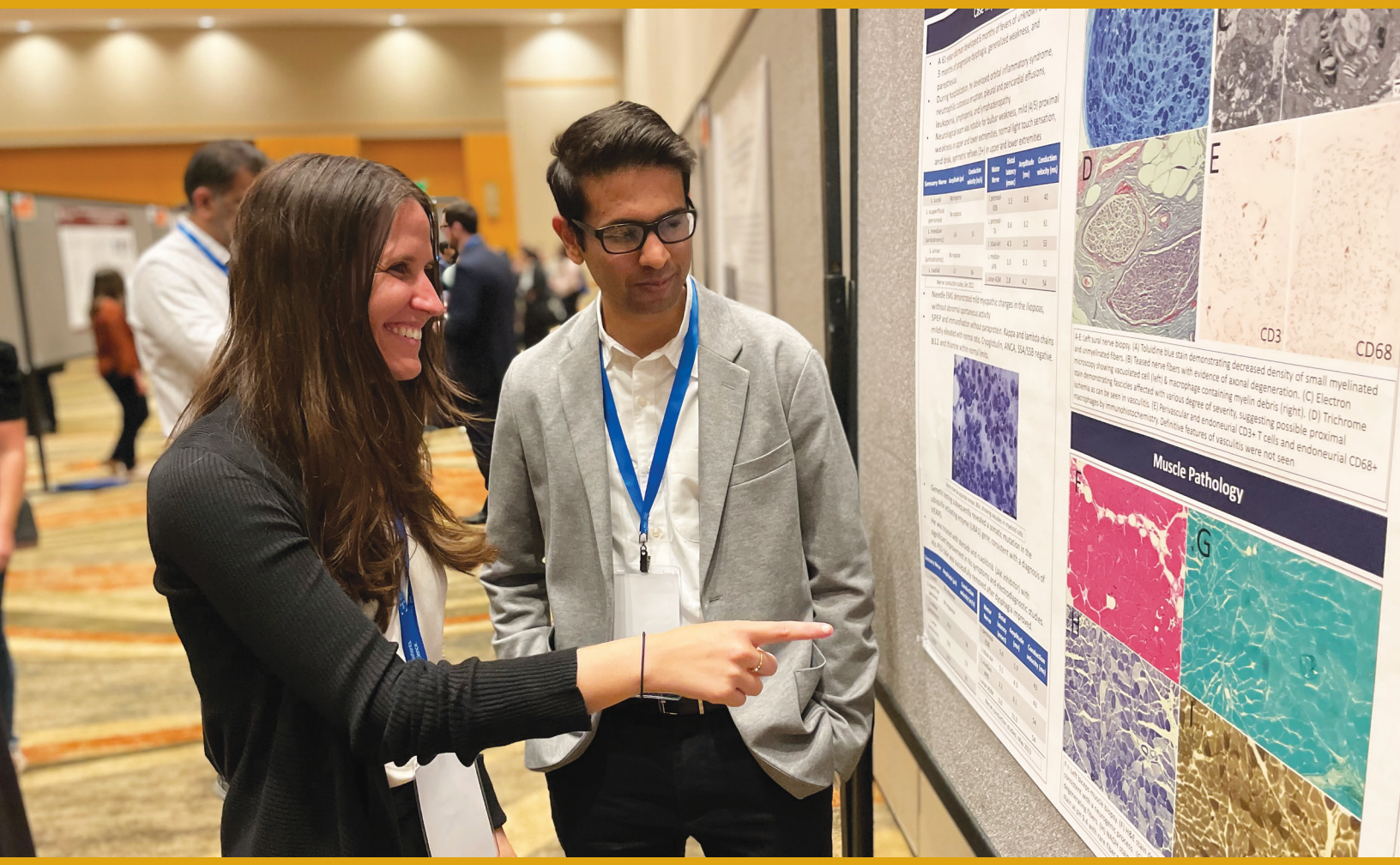
AANEM

ABSTRACT GUIDE



2024 AANEM Annual Meeting

2024 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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ISCHEMIC INJURY AND MICROVASCULITIS IN TREATMENT INDUCED NEUROPATHY OF DIABETES AND TREATMENT INDUCED DIABETIC LUMBOSACRAL RADICULOPLEXUS NEUROPATHY

