared with recommendations outlined in the MG 2016 and 2020 consensus guidelines.

RESULTS: 318 practitioners across 6 continents responded to the survey. Areas of discordance among respondents included the role of thymectomy, management of treatment-related side effects, management of acetylcholine receptor (AChR) antibody-negative MG, and management in preconception and pregnancy. Despite guidelines, only 54% of respondents recommended thymectomy in someone with AChR-MG, 25% recommended vaginal delivery in someone with well controlled MG, and 27% recommended early initiation of rituximab in someone with muscle-specific tyrosine kinase (MuSK) antibody-positive MG.

SUMMARY/CONCLUSION: Our preliminary survey data suggests that despite efforts to create a set of international consensus guidelines, uncertainty persists in the neurology community surrounding MG management. We identify areas of agreement and disagreement that can help clinicians refine their own practice patterns and define the need for modified guidelines that highlight the side effect profiles, cost, and availability of therapies worldwide.

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THE DUKE MYASTHENIA GRAVIS CLINIC REGISTRY: HOW WELL DO CHANGES IN OUTCOME MEASURE SCORES PREDICT CLINICALLY MEANINGFUL IMPROVEMENT?

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INTRODUCTION: Treatment trials in MG use various outcome measures (OMs) to determine if therapeutic interventions produce clinically meaningful improvement. The Duke MG Clinic Registry contains clinician- and patient-derived data including MG OM scores and MGFA Class from patients seen in the Duke MG Clinic since 1980.

OBJECTIVE: To determine the smallest change in scores of the MG-Activity of Daily Living (ADL), Quantitative MG (QMG), MG-Manual Muscle Test (MMT), and MG-Composite (MGC) scales that indicates clinically meaningful improvement (CMI) as defined by a reduction in class.

METHODS: We reviewed registry data from patients with MG initially seen in the Duke MG Clinic between 1980 and 2018 to determine the change in scores of the ADL, QMG, MMT, and MGC scales and the change in class between 2 visits.

RESULTS: Receiver operating characteristic curve (ROC) analyses of change in score vs a reduction in Class demonstrated area under the ROC curve (AUC) values greater than 0.75 for all 4 OMs. The score change that produced the maximal AUC, the AUC value, sensitivity, and specificity were: ADL, 2 point reduction/0.76/0.70/0.71; QMG, 4 point reduction/0.77/0.67/0.76; MMT, 2 point reduction/0.81/0.89/0.59; and MGC, 1 point reduction/1.00/1.00/1.00.

SUMMARY/CONCLUSION: A reduction in score of all 4 assessed OMs predicted CMI, as defined by a reduction in Class. The score change for each OM that best predicted a reduction in Class could be used to indicate CMI. The MG-Composite, which incorporates patient-reported and clinician-reported items that are weighted for clinical significance, best predicted clinically meaningful improvement.

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NETWORK META-ANALYSIS OF TREATMENT OPTIONS IN GENERALIZED MYASTHENIA GRAVIS: IMPACT ON HEALTH-RELATED QUALITY OF LIFE OUTCOME

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INTRODUCTION: As new targeted therapies are being rapidly developed and approved for generalized myasthenia gravis (gMG), there is lack of data comparing these therapies on health-related quality of life (HRQoL) outcomes.

OBJECTIVE: To compare the effect of new and evolving treatments (efgartigimod, ravulizumab, rozanolixizumab 10mg and 7mg, and zilucoplan) on HRQoL outcomes primarily in gMG patients with anti-acetylcholine receptor antibodies.

METHODS: A Bayesian network meta-analysis (NMA) was conducted using published data extracted from 4 phase 3 randomized placebo-controlled trials. Changes in HRQoL outcomes, EQ-5D VAS, and Myasthenia Gravis Quality of Life revised (MG-QoL15r), from baseline to primary assessment timepoints in the respective clinical trials were compared.

RESULTS: NMA indicated significantly more improvement in EQ-5D VAS with efgartigimod vs. ravulizumab (median difference: 10.39; 95% credible interval [CrI]: 2.39, 18.31) and zilucoplan (8.50; 95% CrI: 0.66, 16.48). The improvement in EQ-5D VAS was not significantly different between efgartigimod and rozanolixizumab 10mg and 7 mg. NMA for MG-QoL15r indicated significantly more improvement with efgartigimod vs. ravulizumab (-3.29; 95% CrI: -6.01, -0.61). The improvement in MG-QoL15r was not significantly different between efgartigimod vs. zilucoplan and rozanolixizumab 10mg and 7mg.

SUMMARY/CONCLUSION: The results suggested efgartigimod was associated with greater degree of improvement in EQ-5D VAS (compared to ravulizumab and zilucoplan) and MG-QoL15r (compared to ravulizumab) scores in patients with gMG. This may be related to effectiveness, safety or other characteristics of the treatment.

Disclosures:

Gil Wolfe - Gil Wolfe - Consultant for Grifols, argenx, Alexion, CSL, Takeda, UCB, Cartesian; grant/research support from argenx, Ra/UCB, Roche, Alexion, Sanofi, NINDS/NIH, PCORI

Carolina Barnett-Tapia - Consultant and/or member of advisory board for Sanofi, Alexion, argenx, Janssen; received research grants from industry (Grifols and Octapharma) and DoD, MG Net, and Muscular Dystrophy Canada; primary developer of the MGII and may receive royalties

Tuan Vu - USF Site Principal Investigator for MG clinical trials sponsored by Alexion/AstraZeneca Rare Disease, argenx, Ra Pharmaceuticals/UCB Pharma, Viela Bio/Horizon Therapeutics, Janssen Pharmaceuticals/Momenta, Regeneron, and Cartesian Therapeutics; has received speaking and/or consulting honoraria from Alexion, argenx, and UCB Pharma

Stojan Peric - Site principal investigator for MG clinical trials sponsored by argenx, Ra/UCB, and Takeda/Millennium; consultant for argenx

Pushpa Narayanaswami - Research support from Alexion; on advisory boards for Alexion, argenx, UCB, Janssen; DSMB: Sanofi, Consultant: UCB, Dianthus, Novartis, GSK

Francesco Saccà - received speaking honoraria from Alexion, argenx, Genpharm, Medpharma Madison Pharma; received compensation for advisory boards or consultation fees from Alexion, argenx, Dianthus, Lexeo Therapeutics, Novartis, Reata; PI in clinical trials for Alexion, argenx, Immunovant, Novartis, Prilenia, Sanofi

Glenn Phillips - argenx employee and shareholder

Eddie Brauer - argenx employee and shareholder

Cynthia Qi - argenx employee and shareholder

Hongbo Yang - Consultant of Analysis Group, which received consulting fee from argenx

Mandy Du - Consultant of Analysis Group, which received consulting fee from argenx

Xin Chen - Consultant of Analysis Group, which received consulting fee from argenx

Srikanth Muppidi - Served on advisory board for Alexion, argenx, UCB/Ra, and Horizon Pharma

BATOCLIMAB AS INDUCTION AND MAINTENANCE THERAPY IN PATIENTS WITH MYASTHENIA GRAVIS: RATIONALE AND STUDY DESIGN OF A PHASE 3 CLINICAL TRIAL

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INTRODUCTION: Despite recent advances in the field of myasthenia gravis (MG), there remain unmet treatment needs.

OBJECTIVE: Describe an innovative phase 3 clinical trial of batoclimab, a fully human monoclonal antibody that inhibits the neonatal fragment crystallizable receptor, in generalized MG (gMG).

METHODS: Adults with gMG will be randomized 1:1:1 to induction treatment with batoclimab 680 mg, 340 mg, or placebo, administered once weekly (QW) for 12 weeks as a subcutaneous injection at home or in the clinic. The primary endpoint is the change from baseline to Week 12 on the Myasthenia Gravis Activities of Daily Living (MG-ADL) score. Batoclimab-treated patients achieving a ≥2-point improvement from baseline on MG-ADL at Week 10 or Week 12 (responders) will be re-randomized to maintenance treatment with batoclimab (340 mg QW or every other week [Q2W]) or placebo for 12 weeks; batoclimab non-responders will be switched to placebo for 12 weeks, then discontinued. Placebo-treated patients from the induction period will be re-randomized to batoclimab 340 mg QW or Q2W during maintenance. Patients completing the maintenance period who are responders in the induction and/or maintenance periods will continue their maintenance batoclimab dose (or switch to 340 mg QW if on placebo) for a 52-week long-term extension. Patients experiencing a flare during the extension may receive open-label rescue treatment with batoclimab 680 mg QW for 4 weeks, followed by 340 mg QW.

RESULTS: The FLEX trial (Clincialtrials.gov: NCT05403541) is recruiting participants.

SUMMARY/CONCLUSION: FLEX will explore different induction and maintenance doses of batoclimab in gMG, with a goal of informing clinical practice.

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Heinz Wiendl - Receives research honoraria from Abbvie, Alexion, argenx, Bristol Myers Squibb/Celgene, Janssen, Merck, Novartis, and Sandoz; receives speaker honoraria and travel support from Alexion, Biogen, Bristol Myers Squibb, Genzyme, Merck, Neurodiem, Novartis, Ology, Roche, TEVA, and WebMD Global; consultant for Abbvie, Actelion, argenx, BD, Biogen, Bristol Myers Squibb, EMD Serono, Fondazione Cariplo, Gossamer Bio, Idorsia, Immunic, Immunovant, Janssen, Lundbeck, Merck, NexGen, Novartis, PSI CRO, Roche, Sanofi, The Swiss Multiple Sclerosis Society, UCB, and Worldwide Clinical Trials. His research is funded by the Deutsche Forschungsgesellschaft (DFG), Deutsche Myasthenie Gesellschaft e.V., European Union, Alexion, Amicus Therapeutics Inc, argenx, Biogen, CSL Behring, F. Hoffmann - La Roche, Genzyme, Merck KgaA, Novartis, Roche Pharma, UCB Biopharma

Richard Nowak - Research support from the National Institutes of Health, Genentech, Alexion Pharmaceuticals, Inc., argenx, Annexon Biosciences, Inc., UCB S.A., Myasthenia Gravis Foundation of America, Momenta Pharmaceuticals, Immunovant, Grifols, S.A., Horizon Therapeutics; consultant/advisor for Alexion Pharmaceuticals., argenx, Cabaletta Bio, Cour Pharmaceuticals, UCB S.A., Immunovant, Momenta Pharmaceuticals, Horizon Therapeutics

Yan Zheng - Employee of Immunovant, Inc.

Richard Valanzola - Employee of Immunovant, Inc.

Tess Karlson - Employee of Immunovant, Inc.

Sheetal Patel - Employee of Immunovant, Inc.

William Macias - Employee of Immunovant, Inc.

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ASSOCIATION BETWEEN PATIENT SUPPORT PROGRAM PARTICIPATION AND ACCESS TO EFGARTIGIMOD TREATMENT FOR GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: Efgartigimod (EFG) is a recently FDA-approved therapy for individuals diagnosed with generalized myasthenia gravis. A manufacturer-provided patient support program (PSP) aims to help patients access prescribed EFG treatment, but its effectiveness is unknown.

OBJECTIVE: To compare access to prescribed EFG treatment with and without PSP participation.

METHODS: Using specialty pharmacy data from February 2021–January 2023, patients with an initial EFG script with ≥3 months of follow-up observation were identified and stratified based on concurrent PSP participation. Access outcomes included successful EFG dispensing, approval of the initial script, abandonment of approved treatment, and time to dispense. Multivariate regressions controlling for baseline characteristics estimated risk-adjusted outcomes, odds ratios (ORs), and 95% confidence intervals (CIs).

RESULTS: PSP (N=876) and non-PSP (N=409) cohorts were well-balanced on patient demographics. Relative to non-PSP patients, PSP participants had a 19% higher dispense rate within 3 months of their initial EFG script (56% vs. 47%; OR:1.47; CI:1.14-1.89; p<0.01). Among patients with initial script approval, PSP participants received EFG in 28 fewer days on average (30 vs. 58 days; median: 23 vs. 28; p=0.02). Though not statistically significant, PSP participants also had a 10% higher approval rate (absolute 53% vs. 49%; OR:1.23; CI:0.96-1.59; p=0.11) and a 33% lower abandonment rate (absolute 9% vs. 13%; OR:0.60; CI:0.33-1.11; p=0.11) relative to non-PSP patients. Differences with PSP participation were greatest for the Midwest, Medicaid-insured patients, and patients prescribed EFG by a primary care provider.

SUMMARY/CONCLUSION: This study suggests PSP participation may be associated with improved access to prescribed EFG treatment, including more successful and faster initiation.