Hebatallah Rashed (Cairo, Egypt), Kamal Shouman (Rochester, MN), Marcus Vinicius Pinto (Rochester, MN), Catarina Aragon Pinto (Rochester, MN), Peter Dyck (Rochester, MN), JaNean Engelstad (Rochester, MN), Catherine Daley (Chicago, IL), Christopher Klein (Rochester, MN), Kudva Yogish (Rochester, MN), P. James Dyck (Rochester, MN)

INTRODUCTION: Treatment induced neuropathy of diabetes (TIND) is painful, autonomic, subacute neuropathy after rapid hyperglycemia correction; pathophysiology is unclear. Diabetic lumbosacral radiculoplexus neuropathy (DLRPN) is painful, subacute neuropathy due to ischemic injury and microvasculitis.

OBJECTIVE: Because both can be induced by rapid glycemic correction, we postulate similar pathophysiology.

METHODS: We identified TIND, and treatment induced DLRPN (TI-DLRPN) patients with nerve biopsy. Clinical and pathological characteristics were compared.

RESULTS: Eight TIND and 25 TI-DLRPN patients. TIND were all males, median age 57.5 years (42-70), TI-DLRPN were male (12/25), median age 56 (35-73). Biopsies showed perivascular inflammatory collections (8/8 TIND and 25/25 TI-DLRPN, p=1), with similar inflammatory collection sizes (large 3/8 TIND vs 12/25 TI-DLRPN, p=0.6; moderate 3/8 vs 5/25, p=0.3; and small 2/8 vs 8/25, p= 1). Diagnostic microvasculitis occurred in 2/8 TIND and 7/25 TI-DLRPN biopsies (p=0.8), while suggestive of microvasculitis in 3/8 vs 10/25 (p=0.8). Ischemic injury was commonly seen (7/8 vs 24/25; p=0.4): multifocal fiber loss (5/8 vs 16/25; p=0.9), neovascularization (5/8 vs 16/25; p=0.9), injury neuroma (2/8 vs 11/25; p=0.3) and perineurial thickening (3/8 vs 18/25; p=0.07). Teased fibers showed increased axonal degeneration in 6/8 TIND and 23/25 TI-DLRPN; p=0.2 (TIND, 5.9%, 2.9-60% and TI-DLRPN, 16.7%, 1.6-74.7%; p=0.4) and increased segmental demyelination in 5/8 TIND vs 21/25 TI-DLRPN; p=0.2 (TIND, 4.15%, 0-16.2% and TI-DLRPN, 8.6%, 0-34.5%; p=0.007).

SUMMARY/CONCLUSION: We find evidence of ischemic injury and microvasculitis in TIND and TI-DLRPN. We postulate that rapid hyperglycemia correction triggers an immune attack on nerves which presents as either TIND or TI-DLRPN.

Hebatallah Rashed, MD, PhD

Golseth Young Investigator Award Recipient

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PROFILING GRANZYMES IN ACUTE INFLAMMATORY DEMYELINATING POLYNEUROPATHY

Derek Wu (Vancouver, Canada), Michael Lane (Vancouver, Canada), Hongyan Zhao (Vancouver, Canada), Karen Jung (Vancouver, Canada), Kristine Chapman (Vancouver, Canada), Michelle Mezei (Vancouver, Canada), Kristin Jack (London, Canada), Mike Berger (Victoria, Canada), Katherine Beadon (Vancouver, Canada), David Granville (Vancouver, Canada)

INTRODUCTION: Granzymes (GZMs) are a family of serine proteases implicated in several processes, including pro-inflammatory cytokine release, cell death, extracellular matrix degradation, cell junction disruption, epithelial barrier dysfunction, and/or autoantigen generation, making them prime targets in drug development for inflammatory diseases. Acute inflammatory demyelinating polyneuropathy (AIDP) is an immune-mediated neuropathy with an incompletely understood pathogenesis and lacks targeted treatment. This study investigated whether GZMs are present in the cerebrospinal fluid (CSF) of individuals with AIDP, which could implicate them in the pathophysiology of this condition.

OBJECTIVE: To profile the GZM levels in AIDP and determine their relationship with clinical markers of disease severity.

METHODS: CSF samples (AIDP n=13; Control n=9) were analyzed using enzyme-linked immunosorbent assays for GZMs A, B, H, K, and M. AIDP participants had confirmed diagnoses via clinical, electrodiagnostic, and CSF findings. Control CSF samples were obtained from a spinal cord injury biobank.

RESULTS: CSF GZMA is notably diminished by -61.0% ($p<0.01$), while CSF GZMs B and M are non-significantly elevated by +1030% ($p>0.05$) and +83.8% ($p>0.05$), respectively, in AIDP, relative to control samples. Additionally, CSF protein levels in AIDP patients share a positive correlation with their GZMM levels ($rs=0.79$, $p<0.01$) and GZMB levels ($rs=0.545$, $p>0.05$).

SUMMARY/CONCLUSION: Abnormal CSF GZM levels in AIDP suggest that specific GZMs are involved in AIDP pathology—decreased GZMA may indicate dysfunction in immunoregulation, while increased GZMs B and M could imply extracellular proteolysis in pathogenesis. Moreover, correlations between GZMs and CSF protein levels further support the role of GZMs in disease and/or as possible biomarkers in AIDP.

Derek Wu, BS

Best Abstract Award Recipient

Disclosures:

David Granville - serves as a co-Founder and Chief Scientific Officer of viDA Therapeutics.

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NEUROLOGIC CLINICAL, ELECTROPHYSIOLOGIC, AND PATHOLOGIC CHARACTERISTICS OF PRIMARY VERSUS SECONDARY NEUROLYMPHOMATOSIS

Michael Skolka (Rochester, MN), Narupat Suanprasert (Bangkok, Thailand), Jennifer Martinez-Thompson (Rochester, MN), Rebecca King (Rochester, MN), William Macon (Rochester, MN), Michelle Mauermann (Rochester, MN), Christopher Klein (Rochester, MN), Thomas Habermann (Rochester, MN), Patrick Johnston (Rochester, MN), Ivana Micallef (Rochester, MN), Kimberly Amrami (Rochester, MN), Robert Spinner (Rochester, MN), Jayawant Mandrekar (Rochester, MN), Peter Dyck (Rochester, MN), P. James Dyck (Rochester, MN)

INTRODUCTION: Neurolymphomatosis (NL) is characterized by lymphomatous infiltration of peripheral nerves presenting as the initial manifestation of lymphoma (primary NL, PNL) or in relapse of a known lymphoma (secondary NL, SNL).

OBJECTIVE: To detail and compare the neurologic clinicopathologic characteristics of PNL and SNL.
This retrospective study comprises patients with pathologically confirmed NL in nerve between January 1992 - June 2020. Patient clinical characteristics, exam, imaging studies, EMG, and nerve biopsy data were analyzed.

MEHODS: Fifty-eight patients were identified (34 PNL, 24 SNL). Time from neurologic symptom onset to diagnosis was longer in PNL at 18.5 months versus 5.5 months in SNL (p=0.01). Neurologic symptoms were similar in both groups and included primarily sensory loss (98%), pain (76%), and asymmetric weakness (76%). A wide spectrum of EMG confirmed neuropathy patterns were observed, but SNL patients had increased mononeuropathies (n=8) versus PNL (n=1, p=0.01). MRI studies detected NL more (86%) compared to FDG-PET/CT (60%) (p=0.007).