Disclosures:

Glenn Phillips - Employee of argenx

Ali Habib - Research support from Alexion/Astra Zeneca, argenx, UCB, Immunovant, Regeneron, CabalettaBio, VielaBio/Horizon, Genentech/Roche; honoraria from UCB, argenx, Alexion, Immunovant, Regeneron, and Genentech/Roche

Tom Hughes - Employee of argenx

Cynthia Qi - Employee of argenx

Dominic Nunag - Employee of Medicus Economics, LLC, which received funding from argenx to participate in this research

Matthew Davis - Employee of Medicus Economics, LLC, which received funding from argenx to participate in this research

Jeffrey Rosenfeld - Received research/consulting fees from MT Pharma America, Alexion, argenx, NeuroSource, Biogen, and ML Bio Solutions

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RACIAL DISPARITIES IN ACUTE CARE UTILIZATION OUTCOMES AMONG THOSE WITH MYASTHENIA GRAVIS

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OBJECTIVE: To evaluate the relationship between race and acute care utilization among those with MG.

METHODS: This retrospective cohort study used Optum's de-identified Market Clarity Data from 2010-2019 to assess acute care utilization (emergency department [ED] visits and hospitalizations) among those with newly diagnosed MG. Differences in outcomes between racial subgroups (non-Hispanic Caucasian, Black and Asian, and Hispanic) in Year 1 and Year 2 post-diagnosis were evaluated using multivariable logistic regression models.

RESULTS: Among 7,058 eligible patients with MG, we found significant differences in age, gender, geographic region, insurance status, and rates of hyperlipidemia, thyroid-related disorders, gastroesophageal reflux disease, anxiety, depression, and thymoma among racial subgroups. After adjusting for baseline characteristics using a multivariable model, those who were non-Hispanic Black had a 37% increased odds of experiencing an ED visit compared with those who were non-Hispanic Caucasian ($p = 0.04$) in Year 1. Those who were Hispanic had a 70% increased odds of hospitalization compared with those who were non-Hispanic Caucasian ($p = 0.04$) in Year 2.

SUMMARY/CONCLUSION: This study provided evidence of potential racial disparities in care among those with MG, but further research is needed to characterize factors related to increased acute care utilization. Our findings also indicate that certain factors may be important early after diagnosis, while others may not. Acute care events represent a high burden for payers, hospitals and most importantly, patients. Patient support programs targeted towards at-risk populations may have the potential to improve disease management and reduce acute care utilization.

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SPECIFIC ATTRIBUTES OF MYASTHENIA GRAVIS PATIENTS MAY CORRELATE WITH A HIGHER BURDEN OF DEPRESSION AND ANXIETY: A LITERATURE REVIEW

Louis Jackson (Titusville, NJ), Nizar Souayah (New Brunswick, NJ), Sindhu Ramchandren (Titusville, NJ), Zia Choudhry (Titusville, NJ), Rachelle Rodriguez (Titusville, NJ), Jacqueline Pesa (Superior, CO), Kristin Heerlein (Titusville, NJ), Kelly Gwathmey (Richmond, VA)

INTRODUCTION: Increased rates of depression and anxiety have been identified among patients with myasthenia gravis (MG). Identifying attributes of patients who experience higher mental health burden may offer insight into the means to reduce the overall disease burden.

OBJECTIVE: To ascertain whether a higher prevalence or severity of depression and anxiety is reported for attributes of MG patients.

METHODS: A targeted literature review examined depression and anxiety data from MG observational studies published between January 2018 – December 2022.

RESULTS: Eighteen publications met the selection criteria. Patient-reported outcome tools such as MG-ADL quantified MG severity, while measures such as PHQ-9 and GAD-7 quantified depression/anxiety severity. Depression rates ranged from 17% to 60% (n=12 studies) in MG patients, and anxiety rates ranged from 8% to 64% (n=7 studies). Women presented with higher rates of depression and anxiety in 4 studies, although 1 study found no sex-related differences. Depression (n=8 studies) and anxiety (n=7 studies) severity positively correlated with MG severity. Additionally, 5 studies noted a positive correlation between depression and fatigue severity. Single studies reported a positive relationship between depression severity and younger patients, shorter MG duration, higher level of education, and higher income, but none reported associations with onset age or concomitant medications.

SUMMARY/CONCLUSION: Depression severity in MG is correlated with MG disease severity and fatigue and disproportionately impacts females. Findings highlight the depression and anxiety burden among MG patients and the need for treating neurologists to take a holistic approach in considering treatment options for their MG patients.

Disclosures:

Louis Jackson - Employee of Janssen and a Johnson & Johnson stockholder

Sindhu Ramchandren - Employee of Janssen and a Johnson & Johnson stockholder

Zia Choudhry - Employee of Janssen and owns Takeda and Janssen stock

Rachelle Rodriguez - Employee of Janssen and a Johnson & Johnson stockholder

Jacqueline Pesa - Employee of Janssen

Kristin Heerlein - Employee of Janssen and a Johnson & Johnson stockholder

Kelly Gwathmey - Received consulting honoraria from argenx, Alexion, and UCB, and speaking honoraria from Alexion

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A CASE SERIES OF PATIENTS WITH ACETYLCHOLINE RECEPTOR ANTIBODY-POSITIVE GENERALIZED MYASTHENIA GRAVIS THAT TRANSITIONED FROM EFGARTIGIMOD TO RAVULIZUMAB

Andrew Gordon (Deerfield, IL), Jennifer Buczyner (Jupiter, FL), Rosemarie Walch (Owosso, MI)

INTRODUCTION: Biologic therapies indicated for acetylcholine receptor antibody-positive (AChR-Ab+) generalized myasthenia gravis (gMG) include C5 inhibitors, i.e., ravulizumab and eculizumab, and the neonatal Fc receptor inhibitor, efgartigimod. This case series reports real-world effectiveness, safety, and perceptions for patients that transitioned from efgartigimod to ravulizumab.

CASE PRESENTATION: We report outcomes for 4 patients (ages 44 to 63 years) with AChR-Ab+ gMG who were treated with efgartigimod for at least 1 cycle (median, 2 cycles) and transitioned to ravulizumab. Prior to efgartigimod initiation, Myasthenia Gravis Foundation of America (MGFA) class ranged from MGFA 1 to MGFA 2B and median Myasthenia Gravis Activities of Daily Living (MG-ADL) was 4 (range, 3 to 5). During efgartigimod therapy, MGFA class worsened (from MGFA 1 to MGFA 3A; n=1) or remained unchanged (n=3) while median MG-ADL worsened to 7.5 (range, 5 to 12). After transitioning from efgartigimod to ravulizumab, MGFA class improved (n=3) or remained unchanged (n=1) while median MG-ADL improved to 3.5 (range, 3 to 5) after a median of 3 doses. Throughout efgartigimod and ravulizumab therapy, 2 patients were on concomitant therapy (prednisone, 5-20 mg/d; mycophenolate mofetil, 2000 mg/d); 2 patients were not on concomitant immunosuppressive therapy. Patients perceived improved ability to work and drive a car, and decreased shortness of breath on ravulizumab. No adverse events were reported for patients taking ravulizumab; 1 patient had a potential allergic reaction related to efgartigimod.

SUMMARY: Ravulizumab provided early, sustained improvement in MGFA class and MG-ADL score in the absence of heavy immunosuppression in patients that transitioned from efgartigimod.

Disclosures:

Andrew Gordon - Received consulting honoraria from Alexion, Abbvie, and argenx

Jennifer Buczyner - On the speaker bureau for argenx and Alexion and has received compensation from both

Rosemarie Walch - Received speaker and consulting fees from Alexion; institution has research support from Spheres which is Alexion funded

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PARTNERING WITH PATIENTS AND CARE PARTNERS TO GUIDE THE DESIGN OF A GENERALIZED MYASTHENIA GRAVIS REAL WORLD STUDY

Bruce West (Gilbert, SC), Maria Ait-Tihyaty (Laval, Canada), Catherine Ferrante (Titusville, NJ), Jacqueline Pesa (Superior, CO), Zia Choudhry (Titusville, NJ), Gabrielle Geonnotti (Titusville, NJ), Louis Jackson (Media, PA), Lisa Shea (Titusville, NJ)

INTRODUCTION: Generalized myasthenia gravis (gMG) patients and care partners can bring valuable insights to guide research.

OBJECTIVE: To advance patient-centricity in gMG research by obtaining patient and care partner input on a prospective, real-world study for gMG.

METHODS: Nine gMG patients and 2 care partners from the gMG Patient Engagement Research Council (PERC) participated in 3 virtual 2-hour structured focus groups in March 2023. The PERC is a diverse group of patients with respect to time since diagnosis, disease severity, treatments, age, gender, and race/ethnicity. The sessions focused on impressions, perceived challenges, and logistical burden around participating in a gMG real-world study, as well as feedback on providing data via surveys and wearing monitoring devices.

RESULTS: The PERC insights guided study design, and patients and care partners expressed interest to participate in research that advances MG medication development and treatment. Members provided feedback on logistics, including travel, compensation, time commitment, and burden of data collection. The importance of “meeting patients where they are” in their disease journey to ensure completeness of patient reported data was a key finding. The study design was modified based on gathered input from the PERC.

CONCLUSIONS: Involving patients in the design of research is crucial in understanding how to ensure the outcomes are patient centric and the study burden is reasonable. Insights from this research directly impacted protocol development of a large, global real-world study, thus supporting recruitment goals, adherence to study protocol, and the success and relevance of this research to patients.

Disclosures:

Bruce West - Member of the Janssen Patient Engagement Research Council and receives honoraria for his participation

Maria Ait-Tihyaty - Employee of Janssen and a Johnson & Johnson stockholder

Catherine Ferrante - Employee of Janssen and a Johnson & Johnson stockholder

Jacqueline Pesa - Employee of Janssen Pharmaceuticals

Zia Choudhry - Employee of Janssen; owns Takeda and Janssen stock

Gabrielle Geonnotti - Employee of Janssen and a Johnson & Johnson stockholder

Louis Jackson - Employee of Janssen and a Johnson & Johnson stockholder

Lisa Shea - Employee of Janssen and a Johnson & Johnson stockholder

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ACHIEVEMENT OF MINIMAL SYMPTOM EXPRESSION IN ACETYLCHOLINE-RECEPTOR ANTIBODY-POSITIVE PARTICIPANTS WITH GENERALIZED MYASTHENIA GRAVIS AND EFFECT ON DISEASE-SPECIFIC MEASURES IN ADAPT/ADAPT+ STUDIES

James Howard (Chapel Hill, NC), Hiroyuki Murai (Narita, Japan), Srikanth Muppidi (Palo Alto, CA), Glenn Phillips (Boston, MA), Cynthia Qi (Boston, MA), Deborah Gelinas (Durham, NC), Edward Brauer (Boston, MA), Sihui Zhao (Boston, MA), Vera Bril (Toronto, Canada), John Vissing (Copenhagen, Denmark)

INTRODUCTION: Minimal symptom expression (MSE), defined as Myasthenia Gravis Activities of Daily Living (MG-ADL) total score 0 or 1, is explored as a novel proposed treatment target in generalized MG.

OBJECTIVE: Assess incidence, characteristics, and changes in other MG-specific scales in participants achieving MSE in ADAPT (phase 3 study of efgartigimod IV) and ADAPT+ (open-label extension).

METHODS: Post hoc analyses of ADAPT (n=129) and ADAPT + (n=111).

RESULTS: In AChR-Ab+ participants from ADAPT, 44.6% treated with efgartigimod achieved MSE vs 10.9% of participants given placebo. In ADAPT+, 40.5% of AChR-Ab+ participants achieved MSE. 81% of participants from efgartigimod treatment arm who achieved MSE in ADAPT continued to achieve MSE during ADAPT+; 23% who had not achieved MSE in ADAPT did in ADAPT+. Baseline characteristics for efgartigimod-treated participants who achieved MSE during ADAPT were comparable to those who did not. Although mean (SD) baseline MG-ADL score was statistically significantly lower for those achieving MSE (8.2 [1.8] vs 9.7 [2.7]), difference was not clinically meaningful. Achieving MSE was associated with substantial improvements in Quantitative Myasthenia Gravis (QMG) and Myasthenia Gravis Quality of Life (MG-QoL15r) mean scores: 11.4-point and 12.4-point decreases, respectively, from baseline to best score (across all visits). For QMG, the difference was ~4 times the threshold for clinically meaningful improvement (≥3 points). An increase of 28 points in EuroQoL-5 Dimensions-5 Levels visual analog score was also seen. MSE achievement resulted in QoL comparable to healthy populations.

SUMMARY/CONCLUSION: Participants who achieved MSE had substantial improvement across multiple disease measures and experienced QoL comparable to healthy populations.

Disclosures:

James Howard - Received research support from Alexion Pharmaceuticals, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention, the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health, PCORI, UCB Biosciences, and Millennium Pharmaceuticals/Takeda Pharmaceuticals; honoraria from Alexion Pharmaceuticals, argenx, F. Hoffman-LaRoche Ltd, Immunovant, NMD Pharma, Novartis Pharmaceuticals, UCB Biosciences, Regeneron Pharmaceuticals, and Sanofi US; and non-financial support from Alexion Pharmaceuticals, argenx BVBA, UCB Biosciences, and Toleranzia AB

John Vissing - Received research and travel support, and/or speaker honoraria from Alexion Pharmaceuticals and Sanofi/Genzyme; served on advisory boards or as a consultant for Asklepios Biopharmaceuticals, Audentes Therapeutics, Novartis Pharma AG, PTC Therapeutics, Roche, Sanofi/Genzyme, Santhera Pharmaceuticals, Sarepta Therapeutics, and Stealth Biotherapeutics

Hiroyuki Murai - Consultant for Alexion, AstraZeneca Rare Disease, argenx, UCB Pharma, and Roche; received speaker honoraria from the Japan Blood Products Organization and Chugai Pharmaceutical; received research support from the Ministry of Health, Labour and Welfare, Japan

Srikanth Muppidi - Served on advisory board meetings for Alexion, argenx, UCB/Ra, and Horizon Pharma

Glenn Phillips - Employee of argenx

Cynthia Qi - Employee of argenx

Deborah Gelinas - Employee of argenx

Edward Brauer - Employee of argenx

Sihui Zhao - Employee of argenx

Vera Bril - Served on scientific advisory boards of CSL Behring, Baxalta, Grifols, argenx, Octapharma, Alpha Technologies, Powell Mansfield Inc, Shire, Akcea, UCB, and Alnylam; received funding for travel or speaker honoraria from CSL Behring and consultancies with CSL Behring, Grifols, Bionevia, Octapharma, Powell Mansfield, argenx, Alpha Technologies, Baxalta, Akcea, UCB, Alnylam, and Pfizer

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NEAR FIBER SEGMENT JITTER IN THE DIAGNOSIS OF MYASTHENIA GRAVIS

Ross Mandeville (Boston, MA), Adam Patterson (Boston, MA), Justin Luk (Boston, MA), Oscar Garnes (Madrid, Spain), Daniel Stashuk (Wateroo, Canada)

INTRODUCTION: Near fiber EMG (NFEMG) focuses on the activity of muscle fibers close to the electrode, can be applied to routinely acquired needle EMG, and offers the ability to semi-automatically assess neuromuscular junction stability (akin to jitter/jiggle) in a conceptually similar manner to single fiber EMG (SFEMG).

OBJECTIVE: To compare the accuracy of NFEMG with SFEMG in diagnosing MG.

METHODS: NFEMG was blindly applied to SFEMG recordings of 40 patients tested at BIDMC in the prior 18 months. After analyzing a sample of 5 MG and 5 non-MG patients, a jitter threshold for diagnosing MG was identified and applied across the whole cohort. The performance of NFEMG was then compared to the clinical diagnosis, as well as to SFEMG results.

RESULTS: 11 of 40 patients were diagnosed clinically as MG after SFEMG testing, with 2 diagnosed as myopathy, and 1 as neuropathy. Of those without myopathy or neuropathy, the sensitivity and specificity for detecting a clinical diagnosis of MG were 100% and 88% for NFEMG, respectively, as compared to 91% and 100% for SFEMG.

SUMMARY/CONCLUSION: NFEMG performs well in diagnosing MG, but prospective studies are needed. Due to the ease of application to routine EMG and the minimal need for training, NFEMG may represent a screen prior to referring for SFEMG or as an alternative diagnostic test when SFEMG is not available, potentially addressing a significant national and global healthcare disparity.

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NEAR FIBER EMG: A NEW WAY TO ASSESS MOTOR UNIT INSTABILITY AND ELECTROPHYSIOLOGICAL TEMPORAL DISPERSION

Daniel Stashuk (Wateroo, Canada), Oscar Garnes (Madrid, Spain), Ross Mandeville (Boston, MA)

INTRODUCTION: Assessments of motor unit (MU) electrophysiological instability (jitter) and temporal dispersion (MUP complexity) can detect MG and assist with discrimination relative to neuropathy or myopathy. We describe the principles of a recently developed technique, near fiber EMG (NFEMG), which focuses on contributions from fibers near the needle detection surface and can be used to semi-automatically quantify MU electrophysiological instability and temporal dispersion.

OBJECTIVE: To describe the fundamental principles and potential uses of NFEMG.

METHODS: Motor unit potentials (MUPs) of MUs extracted from conventionally acquired needle EMG signals are band-pass filtered using low-pass double-differentiation to create near fiber (NF) MUPs which, like SFEMG, are mostly comprised of contributions from fibers near to the needle detection surface. Symmetric peaks in NF-MUPs (NFPks) are created by single or small groups of MU fibers. Temporal variability (jitter) of NF-MUP segments (NFM-SJ) and NFPk segments (NFPk-SJ) across a set of isolated NF-MUPs are measured to assess MU electrophysiological instability. Duration of NF-MUPs (NFM-Duration) and temporal spacings between NFPks (NFM-dispersion) are measured to assess MU electrophysiological dispersion.

RESULTS: Preliminary studies demonstrate that NFEMG parameter values provide novel electrophysiological metrics that accurately quantify instability and temporal dispersion and can discriminate between neuromuscular conditions including, disorders of the neuromuscular junction, muscle, and nerve.

SUMMARY/CONCLUSION: NFEMG parameters, which can be readily, semi-automatically obtained from conventionally acquired needle EMG signals, offer a comprehensive evaluation of MU electrophysiological instability and temporal dispersion that can assist with the diagnosis, quantification, and longitudinal assessment of neuromuscular disorders.

COMPARISON OF NEAR FIBER SEGMENT JITTER AND SINGLE FIBER PAIR JITTER VALUES IN MYASTHENIA GRAVIS

Oscar Garnes (Madrid, Spain), Ross Mandeville (Boston, MA), Daniel Stashuk (Wateroo, Canada)

INTRODUCTION: Current SFEMG fiber-pair jitter methods used for assessing NMJ transmission instability in myasthenia gravis (MG) can be time-consuming and require significant expertise. Motor unit potentials (MUPs) extracted from conventionally acquired EMG signals can be low-pass double-differentiated to create near fiber (NF) MUPs that are comprised of contributions from fibers near to the needle. Symmetric peaks in NF-MUPs (NFPks) are created by single or small groups of MU fibers. Temporal variability (jitter) in NFPk segments across isolated NF-MUPs can be obtained quickly and with minimal training to assess NMJ transmission instability.

OBJECTIVE: To directly compare NFPk SJ values to conventional SFEMG fibre-pair jitter values.

METHODS: Conventional SFEMG and novel NFEMG jitter analysis was applied to matched level-triggered and decomposition-extracted MUP trains (MUPTs), respectively, from 8 myasthenic and 2 non-myasthenic subjects and their corresponding jitter values compared.

RESULTS: 80% of level-triggered MUPTs had a matching decomposition-extracted MUPT resulting in 94 matched MUPTs. SFEMG and NFPk jitter values had a Spearman correlation coefficient of 0.76, with 80% of matched values differing by less than 25µs. The mean disparity between SFEMG and NFPk jitter values was 16µs, without trend towards over or underestimation. Using a dichotomic classifier, only 12.8% of SFEMG fiber-pairs with increased jitter values showed normal NFPk-SJ (false negatives), and 9.6% of SFEMG fiber-pairs with normal jitter showed increased NFPk-SJ (false positives).

SUMMARY/CONCLUSION: NFPk-SJ values correlated well with SFEMG jitter values, supporting a potential role for NFPk-SJ as a novel, practical measure of NMJ instability in the diagnosis of MG.

MG-ADL AND QMG SCORES OVER TIME IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: POST-HOC ANALYSIS OF MYCARING AND OPEN-LABEL STUDIES

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INTRODUCTION: In MycarinG (MG0003/NCT03971422), 1 rozanolixizumab cycle (6 weekly infusions) demonstrated efficacy and was generally well tolerated in adults with generalized myasthenia gravis (gMG). Following MycarinG, patients could enroll in open-label extension studies (MG0004/NCT04124965 or MG0007/NCT04650854).

OBJECTIVE: A post-hoc analysis of rozanolixizumab efficacy over time.

METHODS: MG0004 evaluated ≤52 weekly rozanolixizumab infusions. Patients in MG0007, after an initial cycle, received rozanolixizumab based on symptom worsening (investigator's discretion, e.g. ≥2.0 MG-ADL or ≥3.0 QMG score increase). Data were pooled across MycarinG, MG0004 (first 6 weeks), and MG0007 (interim analysis). We assessed change from baseline in MG-ADL and QMG scores over time in patients with ≥2 consecutive symptom-driven cycles.

RESULTS: Patients (n=97) with >12 months in the studies initiated a mean of 4.0 cycles and 21.6 infusions in the first year. For all patients with all available follow-up (n=188), the mean annualized rate was 3.4 cycles and 17.8 infusions per year. At data cutoff, 127/196 (64.8%) patients received ≥2 symptom-driven cycles of rozanolixizumab and 110/196 (56.1%) received ≥2 consecutive symptom-driven cycles. Consistent rozanolixizumab efficacy was observed in MG-specific outcomes across repeated treatment cycles. Post-hoc analysis expanded findings: mean MG-ADL and QMG improvements were maintained for the cohort while individual patients cycled through consecutive treatment and observation periods. Cohort mean MG-ADL and QMG scores stabilized around a 3- and 4-point decrease, respectively, compared to study baseline scores.

SUMMARY/CONCLUSION: Symptom-driven rozanolixizumab treatment maintained a consistent, clinically meaningful level of improvement in gMG symptoms over multiple cycles.
Funded by UCB Pharma.

Disclosures:

Vera Bril - Consultant for Akcea, Alexion, Alnylam, argenx, CSL, Grifols, Ionis, Immunovant, Janssen, Momenta (now J&J), Novo Nordisk, Octapharma, Pfizer, Powell Mansfield, Sanofi, Takeda, Roche, and UCB Pharma; received research support from Akcea, Alexion, argenx, CSL, Grifols, Immunovant, Ionis, Momenta (now J&J), Octapharma, Takeda, UCB Pharma, and Viela Bio (now Horizon Therapeutics)

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PATIENT-REPORTED OUTCOMES DURING REPEATED CYCLES OF ROZANOLIXIZUMAB TREATMENT IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS IN THE PHASE 3 MYCARING AND OPEN-LABEL EXTENSION STUDIES

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INTRODUCTION: Myasthenia Gravis (MG) Symptoms Patient-Reported Outcome (MGSPRO) scales were developed to fully understand patients' experiences of the severity of specific MG symptoms, including physical fatigue, an important symptom not assessed by other MG symptom severity measures.

OBJECTIVE: To assess the effect of rozanolixizumab on patient-reported MG symptom severity across MycarinG (NCT03971422) and open-label extension studies (MG0004/NCT04124965 and MG0007/NCT04650854).

METHODS: Patients received 1 cycle (6 weekly infusions) of rozanolixizumab in MycarinG and ≤52 weeks of weekly rozanolixizumab in MG0004. In MG0007, after an initial cycle, cycles were administered on symptom worsening (investigators ' discretion, e.g. ≥2.0 MG-ADL/≥3.0 QMG score increase). Pooled data are reported across MycarinG, MG0004 (first 6 weeks) and MG0007 (interim analysis), for patients with ≥2 symptom-driven cycles. Change from baseline (CFB) in MGSPRO scales was assessed; higher scores (0–100) represent more severe symptoms.

RESULTS: 127 patients received ≥2 symptom-driven cycles of rozanolixizumab (7mg/kg or 10mg/kg). MGSPRO muscle weakness fatigability scores improved from baseline to end of first cycle (mean [SD] CFB at Day 43, −21.9 [23.3]), and in subsequent cycles. MGSPRO physical fatigue and bulbar muscle weakness scores also improved from baseline to end of first cycle (mean [SD] CFB at Day 43, −20.4 [20.9] and −15.6 [19.1]), and in subsequent cycles. Similar MGSPRO improvements were observed for each rozanolixizumab dose group. Rozanolixizumab was well tolerated with an acceptable safety profile, consistent across cycles.

SUMMARY/CONCLUSION: Rozanolixizumab consistently improved MG symptoms, including physical fatigue, a symptom particularly important to patients, across repeated treatment cycles, as measured by MGSPRO scales. Funded by UCB Pharma.

Disclosures:

Ali A. Habib - Received research support from Alexion/AstraZeneca, argenx, Cabaletta Bio, Genentech, Regeneron, UCB Pharma, and Horizon Therapeutics; received consulting fees/honoraria from Alexion/AstraZeneca, argenx, Genentech/Roche, Immunovant, and UCB Pharma

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Henry J. Kaminski - Consultant for Roche, Cabaletta Bio, Lincoln Therapeutics, Takeda, and UCB Pharma; is CEO and CMO of ARC Biotechnology, LLC, based on US Patent 8,961,98; principal investigator of the Rare Disease Network for Myasthenia Gravis (MGNet) National Institute of Neurological Disorders & Stroke, U54 NS115054, and Targeted Therapy for Myasthenia Gravis; received R41 NS110331-01 to ARC Biotechnology

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ZILUCOPLAN IN PEDIATRIC PATIENTS WITH ACETYLCHOLINE RECEPTOR AUTOANTIBODY-POSITIVE GENERALIZED MYASTHENIA GRAVIS: ZIMYG (MG0014) AND ZIMYG+ (MG0015) CLINICAL STUDY DESIGNS

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INTRODUCTION: Zilucoplan, a macrocyclic peptide complement C5 inhibitor, has demonstrated efficacy and safety in phase 2 and phase 3 studies in an adult population with acetylcholine receptor autoantibody-positive (AChR+) generalized myasthenia gravis (gMG). The phase 2/3 ZiMyG (MG0014) and phase 3 ZiMyG+ (MG0015) studies aim to assess the pharmacokinetics/pharmacodynamics (PK/PD), safety, tolerability and activity of zilucoplan in pediatric patients with AChR+ gMG.