RESULTS: Nerve biopsies revealed predominantly B-cell lymphoma in PNL (n=32) and SNL (n=22) with increased demyelination in both groups and increased axonal degeneration (p=0.02) and multifocal fiber loss (p=0.04) greater in SNL versus PNL. SNL has a worse prognosis (p=0.025).

SUMMARY/CONCLUSION: While PNL and SNL are primarily painful and asymmetric neuropathies with axonal and demyelinating features and are better detected on MRI, SNL may have a distinct profile of fulminant mononeuropathies with increased axonal damage and multifocal fiber loss on nerve biopsy resulting in worse prognosis. Peripheral nerve serves as a safe haven for NL cells.

Michael Skolka, MD

Best Abstract Runner Up Award Recipient

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CUTANEOUS SILENT PERIOD IN A PATIENT WITH WARM COMPLEX REGIONAL PAIN SYNDROME

Isvan Alvarez Herrera (Ridgeland, MS), A. Arturo Leis (Jackson, MS)

INTRODUCTION/BACKGROUND: Complex regional pain syndrome (CRPS) is a persistent condition, usually triggered by injury, with sensory, autonomic, motor, and trophic symptoms. Pathological studies on the affected region have shown degeneration of small nerve fibers. The cutaneous silent period (CSP), a reflex inhibition of EMG activity after nociceptive electrical stimulation, mediated by Aδ fibers, have not been used in the assessment of possible nerve injuries in these patients.

CASE REPORT: A 55-year-old right-handed, otherwise healthy woman, was referred for evaluation of left hand CRPS, warm subtype, which started after a thumb carpo-metacarpal arthroplasty 3 months prior. Examination revealed hyperalgesia, allodynia, forearm, and hand disuse wasting, dystrophic skin changes, increased temperature, sweating and pilosity, and reduced active and passive mobility of digits and wrist. Median and ulnar bilateral sensory and motor NCS, and needle EMG of hand and forearm muscles, showed no abnormalities. A CSP protocol of four trials of middle finger electrical stimulation at 21mA and 60mA intensities (7 and 20 times the sensory threshold of affected hand), recording the surface EMG activity from thenar eminence, was followed bilaterally. The CSP was defined on the resultant rectified and averaged signal by an 80% drop on pre-stimulation activity, onset (latency) and termination marked, and duration calculated. At 60mA stimulation intensity, CSP latency and duration were similar bilaterally (Left latency=78ms, duration=48ms; Right latency=83ms, duration=43ms). At 21mA intensity, CSP was more robust on the affected side (Left latency=107ms, duration=27ms; Right latency=131ms, duration=17ms).

SUMMARY/CONCLUSION: CSP can provide important information about the functioning of Aδ fibers in CRPS patients.

Isvan Alvarez Herrera, CNCT

Technologist Member Recognition Award Recipient

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EARLY NERVE CONDUCTION FINDINGS PREDICT TREATMENT OUTCOMES IN CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY

Thapat Wannarong (Rochester, MN), Michael Skolka (Rochester, MN), Grace Swart (Rochester, MN), Natthapon Rattanathamsakul (Rochester, MN), P. James Dyck (Rochester, MN), Sarah Berini (Northfield, MN), Divyanshu Dubey (Rochester, MN), Kamal Shouman (Rochester, MN), Marcus Vinicius Pinto (Rochester, MN), Michelle Mauermann (Rochester, MN), Anthony Windebank (Rochester, MN), Nathan Staff (Rochester, MN), Christopher Klein (Rochester, MN)

INTRODUCTION: NCS aids chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) diagnosis but their role in therapy monitoring is less utilized in clinical practice.

OBJECTIVE: To study whether the early changes in NCS variables can predict treatment outcomes.

METHODS: Utilizing 2021 European Academy of Neurology/Peripheral Nerve Society criteria, newly diagnosed CIDP patients were identified. Changes in NCS from baseline to first follow-up were compared with neuropathy impairment scores (NIS) changes and treatment response groups (responders versus non-responders).