METHODS: ZiMyG (MG0014), a multicenter, open-label study will enroll pediatric patients aged 2 to <18 years with AChR+ gMG and MGFA Disease Class II-IV. Patients will receive once-daily subcutaneous zilucoplan for 4 weeks. Two cohorts are planned: Cohort A will include adolescents, aged 12 to <18 years and Cohort B will include children, aged 2 to <12 years. Primary endpoints are plasma concentration of zilucoplan and complement inhibition, measured by change from baseline (CFB) in sheep red blood cell lysis and C5 levels at Week 4 (Day 29). Secondary endpoints include incidence of treatment-emergent adverse events, anti-drug antibodies at Day 29, and CFB to Day 29 in Myasthenia Gravis Activities of Daily Living, Quantitative Myasthenia Gravis, MGFA Post-Interventional Status and Pediatric Quality of Life Inventory scores. At the end of the 4-week treatment period, patients may continue treatment in an open-label extension study ZiMyG+ (MG0015), where long-term safety up to 52 weeks will be assessed.

SUMMARY/CONCLUSION: The ZiMyG 4-week study (MG0014) and its 52-week extension study ZiMyG+ (MG0015) will evaluate the PK/PD, safety, tolerability, and activity of once-daily subcutaneous zilucoplan in pediatric patients. Funded by UCB Pharma.

Disclosures:

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A PHASE 0 STUDY ESTABLISHING A ROBUST T CELL ASSAY FOR THE FIRST IN HUMAN TRIAL OF CNP-106 FOR GENERALIZED ACHR+ MG

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INTRODUCTION: Acetylcholine receptor (AChR) antibodies are detected in approximately 80-90% of generalized myasthenia gravis (MG) patients and directly lead to immune-mediated damage at the motor endplate causing fatigable muscle weakness. Current treatments for MG do not directly address the underlying T cell mediated component of this autoimmune condition. CNP-106, a nanoparticle that contains a pool of AChR-derived peptides to induce antigen-specific tolerance to AChR, is being investigated in an effort to develop a novel therapeutic class for MG.

OBJECTIVE: The primary objectives of this study were to confirm the presence of AChR-specific T cells in MG patients and to confirm the antigen set encapsulated in CNP-106. The goal was to establish this approach as a biomarker for measuring the pharmacodynamic activity of CNP-106.

METHODS: Ten AChR+ MG patients were recruited, and HLA-typing was performed. The patients' PBMCs were subjected to an ex vivo activation-induced marker assay using either the AChR peptide pool in CNP-106 or control peptides. The number of circulating activated AChR-specific T cells was counted, and the frequency of patients with measurable circulating T cells determined.

RESULTS: Eight out of 10patients had MG-associated HLA-haplotypes and showed measurable T cell responses to the AChR peptide pool. The remaining 2 patients had different HLA types, with only 1 showing detectable T cell responses.

SUMMARY/CONCLUSION: These findings are encouraging and support further development in the clinic of CNP-106 for AChR+ MG. Nanoparticles inducing antigen-specific T cell tolerance has the potential to be a novel class of therapy for MG.

Disclosures:

Irawati Kandela - Employed by COUR Pharmaceutical Development Co.

Adam Elhofy - Employed by COUR Pharmaceutical Development Co.

Michael Boyne - Employed by COUR Pharmaceutical Development Co.

Samantha Genardi - Employed by COUR Pharmaceutical Development Co.

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ANTIGEN-SPECIFIC IMMUNE THERAPY (CNP-106) FOR TREATMENT OF GENERALIZED MYASTHENIA GRAVIS: RATIONALE AND DESIGN OF FIRST-IN-HUMAN RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION: Myasthenia gravis (MG) is a T cell-dependent B-cell mediated autoimmune disease with pathogenic antibodies directed against the acetylcholine receptor (AChR). Current therapies do not completely address autoimmune recognition of AChR, the root cause of disease, and are associated with possible serious side effects. New therapeutics targeting antigen specific autoimmunity are needed for this significant unmet medical need.

OBJECTIVE: A phase 1/2a celiac disease clinical trial demonstrated that CNPs encapsulating gliadin is safe and effective at inducing antigen-specific tolerance. This trial will investigate antigen-specific tolerance induced by CNPs encapsulating multiple AChR epitopes (CNP-106) in MG patients.

METHODS: The study is a multi-center phase 1b/2a double blind, placebo-controlled trial with enrollment target of 40 AChR antibody positive generalized MG participants. The aim of this study is to determine safety, evaluate antigen specific T cells and other immunologic markers, and assess preliminary efficacy of CNP-106.

RESULTS: Data from pre-clinical models demonstrated that CNP-106 reprogrammed antigen specific T cells and reduced myasthenia clinical symptoms, highlighting the potential benefit of CNP-106 to stop progression of disease in MG patients.

SUMMARY/CONCLUSION: This study is the first to explore novel antigen specific therapy in MG. CNP-106 has the potential to induce tolerance to AChR and improve myasthenia clinical symptoms without the need for broad immunosuppression or chronic dosing. Results of this study will pave the way for a new class of therapeutics targeting antigen specific autoimmunity, leading to improvement in clinical disease and immune tolerance. The study rationale, design, and study status update will be presented.

Disclosures:

Samantha Genardi - Employed by COUR Pharma

Greta Wodarcyk - Employed by COUR Pharma

Derrick McCarthy - Employed by COUR Pharma

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RISK OF MYASTHENIA GRAVIS EXACERBATION AND LEVEL OF HEALTHCARE RESOURCE UTILIZATION BY MYASTHENIA GRAVIS ACTIVITIES OF DAILY LIVING SCORE

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INTRODUCTION: There are limited data available on the relationship of MG-ADL scores to MG exacerbations (>7 day duration of new symptoms or worsening of old symptoms) and healthcare resource utilization (HCRU).

OBJECTIVE: Retrospective, cross-sectional, observational registry study to assess patient characteristics, HCRU, and exacerbation risk in relation to MG-ADL score.

METHODS: The Myasthenia Gravis Foundation of America (MGFA) Global MG Patient Registry is an online patient-reported registry hosted on the Alira Health, Health Storylines platform. The study included participants in the United States, aged ≥18 years, with a self-reported diagnosis for MG and complete MG-ADL data who enrolled in the registry between July 01, 2013, and September 30, 2022. Patient demographics, disease characteristics, and HCRU were stratified by MG-ADL score (0–1/2–4/5–7/8–10/11–13/14+). Negative binomial regression was used to assess the association between MG-ADL score and exacerbation.

RESULTS: Of 3416 eligible patients, 2092 (61%) were female, including ≥78% of patients with MG-ADL scores ≥11. There were sociodemographic disparities in disease severity at enrollment and greater HCRU occurred in the higher MG-ADL score groups. A positive association between exacerbation and MG-ADL score (incidence rate ratio [IRR]: 1.13; 95% CI: 1.11–1.15) was observed at enrollment. Compared with MG-ADL scores of 0–1, exacerbation IRRs increased with higher MG-ADL scores from 2 (2–4) to 7.22 (≥14) ($p<0.001$). At enrollment, 50% (386/778) of patients with 1 exacerbation required treatment with IVIg, plasma exchange, or overnight hospitalization following exacerbation.

SUMMARY/CONCLUSION: Exacerbation risk and HCRU increase with higher MG-ADL scores. Funded by UCB Pharma.

Disclosures:

Angela Ting - Employee and shareholder of UCB Pharma

Minjee Park - Employee of Alira Health

Oshin Sangha - Employee of Alira Health and a member of MGFA Registry Advisory Council

Wendi Huff - Employee of the MGFA

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LOOKING BEYOND THE NUMBERS: INTERPRETING PATIENT EXPERIENCE OF ROZANOLIXIZUMAB IN GENERALIZED MYASTHENIA GRAVIS FROM THE MYCARING CLINICAL TRIAL

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INTRODUCTION: In the MycarinG phase 3 study (NCT03971422), rozanolixizumab demonstrated statistically significant improvements for primary and secondary endpoints compared with placebo in patients with generalized myasthenia gravis (gMG).

OBJECTIVE: Here we explore how the results may be interpreted to better understand patients' experiences.

METHODS: 200 adults with gMG were randomly assigned to receive rozanolixizumab 7 mg/kg, rozanolixizumab 10 mg/kg, or placebo. In a post-hoc analysis, the Rasch model was used to determine the most probable responses to items of the MG Symptoms PRO muscle weakness fatigability, physical fatigue, and bulbar muscle weakness scales, given the mean scores observed at baseline and at day 43 (after 6 weekly infusions of rozanolixizumab or placebo).

RESULTS: Mean MG Symptoms PRO physical fatigue score observed in patients who received rozanolixizumab suggests they typically no longer experience the more severe symptoms (heaviness of the whole body and weakness in the neck, finding it hard to move their body and to get up) and 'rarely' experience the less severe symptoms (feeling tired, lacking energy and weakness in their arms or legs), whereas placebo patients continue to experience these symptoms 'some of the time'. Similar results of patient experience were obtained across muscle weakness fatigability and bulbar muscle weakness scales, documenting a less severe symptom experience in the rozanolixizumab group than placebo.

SUMMARY/CONCLUSION: This post-hoc analysis of the MycarinG study further supports the meaningfulness of the positive clinical trial results and may facilitate communication about patients' experiences with rozanolixizumab.

Disclosures:

Antoine Regnault - Employee of Modus Outcomes, a patient-centered outcome research consultancy that received payment from UCB to conduct this research

Asha Hareendran - Employee and shareholder of UCB Pharma

Thomas Morel - Employee and shareholder of UCB Pharma

Ali A. Habib - Received research support from Alexion/AstraZeneca, argenx, Cabaletta Bio, Genentech, Regeneron, UCB Pharma, and Viela Bio (now Horizon Therapeutics); received consulting fees/honoraria from Alexion/AstraZeneca, argenx, Genentech/Roche, Immunovant, and UCB Pharma

Henry J. Kaminski - Consultant for Roche, Cabaletta Bio, Lincoln Therapeutics, Takeda, and UCB Pharma; CEO and CMO of ARC Biotechnology, LLC, based on US Patent 8,961,98; principal investigator of the Rare Disease Network for Myasthenia Gravis (MGNet) National Institute of Neurological Disorders & Stroke, U54 NS115054 and Targeted Therapy for Myasthenia Gravis; R41 NS110331-01 to ARC Biotechnology

Ann-Christin Mork - Employee and shareholder of UCB Pharma

EFFICACY OF REPEATED CYCLES OF ROZANOLIXIZUMAB TREATMENT IN SUBGROUPS OF PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: A POOLED ANALYSIS OF A PHASE 3 STUDY AND TWO PHASE 3 OPEN-LABEL EXTENSION STUDIES

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INTRODUCTION: The phase 3 MycarinG study (MG0003/NCT03971422) demonstrated efficacy of a single 6-week cycle of rozanolixizumab in patients with generalized myasthenia gravis (gMG). Following MycarinG, patients could enroll in open-label extension studies (MG0004/NCT04124965 or MG0007/NCT04650854).

OBJECTIVE: A subgroup analysis of rozanolixizumab efficacy over repeated cycles of treatment in patients with gMG.

METHODS: MG0004 evaluated ≤52 weeks of weekly rozanolixizumab infusions. In MG0007, after an initial rozanolixizumab treatment cycle, cycles were administered based on symptom worsening (investigators' discretion, e.g. ≥2.0 MG-ADL or ≥3.0 QMG score increase). Data were pooled across MycarinG, MG0004 (first 6 weeks) and MG0007 (interim analysis): efficacy pool, patients with ≥2 symptom-driven cycles; safety pool, ≥1 cycle including observation periods across MycarinG (symptom-driven) and MG0007 (fixed/symptom-driven).

RESULTS: 127 patients received ≥2 symptom-driven cycles of rozanolixizumab. Mean changes from baseline in MG-ADL scores at Day 43 for the overall population were: Cycle 1, −3.7; Cycle 2, −3.9; Cycle 3, −3.4; Cycle 4, −3.8; Cycle 5, −3.9; Cycle 6, −4.5. Improvements from baseline in MG-ADL scores at Day 43 were consistent across repeated cycles of rozanolixizumab treatment in prespecified subgroups: autoantibody status (MuSK/AChR autoantibody positive), baseline duration of disease (<5.4 and ≥5.4 years), age (<65 and ≥65 years), baseline MG-ADL (<5 and ≥5) and thymectomy status. Overall, treatment-emergent adverse events occurred in 169/188 (89.9%) patients; most were mild to moderate in severity.

SUMMARY/CONCLUSION: Rozanolixizumab efficacy was maintained across multiple treatment cycles in a broad population of patients with gMG, regardless of autoantibody status, disease duration, age, disease severity and thymectomy status.

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Marion Boehnlein - Employee and shareholder of UCB Pharma

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Franz Woltering - Employee and shareholder of UCB Pharma

Maryam Gayfieva - Employee and shareholder of UCB Pharma

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EARLY RESPONDERS WITH ZILUCOPLAN: AN INTERIM ANALYSIS OF RAISE-XT IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: Zilucoplan, a complement component 5 inhibitor, showed clinically meaningful and significant improvements in myasthenia gravis (MG)-specific outcomes in the phase 3 RAISE study in patients with acetylcholine receptor autoantibody-positive generalized MG (AChR+ gMG). Interim analyses of RAISE-XT, an ongoing open-label extension study, demonstrated that zilucoplan was efficacious and well-tolerated in the long term.

OBJECTIVE: A post-hoc analysis to assess baseline characteristics and long-term outcomes for MG Activities of Daily Living (MG-ADL) and Quantitative MG (QMG) responders at Week 1.

METHODS: Adults with AChR+ gMG (MGFA Class II-IV) who completed a qualifying randomized, placebo-controlled, double-blind study of zilucoplan (phase 2, NCT03315130; phase 3, NCT04115293) could opt to receive daily, subcutaneous zilucoplan 0.3 mg/kg in RAISE-XT (NCT04225871). MG-ADL and QMG responders were defined by ≥3-point and ≥5-point reductions from double-blind baseline without rescue therapy, respectively.

RESULTS: Of patients randomized to zilucoplan 0.3 mg/kg in the double-blind studies (n=93), 40 (43.0%) were MG-ADL and 31 (33.3%) were QMG responders at Week 1, of whom >80% and >85%, respectively, remained responders at each assessment through Week 60. Additionally, Week 1 responders maintained their response for 88.1% and 88.8% of their total time on treatment, respectively, for a median zilucoplan treatment duration of 450 days. There were no relevant differences in baseline characteristics of Week 1 responders compared to the overall population.

SUMMARY/CONCLUSION: Week 1 responders maintained their response for almost 90% of their time on long-term zilucoplan treatment, regardless of baseline characteristics, thus supporting its early use in a broad patient population. Funded by UCB Pharma.

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Tuan Vu - USF Site Principal Investigator for trials sponsored by Alexion/AstraZeneca Rare Disease, argenx, Ra Pharmaceuticals/UCB Pharma, Horizon Therapeutics, Janssen Pharmaceuticals/Momenta, Regeneron, and Cartesian Therapeutics; received speaking and/or consulting honoraria from Alexion, argenx, and UCB Pharma

Raphaelle Beau Lejdstrom - Employee and shareholder of UCB Pharma

Babak Boroojerdi - Employee and shareholder of UCB Pharma

Fiona Grimson - Employee and shareholder of UCB Pharma

Pauline Payen - Employee and shareholder of UCB Pharma

Natasa Savic - Employee and shareholder of UCB Pharma

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SOCIAL DETERMINANTS OF HEALTH ARE ASSOCIATED WITH SUBOPTIMAL TREATMENT AMONG INDIVIDUALS WITH MYASTHENIA GRAVIS

Judith Thompson (Smyrna, GA), Bo Zhang (Atlanta, GA), Joshua N. Liberman (Clarksville, MD), Jonathan Darer (Lewisburg, PA)

INTRODUCTION: Social determinants of health (SDoH) can significantly impact health care access.

OBJECTIVE: To investigate the association between SDoH and suboptimal therapy among individuals with myasthenia gravis (MG).

METHODS: We conducted a retrospective observational cohort study among adults diagnosed with MG between 10/1/18 and 9/30/20 using IQVIA LAAD medical and pharmacy claims data linked to Socially Determined SDoH indices measured at the level of 5-digit ZIP code. Eligible participants had no MG diagnosis or treatment at baseline (12 months before index diagnosis). Follow up (24 months following index) was used to identify treatment. Suboptimal treatment, defined as beginning therapy without acetylcholinesterase inhibitor, >10mg/day of corticosteroids for 6 months, >300 mg/day of azathioprine for 24 months, or >3,000 mg/day of mycophenolate for 12 months. Demographics, comorbidities, and 7 SDoH risk indices were regressed (logistic regression) on suboptimal treatment.

RESULTS: Of 8,839 participants, 3,091 (35.0%) received suboptimal treatment. Compared to individuals with no evidence of suboptimal treatment, individuals receiving suboptimal treatment were more likely male (52.9% vs. 46.0%, $p<0.01$), to have fewer comorbidities (Charlson Index 0.41 vs. 0.46, $p<0.01$), and to initiate treatment within 30 days of index (64.6% vs. 47.7%, $p<0.001$). After adjustment, regions with high-risk (vs. low-risk) housing environment index score (OR 1.17; 95% CI: 1.02,1.35) and high-risk food landscape index score (OR 1.13; 95% CI: 0.99, 1.28) had elevated risk of suboptimal therapy.

SUMMARY/CONCLUSION: SDoH are associated with the receipt of suboptimal treatment among individuals with MG. Providers may need to identify patients from at-risk communities who require additional support. Funded by UCB Pharma.

Disclosures:

Judith Thompson - Employee of UCB Pharma

Bo Zhang - Employee of UCB Pharma

Joshua N. Liberman - Employee of Health Analytics, LLC

Jonathan Darer - Employee of Health Analytics, LLC

INVESTIGATING IMMUNOLOGICAL PROFILES OF THYMUS IN ACHR-MG BY SCRNA-SEQ

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INTRODUCTION: Thymic hyperplasia has been associated with early-onset AChR-myasthenia gravis (MG). However, thymus complexities hinder comprehensive analysis by traditional techniques, limiting our understanding of thymic immunological profiles in MG.

OBJECTIVE: To characterize the immunological signatures of thymus in patients with AChR-MG.

METHODS: We collected matched thymus samples and peripheral blood monocytes (PBMCs) from 2 patients diagnosed with early-onset AchR-MG. To identify and characterize immune cell subsets within the thymus and PBMCs, we applied high-resolution single-cell RNA sequencing (scRNA-seq) technology. After removing the dead cells and following sequencing, we performed bioinformatic analysis. Public available dataset of age and sex-matched healthy controls (HC) were also included.

RESULTS: A total of 39,943 single cells derived from thymocytes and PBMCs passed QC. Twenty-four immune cell clusters were identified. Comparing thymocytes, we observed a significant decrease in double positive T cells, along with an increase in CD4 T cells, B cells, NK and DCs in MG patients than HC. In PBMCs, we observed a significant increase in double positive T cells and CD4 T cells, while NK cells, DCs and monocytes were decreased in MG patients. Overall, our findings indicate a shift of double positive T cells from thymus to periphery, and an increase of B cells, NK cells, and DCs in the thymus of MG patients.

SUMMARY/CONCLUSION: Our study highlights the presence of an immune cell imbalance between the thymus and peripheral circulation in MG patients. Further investigations are necessary to confirm the underlying mechanisms and elucidate the role of these imbalanced immune cells in the pathogenesis of MG.

OVERVIEW OF THE SAFETY PROFILE FROM EFGARTIGIMOD CLINICAL TRIALS IN PARTICIPANTS WITH DIVERSE IMMUNOGLOBULIN G-MEDIATED AUTOIMMUNE DISEASES

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INTRODUCTION: Efgartigimod is a first-in-class human immunoglobulin G (IgG) Fc fragment that inhibits the neonatal Fc receptor (FcRn) and outcompetes endogenous IgG binding. This results in reduced recycling and increased degradation of IgGs, including pathogenic IgG autoantibodies. FcRn inhibition by efgartigimod is a rational therapeutic option for IgG-mediated autoimmune disorders.

METHODS: Intravenous efgartigimod safety was assessed in generalized myasthenia gravis (gMG) in phase 2 and 3 (ADAPT) trials and a 3-year open-label extension (ADAPT+) trial, in primary immune thrombocytopenia (ITP) in a phase 3 trial (ADVANCE), and in pemphigus (vulgaris and foliaceus) in an open-label phase 2 trial. These studies examined different dosing regimens of efgartigimod (10–25 mg/kg), including cyclical dosing in gMG and continuous weekly dosing in ITP and pemphigus.

RESULTS: Across all indications and doses studied, efgartigimod demonstrated a consistent safety profile, with comparable treatment-emergent adverse event (TEAE) rates to placebo (ADAPT 77.4% efgartigimod/84.3% placebo; ADVANCE 93.0% efgartigimod/95.6% placebo; and pemphigus 85% efgartigimod). Most TEAEs were mild to moderate in severity. Discontinuation rates due to adverse events were consistently low (ADAPT 3.6% efgartigimod group/3.6% placebo; ADVANCE 3.5% efgartigimod/2.2% placebo; and 3% of pemphigus study participants). Efgartigimod was well tolerated in ADAPT+, with no increase in TEAE incidence rates, including infections, with repeated efgartigimod cycles (up to 19). Efgartigimod treatment did not reduce albumin levels or increase cholesterol levels.

SUMMARY/CONCLUSION: Efgartigimod is well tolerated across indications and doses studied. Most TEAEs, including infections, were mild or moderate in severity and did not increase in frequency with recurrent dosing.

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Matthias Goebeler - Consultant for argenx, Almirall; honoraria from Biotest, GSK, Janssen, Leo Pharma, Lilly, Novartis, and UCB

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EFFECTIVENESS AND SAFETY OF TRANSITIONING TO RAVULIZUMAB FROM ECULIZUMAB IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: EVIDENCE FROM THE MG501 REGISTRY

Andrew Gordon (Lake Barrington, IL), Pushpa Narayanaswami (Boston, MA), Michael Pulley (Jacksonville, FL), Saida Sharapova (Boston, MA), Guido Sabatella (Boston, MA), James F Howard Jr (Chapel Hill, NC)

INTRODUCTION: Complement component 5 inhibitors eculizumab and ravulizumab are approved treatments for generalized myasthenia gravis (gMG), dosed every 2 (Q2W) and 8 weeks (Q8W), respectively. The MG501 registry collects data on eculizumab and ravulizumab effectiveness and safety.

OBJECTIVE: To assess the effectiveness and safety of transitioning patients with gMG from eculizumab to ravulizumab in clinical practice using the Myasthenia Gravis Activities of Daily Living (MG-ADL) total score and Myasthenia Gravis Foundation of America (MGFA) classification.

METHODS: Registry patients who transitioned from eculizumab to ravulizumab were included if they had MG-ADL total scores and MGFA classifications before initiating and during eculizumab treatment, and after transitioning to ravulizumab treatment. Descriptive statistics were performed and are presented as mean (standard deviation). Safety data will be reported.

RESULTS: Of the 188 registry patients enrolled, 38 (20%; 66% male) transitioned from eculizumab to ravulizumab. Patient age at eculizumab and ravulizumab initiation was 65.1 (15.4) and 68.0 (16.0) years, respectively. For 16 patients with MG-ADL total scores, a 4.2-point reduction from 8.1 (4.0) to 3.9 (4.5) was observed after 31.5 (22.4) months of eculizumab treatment. After transitioning to ravulizumab, MG-ADL total scores remained stable at 3.3 (3.6) after 5.2 (2.2) months of treatment. In patients with MGFA classifications, improvements were noted during eculizumab treatment and remained stable over 5.3 (2.3) months after transitioning to ravulizumab.

SUMMARY/CONCLUSION: These initial results from the MG501 registry, representing clinical practice, demonstrate that average improvements achieved during Q2W eculizumab treatment were maintained when patients with gMG transitioned to Q8W ravulizumab.

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Pushpa Narayanaswami - Received research support from Alexion, AstraZeneca Rare Disease, Momenta/Janssen, PCORI, and UCB S.A.; served on advisory boards for Janssen and as a Data Monitoring Committee Chair for Sanofi; speaker for Alexion, AstraZeneca Rare Disease, argenx, and UCB S.A.

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Saida Sharapova - Employee of Alexion, AstraZeneca Rare Disease

Guido Sabatella - Employee of Alexion, AstraZeneca Rare Disease and also owns stocks in Alexion

James F Howard Jr - Received research support from Alexion, AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention, the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health, PCORI, UCB S.A., and Takeda Pharmaceuticals; honoraria from Alexion Pharmaceuticals, argenx, F. Hoffman LaRoche Ltd, Immunovant., Merck EMD Serono, NMD Pharma, Novartis Pharmaceuticals, UCB S.A., Regeneron Pharmaceuticals, and Sanofi US; non-financial support from Alexion, AstraZeneca Rare Disease, argenx, UCB S.A., and Toleranzia AB

STUDY DESIGN AND METHODOLOGY OF PREVAIL: A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF THE SAFETY AND EFFICACY OF SUBCUTANEOUS ALXN1720 IN ADULTS WITH GENERALIZED MYASTHENIA GRAVIS

James F Howard Jr (Chapel Hill, NC), Sanjay Rakhade (Boston, MA), Joachim Scholz (Boston, MA), Stephan Ortiz (Boston, MA), Shulian Shang (Boston, MA), Tuan Vu (Tampa, FL)

INTRODUCTION: ALXN1720, a novel bispecific variable domain on a heavy chain antibody, binds complement component 5 (C5) and inhibits its cleavage into C5a and C5b, thus preventing the formation of membrane attack complex. ALXN1720 binding to albumin extends its half life and enables self administered subcutaneous (SC) dosing at weekly intervals. Previous studies of eculizumab and ravulizumab have demonstrated the safety and efficacy of C5 inhibitors in generalized myasthenia gravis (gMG).

OBJECTIVE: To present the rationale and design for PREVAIL (ALXN1720-MG-301; NCT05556096), an international phase 3 study of ALXN1720 in adults with acetylcholine receptor antibody positive (AChR Ab+) gMG.

METHODS: PREVAIL consists of a 4-week screening period, a 26-week randomized controlled treatment period and a 105-week open-label extension period. Approximately 200 patients are randomized 1:1 to receive ALXN1720 (comprised of an initial weight-based loading dose, followed by weekly weight-based maintenance doses) or placebo. The primary outcome is change from baseline in Myasthenia Gravis-Activities of Daily Living (MG ADL) total scores at week 26. Secondary outcomes include changes from baseline in Quantitative Myasthenia Gravis (QMG) and Myasthenia Gravis Composite total scores, and MG-ADL 3 point improvement and QMG 5-point improvement. The safety, pharmacokinetics, pharmacodynamics, and immunogenicity of ALXN1720 will be assessed. Key eligibility criteria include diagnosis of gMG ≥ 3 months ago; positive serological test for AChR autoantibody; Myasthenia Gravis Foundation of America disease classification II- IV; and MG-ADL total score ≥ 5.

RESULTS: PREVAIL is actively recruiting patients.

SUMMARY/CONCLUSION: PREVAIL will assess the safety and efficacy of SC ALXN1720 in patients with AChR Ab+ gMG.

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Tuan Vu - Received research or grant support from Alexion/AstraZeneca Rare Disease, argenx, Horizon/Viela Bio, Immunovant, Janssen/Momenta, RA Pharmaceuticals/UCB Biosciences, Regeneron, and Sanofi; serves on advisory board and/or speaker bureau for Alexion/AstraZeneca Rare Disease, argenx, and UCB Biosciences

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DIFFERENCES IN CLINICAL CARE BETWEEN BLACK AND NON-BLACK PATIENTS WITH GMG RECEIVING ECULIZUMAB IN THE UNITED STATES

Adrian Kielhorn (Boston, MA), Justin Lee (Boston, MA), James F Howard Jr (Chapel Hill, NC), Ali Habib (Irvine, CA), Barbara Mungin (Boston, MA), Marla Morgan (Albany, GA)

INTRODUCTION: Racial inequities have been observed in healthcare access and treatment. Myasthenia gravis (MG) is a rare autoimmune neuromuscular disease resulting in muscle weakness and functional impairment affecting 6.2% of Black patients in a US-based registry.

OBJECTIVE: To explore differences in care approaches between Black and non-Black patients with generalized MG (gMG) receiving eculizumab in the US.

METHODS: This study was a retrospective data analysis of adults with gMG from physician-reported electronic medical record data at 14 US sites. gMG severity and treatment outcomes 2 years before and 2 years after eculizumab initiation were analyzed for Black and non-Black patients.

RESULTS: Compared with non-Black patients (n=100), Black patients (n=19) were predominantly female (84.2% vs 55.0%), diagnosed at a younger age (mean: 33.3 vs 53.8 years), treated in academic medical centers (78.9% vs 50.0%), and had commercial insurance (68.4% vs 40.0%). Black patients experienced a longer time from diagnosis to initiation of eculizumab (mean: 10.2 vs 7.5 years) and initiated eculizumab with higher disease severity (mean MG-ADL score: 9.3 vs 7.7 points). Eculizumab was initiated in Black patients more frequently due to prior therapy intolerance (47% vs 39%), gMG crises (11% vs 6%), and exacerbations (42% vs 34%) compared with non-Black patients. Differences were also observed in percentages of Black vs non-Black patients receiving concomitant medications prior to and at eculizumab initiation.

SUMMARY/CONCLUSION: In US clinical practice, differences in clinical care were observed between Black and non-Black patients; these differences may indicate health inequities and warrant further investigation.

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Adrian Kielhorn - Employed by and owns stock in AstraZeneca

Justin Lee - Employed by and owns stock in AstraZeneca

James F Howard Jr - - Received research support from Alexion Pharmaceuticals, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention, the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health, PCORI, UCB Biosciences, and Takeda Pharmaceuticals; honoraria from Alexion Pharmaceuticals, argenx, F. Hoffman-LaRoche Ltd, Immunovant., Merck EMD Serono, NMD Pharma, Novartis Pharmaceuticals, UCB Biosciences, Regeneron Pharmaceuticals, and Sanofi US; non-financial support from Alexion Pharmaceuticals, argenx, UCB Biosciences, and Toleranzia AB

Ali Habib - Received research support from Alexion, AstraZeneca Rare Disease, argenx, Cabealetta Bio, Genentech, Immunovant, Pfizer, Regeneron Pharmaceuticals, UCB Pharma, and Viela Bio (part of Horizon Therapeutics); received fees from Alexion, AstraZeneca Rare Disease, argenx, Immunovant, Regeneron Pharmaceuticals, and UCB Pharma

Barbara Mungin - Employed by and owns stock in AstraZeneca

Marla Morgan - Member of a Scientific Advisory Committee for Alexion, AstraZeneca Rare Disease

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MGNATION: A REAL WORLD STUDY CAPTURING PATIENT, HEALTHCARE PROFESSIONAL, AND CAREGIVER PERSPECTIVES

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INTRODUCTION: Myasthenia gravis (MG) is a rare, chronic, IgG autoantibody-mediated disease, characterized by debilitating and unpredictable muscle weakness. Despite commonly used standard-of-care (SoC) treatments such as corticosteroids and immunosuppressants, many patients only have a suboptimal response that may be improved by newer targeted immunotherapies.

OBJECTIVE: To evaluate this patient population to report on how patients feel, function, and cope.

METHODS: MGNation is a prospective, longitudinal, global, non-interventional real-world cohort study collecting patient-, HCP-, and caregiver-reported outcomes in a patient population with uncontrolled moderate-to-severe generalized MG (gMG) despite SoC treatment and who are initiating a new targeted immunotherapy. Enrollment is planned for ≥ 200 patients and the follow-up period is up to 2 years. Patients will be followed per routine clinical practice and will have access to a device to assist collecting data on patient reported outcomes and the impact of the disease on the patient as well as their caregiver.

RESULTS: MGNation will help describe this patient population with gMG with suboptimal response to SoC in terms of demographics, disease characteristics as well as real-world treatment patterns, treatment effectiveness, safety, and medical resources utilization. This study will provide summary statistics by treatment cohorts overtime for changes in patient, clinician, and caregiver reported outcomes.

SUMMARY/CONCLUSION: MGNation, an innovative non-interventional study, will collect robust data from key stakeholders, to give the most complete understanding on how patients with moderate to severe uncontrolled gMG and suboptimal response to SoC are managed in the real world.

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Shirley Pullan - Johnson & Johnson employee and might hold Johnson & Johnson stock

Ibrahim Turkoz - Johnson & Johnson employee and might hold Johnson & Johnson stock

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ACUPUNCTURE TREATMENT FOR INDIVIDUALS WITH MYASTHENIA GRAVIS

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INTRODUCTION: Acupuncture has been shown to be safe and effective for treating many conditions and involves inserting fine needles into specific areas of the body. It has been practiced for over 4,000 years and is accepted by many cultures. A recent systematic review concluded that acupuncture for 12 or more weeks, combined with medication use, may be beneficial for individuals with myasthenia gravis (MG).

OBJECTIVE: The primary goal of this study is to examine the effect of acupuncture on quality of life and activities of daily living in individuals with MG.

METHODS: Twenty participants will receive acupuncture twice a week for 12 weeks. Participants are randomized into an immediate or a delayed start group. Acupuncture points are chosen based on classical Traditional Chinese Medicine (TCM) indications and modern biomedical applications. MG symptom pathology, along with muscular, immunological, and neurological actions were considered. During treatment, 21 needles are inserted, with up to 9 additional needles based on individual presentation, and TCM pattern differentiation.

RESULTS: To date, we have enrolled 12 participants. Four participants have completed treatment, 3 are active, and 5 have withdrawn. Withdrawal reasons include unrelated health complications, scheduling difficulties, and the frequency/duration of the intervention.

SUMMARY/CONCLUSION: We aim to demonstrate that acupuncture can improve the quality of life and daily living activities for individuals with MG. This study is crucial to inform the design of a larger trial, including taking into consideration reasons for withdrawal. Next steps include increasing recruitment by sending targeted recruitment letters to patients with MG within our healthcare system.

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PREVALENCE OF SMALL CELL LUNG CANCER IN US PATIENTS WITH LAMBERT-EATON MYASTHENIC SYNDROME: A CONTEMPORARY REAL-WORLD DATA ANALYSIS

David Morrell (Coral Gables, FL), Nicholas Streicher (Chevy Chase, MD), Benjamin Drapkin (Dallas, TX), Regina Grebla (Bradford, NH), Guy Shechter (Lexington, MA)

INTRODUCTION: Small cell lung cancer (SCLC) is estimated to occur in approximately 40%-60% of Lambert-Eaton myasthenic syndrome (LEMS) patients and has been associated with improved survival. Recent data evaluating SCLC among United States (US) LEMS patients is lacking.

OBJECTIVE: To investigate the frequency of SCLC among patients with LEMS in the US.

METHODS: Healthcare claims from longitudinal databases representing >300 million US patients between 2014-2022 were evaluated. Patients with LEMS (ICD-9-CM: 358.3, 358.30, 358.31, 358.39 or ICD-10-CM: G70.80, G70.81, G73.1), lung cancer (ICD-9-CM 162.X excluding 162.0, ICD-10-CM C34.X), and/or SCLC-related therapies (etoposide and platinum) were identified based on ≥2 claims ≥30 days apart. The prevalence of SCLC among patients with LEMS overall and with continuous healthcare utilization (≥12 months pre- and post-index LEMS claim) was quantified.

RESULTS: Among 1,836 LEMS patients eligible for inclusion in the study, 390 (21%) had lung cancer-related claims. In 50% (n=195/390), the first observed lung cancer claim preceded the index LEMS claim by >14 days. 30.8% (n=120/390) of LEMS-SCLC patients (6.5% overall) received SCLC treatment. Among the subset of 1,153 patients with continuous healthcare utilization, 76 (6.6%) had treated SCLC (53% female, mean age 64.8 ± 7.0 years).

SUMMARY/CONCLUSION: SCLC has been reported among half of LEMS patients in prospective international studies, but among US-diagnosed LEMS patients, SCLC is found in approximately 20%. Future analyses examining additional data sources to verify the data presented in this abstract are planned.

Disclosures:

David Morrell - Employee and stockholder of Catalyst Pharmaceuticals

Benjamin Drapkin - Consultant for Sonata Therapeutics

Regina Grebla - Consultant for Catalyst Pharmaceuticals

Guy Shechter - Consultant for Catalyst Pharmaceuticals

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CLINICAL OUTCOMES OF FCRN INHIBITORS IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Amanda Cyntia Lima Fonseca Rodrigues (Curitiba, Brazil), James Howard (Chapel Hill, NC)

INTRODUCTION: Generalized myasthenia gravis (gMG) is a rare, chronic, neuromuscular autoimmune disease mediated by pathogenic immunoglobulin G (IgG) autoantibodies against the acetylcholine receptor. Neonatal Fc receptor (FcRn) blockade competitively inhibits endogenous IgG binding, leading to reduced IgG recycling and increased degradation resulting in lower IgG concentration. FcRn inhibition may provide an efficient treatment alternative for gMG.

OBJECTIVE: To conduct a meta-analysis of randomized controlled trials (RCTs) to investigate clinical outcomes of FcRn inhibitors compared with placebo in gMG patients.

METHODS: PubMed, Embase, and Cochrane databases were searched through June 2023. We conducted the statistical analysis in R version 4.3.0 using random-effects models that were estimated using the inverse variance with Mantel-Haenszel method. The outcomes assessed were MG-Activities of Daily Living (MG-ADL) responders (improvement of ≥ 2 points), Quantitative MG (QMG) and MG Composite (MGC) responders (≥ 3 points).

RESULTS: Three RCTs were included with 300 patients. The total mean age was 50 years old, and 199 were women (66.33%). FcRn inhibitors had a significant positive response rate on MG-ADL (OR 5.33, 95% CI 3.23 to 8.80, $p<0.001$), $I^2 = 0\%$), QMG (OR 3.53, 95% CI 1.14 to 10.95, $p=0.029$, $I^2 = 79\%$), and MGC (OR 2.31, 95% CI 1.25 to 4.29, $p=0.008$, $I^2 = 0\%$) scores.

SUMMARY/CONCLUSION: FcRn inhibitors demonstrated a significant positive effect and had a statistically positive impact on all 3 outcome measures. MG-ADL, MGC, and QMG demonstrated consistency across studies. These findings highlight the potential benefits of FcRn inhibition for patients with gMG.

Disclosures:

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RATES OF MYASTHENIC CRISIS, EXACERBATION AND HEALTHCARE RESOURCE UTILIZATION IN ECULIZUMAB-TREATED PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS FROM THE MG501 REGISTRY

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INTRODUCTION: Generalized myasthenia gravis (gMG) is a rare autoimmune disorder characterized by fatigable muscle weakness. Myasthenic crisis is a potentially life-threatening complication of gMG. Complement C5 inhibitor eculizumab has been shown to be effective and well-tolerated in treating patients with acetylcholine receptor antibody-positive gMG.

OBJECTIVE: To assess the rates of myasthenic crisis, exacerbations and hospitalizations/emergency room (ER) visits among US patients with gMG treated with eculizumab in clinical practice.

METHODS: Frequency and type of hospitalizations were evaluated for patients enrolled in the MG501 registry from 12 months prior to eculizumab and following initiation up to January 2, 2023. Demographics, hospitalizations/ER visits, and intensive care unit (ICU) admissions were analyzed, irrespective of eculizumab treatment. In patients with known treatment dates, rates of myasthenic crisis, exacerbations, and hospitalizations per 100 person-years were calculated before/during eculizumab treatment.

RESULTS: Of 155 patients with completed hospitalization forms, 120 (77.4%) had complete eculizumab records. Demographic data were similar among patients with (n=61 [39%]) or without hospitalizations/ER visits (n=94 [61%]). Twenty-three (37.7%) hospitalized patients were admitted to an ICU (34 total ICU admissions, of which 27 [79.4%] were MG-related). Following eculizumab initiation, rates of myasthenic crisis, exacerbations, and hospitalizations all decreased (from 12 to 2; 39 to 3; 79 to 26 per 100 person-years, respectively), whereas rates of non-MG-related hospital visits remained unchanged. Patients without hospitalizations/ER visits increased from 71 (59.2%) to 90 (75.0%) following eculizumab initiation.

SUMMARY/CONCLUSION: Eculizumab is associated with decreased rates of myasthenic crisis, exacerbations, and hospitalizations among patients with gMG in clinical practice.

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Rup Tandan - Site principal investigator for Apellis, Alexion, Cytokinetics, and Mitsubishi Tanabe; consultant for Apellis and Biogen; and speaker for Amylyx

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Ericka Greene - Speaker for Alexion Pharmaceuticals

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Samir Macwan - Consultant for Abbvie, Alexion, argenx, Catalyst, Grifols, Kabafusion, Supernus, UCB

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CLEARANCE OF IMMUNOGLOBULIN G BY PLASMA EXCHANGE AND RISK OF INFECTIONS IN MYASTHENIA GRAVIS: A RETROSPECTIVE ELECTRONIC MEDICAL RECORD REVIEW

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INTRODUCTION: Myasthenia gravis (MG) is a chronic autoimmune, immunoglobulin G (IgG) mediated disorder. Management includes reduction of pathogenic IgG autoantibodies by plasma exchange (TPE) and neonatal Fc receptor inhibition (FcRn). Both techniques reduce IgG levels between 52% and 73%. There are concerns that chronic IgG reduction of this magnitude could lead to more frequent infections.

OBJECTIVE: Assess frequency and severity of infections in inpatient and outpatient settings and associated serum IgG levels in MG patients treated with chronic TPE.

METHODS: Adult-MG patients treated with chronic TPE between April 2014 and December 2022 at a single center were included. All serum IgG levels from these patients were recorded. Reported infections were limited to those that had clinically reported symptoms, supportive laboratory findings, or treatment using prescription medications.

RESULTS: Twenty-five patients received a total of 2,447 TPE procedures (median 67/patient, range 14-488) and achieved a median serum IgG of 564mg/dL (reference range: 646-2,013mg/dL). Ninety-nine infections were identified. The majority of infections were respiratory (35%) and urinary (22%). There were no significant differences in serum IgG levels during active infection versus steady-state (638.5 and 518mg/dL, respectively, p=0.63). Infections necessitating inpatient admission did not have reduced serum IgG compared with less-severe infections or steady-state (514, 661, and 518mg/dL, respectively, p=0.87). There was no correlation between the number of reported infections per patient and their median serum IgG levels (r=0.25, p=0.24).

SUMMARY/CONCLUSION: This retrospective analysis demonstrates no clear association between serum IgG levels and the occurrence or frequency of infection in MG patients treated with chronic TPE.

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Matthew Karafin - Consultant for Westat, Inc

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PREVALENCE AND DIVERSITY OF MYASTHENIA GRAVIS IN THE UNITED STATES: A CROSS-SECTIONAL STUDY OF THE NIH ALL OF US RESEARCH PROGRAM DATABASE

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INTRODUCTION: The All of Us Research Program was developed by the National Institutes of Health (NIH) in order to establish a diverse health database of patients across the United States. It aims to represent the diversity of the US population including race, ethnicity, sex, gender, and sexual orientation.

OBJECTIVE: To examine the prevalence of myasthenia gravis (MG) using the All of Us Research Program.

METHODS: A cross-sectional analysis utilizing the electronic health records (EHRs) of 369,297 All of US adult participants (age ≥ 18 years) was performed. Participants with a myasthenia gravis diagnosis were identified by observational medical outcome partnership (OMOP) concept IDs for the condition, which includes Systemized Nomenclature of Medicine (SNOMED) and International Classification of Diseases (ICD) codes.

RESULTS: 479 total cases of MG were identified in the available All of Us dataset, with an overall prevalence of 0.13 % (95% CI 0.12-0.14). Participants with MG had an average age of 64 (SD 16) and were predominantly white (Race/Ethnicity distribution: 68% White, 12% Black, 11% Hispanic, 1% Asian, and 8% other) and female (65%).

SUMMARY/CONCLUSION: The prevalence of MG utilizing a US-based inclusive database suggests that the frequency of this condition has increased as compared to prior estimates. It is unclear as to whether this is due to better identification of patients or other factors (i.e., life expectancy, improved treatment). Further investigation into the epidemiology of MG remains critical in order to better understand the impact/burden of disease across a diverse population and to improve patient care.

Disclosures:

Bhaskar Roy - Consultant for argenx, Takeda pharmaceuticals; own stocks in Cabaletta Bio

Richard Nowak - On scientific advisory board for Ra Pharma, Alexion, argenx, Immunovant, Momenta; consultant for Alexion, Grifols, Ra Pharma, Momenta, Immunovant, CSL Behring; while drug/placebo were provided by Genentech through an investigator-initiated trial agreement with Dr. Nowak, they were not involved in trial design, implementation, or data analysis. Dr. Nowak is Global Principal Investigator for a phase 3 trial in myasthenia gravis through a research agreement (Viela Bio, a part of Horizon Therapeutics). (1) National Institute of Neurological Disorders and Stroke (NINDS) of the National Institutes of Health under award number U01NS084495, PI, 2013-2019. (1) Alexion, (2) Genentech, (3) Grifols, (4) Ra Pharma, (5) argenx, (6) Momenta, (7) Immunovant, (8) Viela Bio. Research support: (1) Myasthenia Gravis Foundation of America (MGFA)

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EVALUATING DISPARITIES IN TREATMENT AND OUTCOMES AMONG MYASTHENIA GRAVIS PATIENTS IN COLORADO: A REAL-WORLD DATA ANALYSIS

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INTRODUCTION: Limited real-world data exists regarding differences in outcomes, disparities, effects of comorbid conditions, and treatment choices in patients with myasthenia gravis (MG).

OBJECTIVE: To characterize treatments, complications and healthcare utilization of adult MG patients in Colorado with respect to epidemiologic factors.

METHODS: We included adults from a large health system in Colorado with MG between January 2019 and December 2021. Exploration of the dataset was performed to evaluate associations between demographic factors, common comorbid conditions, and key outcomes and medications utilized.

RESULTS: The sample included 270 patients. 81.5% identified as Caucasian, 5.6% as African American, and 13.0% reported Hispanic ethnicity. 40.4% of patients had hypertension, 24.4% had diabetes, 15.6% had obesity, 15.2% had depression/anxiety. Higher rates of infused medications were seen in Medicaid patients (RR=1.55, p=0.02) and in patients with comorbidities. Diabetic patients had higher rates of rituximab use specifically (RR 3.27 p = 0.04). No differences were seen in outcomes or treatments for non-white or Hispanic patients. However, these populations were significantly younger and more likely to be on Medicaid. Patients with Medicaid (11.1%) had more MG-related hospitalization (40.0% vs 21.7% p = 0.03). Hypertension was associated with increased risk of MG-related hospitalization (RR=1.83 p =0.02).

SUMMARY/CONCLUSION: We highlight higher use of infusion therapies in patients with common comorbidities and with Medicaid. Our findings suggest disparities in hospitalization rates and treatment preferences between Medicaid and non-Medicaid patients. Further research is needed to explore potential underlying causes of these disparities and to develop strategies to improve healthcare access and outcomes for all MG patients.

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THE EFFECT OF STATINS ON LIPID-LOWERING TREATMENT IN MYASTHENIA GRAVIS PATIENTS WITH HYPERLIPIDEMIA

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INTRODUCTION: The burden of multimorbidity can lead to administration of medications that may worsen myasthenia gravis (MG). Statins are frequently used for hyperlipidemia or secondary prevention in cardio-cerebral vascular disease. This is a prospective cohort study to observe the effect of statins on MG patients with hyperlipidemia.

OBJECTIVE: To evaluate the efficacy and safety of statin usage in MG patients with hyperlipidemia.

METHODS: MG patients with hyperlipidemia were recruited from May 2019 to May 2022, grouped as “statin group” and “no-statin group”. All included patients will receive regular follow-ups to evaluate the clinical symptoms and adverse events in at least 6 months. The primary outcome is the decrease of MG-ADL score. Decrease of blood lipids and statin-related adverse events were recorded.

RESULTS: Statin information was systemically obtained from 86 patients (45 in statin group and 41 in no-statin group) being treated. Patients in statin group had more comorbidities (hypertension, diabetes, cardiovascular diseases). There was no difference in change in MG-ADL scores between 2 groups. No new myalgic syndrome or worsening of MG developed in statin group. One patient developed skin rash and 1 patient develop elevated liver enzyme during statin treatment.

SUMMARY/CONCLUSION: There is no evidence of statin related worsening of MG in patients with hyperlipidemia. Statins are safe in MG patients while being used under close monitor.

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RESULTS OF THE MGNET ADAPTING DISEASE-SPECIFIC OUTCOME MEASURES PILOT TRIAL FOR TELEHEALTH IN MYASTHENIA GRAVIS (ADAPT-TELEMG)

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INTRODUCTION/OBJECTIVE: Validated myasthenia gravis (MG)-specific outcome measures performed remotely are an unmet need for patient care and clinical trial readiness. ADAPT-teleMG launched in response to the COVID-19 pandemic to develop MG-specific outcome measures for the telemedicine environment.

METHODS: Adults with stable MG performed 2 video visits within approximately 7 days. Scales were scored synchronously by site “observers” and offline by 2 independent raters (IRs) and, if needed, by a third rater for adjudication. Average of most concordant pair of raters was the “gold standard.” MG Composite Virtual (MGCv), MG-ADL, MG Core Exam, MG-QOL15r, MGFA Severity Class, global impression of disease, fatigue, and telehealth satisfaction scales were performed. Primary outcomes were intra-rater correlation and inter-rater reliability of MGCv. Adjudication threshold for MGCv was ≥3 points in IR's scores.

RESULTS: Fifty-two participants from 5 MGNet* sites were enrolled with 100% study completion. Participant baseline characteristics: median age 63.3 years, 50% female, 30.8% MGFA Severity Class I, 61.5%, Class II/III. Mean MGCv scores 7.89 (observer), 7.61 (gold standard). MGCv intra-rater correlation between observer and gold standard was high with R-squared=0.89, Pearson/Spearman=0.94/0.93 ($p<0.0001$), interclass correlation coefficient = 0.93. IR’s scoring “agreed” for 77/87 (88.5%) MGCv scales. 14/87 (16%) complete MGCvs required adjudication. 17/104 (16%) total MGCvs had ≥1 missing sub-score, mainly related to technology platform.

SUMMARY/CONCLUSION: MGCv exam had high inter-rater reliability and intra-rater correlation when performed virtually and the recorded video was interpreted offline by 2-3 raters. ADAPT-teleMG represents an important step in the development of remote MG-specific outcome measures. Secondary and exploratory outcomes data will be presented.

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Jeffrey Guptill - Employee of argenx

Michael Hehir - Consultant for Alexion, argenx, Janssen, UCB, and Immunovant

Katherine Ruzhansky - On advisory boards for Alexion, argenx, Immunovant, UCB/Ra; served as site PI for Alexion, argenx, UCB, Janssen; received grant funding from MGFA

IMMUNOGLOBULIN USE AMONG PROMISE-MG PATIENTS

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INTRODUCTION: International consensus guidance recommends short-term use of immunoglobulins in the treatment of myasthenia gravis (MG); however, there is clinical equipoise regarding the benefit of maintenance immunoglobulins, particularly their use to reduce steroid exposure.

OBJECTIVE: To determine if maintenance immunoglobulin use reduced the cumulative steroid dose among patients in the Prospective Multicenter Observational Cohort Study of Comparative Effectiveness of Disease-Modifying Treatments for Myasthenia Gravis (PROMISE-MG) study.

METHODS: “Maintenance” immunoglobulin was defined as more than 1 immunoglobulin course within a 6-week period. Descriptive statistics were used to compare outcomes in patients with generalized MG (GMG) receiving immunoglobulin with those receiving any non-immunoglobulin-based immunomodulatory (steroids with or without azathioprine, mycophenolate mofetil, tacrolimus or rituximab) drug (n=89).

RESULTS: Among the 17 patients receiving maintenance immunoglobulin, 16 had generalized GMG and 12 of these received oral corticosteroids along with a non-steroidal immunosuppressant drug. Of the 11 with GMG who received steroids and maintenance immunoglobulin, the mean cumulative prednisone dose was 14,018±6333 mg. Among patients receiving immunomodulatory drugs without immunoglobulins, 58 had GMG and received a cumulative steroid dose of 8,332±5540 mg prednisone.

SUMMARY/CONCLUSION: PROMISE-MG patients with generalized disease who received maintenance immunoglobulins received higher mean cumulative steroid doses, regardless of the concomitant non-steroidal immunomodulatory drug received. These results should be interpreted with caution due to the observational nature of the study and the small number of patients in each group. Further studies would be needed to clarify the role of maintenance immunoglobulins in steroid dose reduction in patients with MG.

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HOSPITALIZATIONS FOR MYASTHENIA GRAVIS EXACERBATION AND CRISIS IN THE PREDICT STUDY

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INTRODUCTION: A subset of patients with myasthenia gravis (MG) require hospitalization for MG exacerbation (ME) or crisis (MC). Clinical features of these patients and hospitalizations in a contemporary cohort are not well described.

OBJECTIVE: To describe the clinical characteristics of patients with ME/MC-related hospitalizations and to characterize these hospitalizations.

METHODS: Data was extracted by chart review for 30 randomly selected patients ≥18 years of age, who received care for generalized MG (gMG) for ≥1 year between 2010-2023 at an integrated health care system (Mass General Brigham) and were hospitalized for ME or MC.

RESULTS: Fifty-three ME/MC-related hospitalizations occurred. Fourteen patients had ≥2 hospitalizations. Fourteen MC-related hospitalizations were seen in 12 patients, and 39 ME-related hospitalizations in 22. Thirteen patients required intensive care. Median age at first hospitalization was 69.5 years (range 29-93) and 50% were female. Eighty-seven percent had AChR antibodies. Median time from generalized MG diagnosis to first hospitalization was 13.5 days (range 0-3557). In 3 patients, MG diagnosis was made during the first hospitalization. Outpatient therapies during the observed timeframe included corticosteroids (27 patients), pyridostigmine (≥29), azathioprine (≥19), mycophenolate mofetil (≥11), IVIg (≥16), PLEX (≥2), eculizumab (≥3), ravulizumab (≥2), and FcRn inhibitor (≥1). Rescue therapies included IVIg (26 patients), PLEX (9), eculizumab (1), and ravulizumab (1). The median duration of hospitalization was 8 days (range 1-38); 1 patient died.

SUMMARY/CONCLUSION: In a contemporary cohort of patients with ME/MC-related hospitalizations, MC occurred in 40%. Recurrent hospitalization was common, observed in 47% of patients. Analysis of a larger cohort from the PREDICT study will follow.

Disclosures:

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Shamik Bhattacharyya - Research funding from Alexion, UCB, NIH

SUBCUTANEOUS EFGARTIGIMOD PH20 TREATMENT IN PARTICIPANTS WITH GENERALIZED MYASTHENIA GRAVIS IN ADAPT-SC+: INTERIM ANALYSES ON QUALITY OF LIFE, EFFICACY, TOLERABILITY, AND LONG-TERM SAFETY

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INTRODUCTION: In ADAPT-SC, subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20) demonstrated noninferior total IgG reduction to efgartigimod IV, resulting in similar clinical improvement in participants with generalized myasthenia gravis (gMG). Participants completing ADAPT-SC, or enrolled in ADAPT+, could roll over into the ongoing open-label extension, ADAPT-SC+.

OBJECTIVE: Evaluate quality of life (QoL), efficacy, tolerability, and long-term safety of efgartigimod PH20 SC in participants with gMG in ADAPT-SC+.

METHODS: Efgartigimod PH20 SC 1000 mg was administered in cycles of 4 weekly injections. Subsequent cycles were initiated ≥4 weeks from the last dose based on clinical evaluation.

RESULTS: As of March 2022, 164 participants received ≥1 dose of efgartigimod PH20 SC. Most participants completed ≈3 cycles. Mean (SD) study duration was 170(59) days (72 patient-years). Mean (SE) MG-QoL15r scores (range 0-30, higher=worse QoL) improved from 13.7(0.52) at baseline to 8.8(0.50) at week 4 of cycle 1. Similarly, EQ-5D-5L VAS scores (range 0-100, higher=better QoL) improved from 59.3(1.46) to 73.0(1.35). QoL and total MG-ADL score improvements consistently occurred across multiple subsequent cycles. Speed of onset, magnitude, and repeatability of MG-ADL improvements were similar to efgartigimod IV in ADAPT/ADAPT+. The most frequent adverse events were injection site erythema (25.6%), headache (15.2%), and COVID-19 (11.6%). All injection site reactions (ISRs) were mild/moderate. Most ISRs resolved spontaneously, and incidence decreased with subsequent cycles.

SUMMARY/CONCLUSION: Treatment with efgartigimod PH20 SC improves QoL and function in participants with gMG. Safety and tolerability of efgartigimod PH20 SC was similar to efgartigimod IV, except mild/moderate ISRs, none of which led to treatment discontinuation.

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Fien Gistelinck - Employee of argenx BV

Sophie Steeland - Employee of argenx BV

Jan Noukens - Consultant for argenx BV

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Yuebing Li - Consultant for argenx BV, UCB Pharma, Alexion, Catalyst, and Immunovant

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HUMORAL IMMUNE RESPONSE TO POLYVALENT PNEUMOCOCCAL VACCINE IN HEALTHY PARTICIPANTS RECEIVING EFGARTIGIMOD

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INTRODUCTION: Efgartigimod, a human immunoglobulin G (IgG)1 antibody Fc-fragment, reduces IgG levels through neonatal Fc receptor (FcRn) blockade. Preliminary observational data suggest efgartigimod does not impair vaccine-induced T-cell-dependent antibody responses.

OBJECTIVE: To determine effect of efgartigimod on T-cell-independent humoral immune response to immunization with PNEUMOVAX 23 (23-valent polysaccharide pneumococcal vaccine).

METHODS: In this phase 1 open-label study, healthy adults were randomized 1:1:1 into 3 cohorts: EFG-1 (n=12), EFG-2 (n=12), and PBO (n=13). Four weekly infusions of efgartigimod (10 mg/kg IV) or placebo were administered with a 6-week follow-up. PNEUMOVAX 23 was either administered on Day 22 (EFG-1/PBO cohorts; before 4th infusion) or Day 36 (EFG-2 cohort; 2 weeks after 4th infusion). Pneumococcal capsular polysaccharide IgG titers were examined for all 23 serotypes before and 4 weeks after vaccine administration.

RESULTS: Ninety percent (EFG-1; n=9/10), 72.7% (EFG-2; n=8/11), and 75.0% (PBO; n=9/12) of participants completing the study had a ≥2-fold increase in antibody concentration for ≥70% of serotypes. Proportions of participants with antibody titers >1.3 mg/L (protective level) for ≥70% of serotypes were: 90.0% (EFG-1; n=9/10), 54.5% (EFG-2; n=6/11), 83.3% (PBO; n=10/12). Considerable variability was observed across participants and serotypes. No serious/severe adverse events occurred.

SUMMARY/CONCLUSION: Most participants exhibited good post-vaccination pneumococcal responses with little difference between cohorts, suggesting efgartigimod does not interfere with vaccine-induced, T-cell-independent humoral immunity in healthy participants. There were no observed differences between administering vaccines during the cycle (EFG-1) as compared to PBO. Vaccine response in efgartigimod-treated patients will continue to be an important area of study.

Disclosures:

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John W. Sleasman - Receives research and salary support from the National Institutes of Health, Cellective Inc., Enzyvant Therpeutics GmbH, and the Jeffrey Modell Foundation and is a consultant for argenx BV

Fien M. Verhamme - Employee of argenx BV

Kevin Winthrop - Received research support from BMS and Pfizer; received consulting honoraria from Pfizer, AbbVie, UCB, Eli Lilly & Company, Galapagos, GSK, Roche, Gilead, Bristol Myers Squibb (BMS), Regeneron, Sanofi, AstraZeneca, and Novartis

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EFGARTIGIMOD INFUSION IN TREATING A PATIENT WITH MYASTHENIC CRISIS

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INTRODUCTION: Myasthenic crisis in refractory cases can be challenging to manage. Other than plasmapheresis, IVIg, and supportive therapy, treatment options remain limited (Sanders, Neurology, 2016; Narayanaswami, Neurology, 2021). The status of crisis is often excluded in clinical trial design including recent trials testing targeted therapies (Howard et al., Lancet Neurology, 2017, 2021). Here we report the use of efgartigimod in a case of myasthenic crisis requiring intubation.

CASE DESCRIPTION: A 48-year-old woman has a longstanding history of acetylcholine receptor (AChR) antibody positive generalized myasthenia gravis (MG). Chronic maintenance therapeutic regimen included weekly plasmapheresis, prednisone 20 mg daily, azathioprine 150 mg daily, and pyridostigmine. Six months prior to the presentation, azathioprine was discontinued due to bone marrow toxicity, and 1 dose of rituximab was given instead. At the time of this presentation, she was in myasthenic crisis and was intubated for respiratory failure. Prednisone was increased to 40 mg daily and plasmapheresis was started for crisis. Her course was complicated by fungemia and pulmonary embolism which were treated medically. Eight sessions of plasmapheresis lead to transient improvement but failed extubation. Efgartigimod was initiated following plasmapheresis and she was extubated 2 days later. By completing the 4 weekly infusions, she was discharged home. She continued with efgartigimod cycles and reported continued improvement. Her prednisone was tapered to previous chronic regimen of 20 mg daily and she has remained at previous baseline.

DISCUSSION: In this case, efgartigimod was used in refractory myasthenic crisis. It likely contributed to sustained improvement from the crisis, and discontinuation of chronic weekly plasmapheresis.

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Yuebing Li - Received grant support from argenx; served as a consultant for Advisory Board Meeting by argenx, Catalyst, Immunovant, and UCB Pharma

EFFECT OF APPLYING INCLUSION AND EXCLUSION CRITERIA OF PHASE III TRIALS TO MYASTHENIA GRAVIS PATIENTS IN ROUTINE CLINICAL CARE

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INTRODUCTION: Recent and ongoing phase 3 MG clinical trials use strict inclusion and exclusion criteria. This leads to difficulty in recruiting patients to clinical trials and also potentially limits the generalizability of these results to a heterogenous clinic population.

OBJECTIVE: To evaluate the percentage of MG patients receiving routine clinical care who meet clinical trial eligibility criteria and the main reasons for failure to meet study criteria.

METHODS: We conducted a retrospective study of AChR+ve gMG patients with documented Myasthenia Gravis Activities of Daily Living (MG-ADL) scores, seen in our clinic from January-June 2021. Clinical data including MG history, concomitant treatment(s) and MG-ADL score from both new and follow up visits through June 2023 were analyzed to determine the eligibility of patients into the clinical trials.

RESULTS: We identified 67 AChR+ve MG patients during the study period who had a total of 330 visits between January 2021-June 2023. Sixty out 67 (89.5%) patients at 315 out of 330 (95%) clinic visits did not meet inclusion criteria for the clinical trial participation. The most common reason for not meeting criteria was MG-ADL<5 at 77.5% of visits. In the subgroup of symptomatic patients with MG-ADL>5, the most common reasons for not meeting criteria were complement inhibitor use, IVIg use within the last 4 weeks, and recent medication changes.

SUMMARY/CONCLUSION: Majority of AChR+ gMG patients treated in routine care did not meet clinical trials criteria for phase 3 trials. Broader inclusion criteria would increase eligibility and study results are more likely generalizable to all patient population.

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Neelam Goyal - Served on advisory board meetings for argenx, Alexion, and UCB Pharma

Srikanth Muppidi - Served on advisory board meeting for argenx, Alexion/Astra Zaneca, ra/UCB, and Horizon Pharma


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