RESULTS: Of 39 identified patients (61.5% male, mean age 52.2 years, total follow-up median 39.5 months, time to first follow-up median 4.9 months), all received at least one first-line treatment, predominantly intravenous immunoglobulin (36/39). NIS changes identified 26 responders (reduced NIS) and 13 nonresponders (worsened/stable NIS). Median baseline NIS changes for responders versus nonresponders were -28.0 versus 4.0 ($p<0.001$) and -34.5 versus 12.0 ($p<0.001$) at first and last follow-up, respectively. Responders showed significant improvements in the amplitudes of ulnar coumpound muscle action potentials (CMAPs) (1.0mV versus -0.4mV, $p=0.036$), fibular CMAPs (0.3mV versus -0.3mV, $p=0.003$), summated CMAPs (1.7mV versus -1.5mV, $p=0.003$), and fibular conduction velocity (3m/s versus -1m/s, $p=0.034$). Only fibular CMAP amplitude changes negatively correlated with NIS changes throughout the entire follow-up (6 to ≥60 months, R -0.6 to -0.8, $p\leq0.003$). Three patients showed no fibular response at baseline and follow-up despite improved NIS, but all had ulnar and summated CMAP responses.

SUMMARY/CONCLUSION: Early NCS changes can predict clinical outcomes in CIDP, distinguishing responders from nonresponders initially and long-term. Small fibular CMAP improvements often accompany dramatic NIS improvements. Ulnar and summated CMAP improvements are viable secondary indicators when fibular response is absent.

Thapat Wannarong, MD

President's Research Initiative Award Recipient

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MYO-GUIDE MODEL: AUTOMATING NEUROMUSCULAR DISEASE DIAGNOSIS WITH MRI AND ARTIFICIAL INTELLIGENCE

Goknur Selen Kocak (Newcastle upon Tyne, United Kingdom), Jose Verdu-Diaz (Newcastle upon Tyne, United Kingdom), Carla Bolano-Diaz (Newcastle upon Tyne, United Kingdom), Alejandro Gonzalez Chamorro (Newcastle upon Tyne, United Kingdom), Sam Fitzsimmons (Newcastle upon Tyne, United Kingdom), Chiara Marini Bettolo (Newcastle, United Kingdom), Michela Guglieri (Newcastle, United Kingdom), Giorgio Tasca (Newcastle upon Tyne, United Kingdom), Volker Straub (Newcastle upon Tyne, United Kingdom), Jaume Bacardit (Newcastle upon Tyne, United Kingdom), Jordi Díaz-Manera (Newcastle upon Tyne, United Kingdom)

INTRODUCTION: Muscle MRI is a valuable tool for assessing muscle structure and identifying characteristic patterns of muscle involvement in various neuromuscular diseases (NMDs). These patterns, involving fat replacement and changes in water content within muscle groups, are complex and often overlap, posing challenges for accurate diagnosis.

OBJECTIVE: This issue prompted the development of Myo-Guide, an artificial intelligence (AI)-driven methodology designed to automate the diagnosis of NMDs through the analysis of muscle MRI data.

METHODS: Our dataset comprises 3462 muscle fat scores from 43 different NMDs, collected through extensive international collaboration involving 27 sites across 20 countries. Based on data availability, we focused on a subset of 21 NMDs and evaluated muscle fat using the 5-point Mercuri scale. We trained a decision tree-based classification model incorporating muscle fat scores, patient age, and sex as variables.

RESULTS: We attained a mean balanced accuracy of 65.125% ± 2.194% and a mean top-three accuracy of 88.645% ± 1.191%.

SUMMARY/CONCLUSION: We deployed The Myo-Guide model in a user-friendly web application, simplifying the input of muscle fat scores for diagnosis. This project demonstrates the effectiveness of machine learning in automating NMD diagnosis and underscores the significance of international collaboration in data collection. Furthermore, it showcases the translation of research findings into practical applications through the deployment of machine learning models as web tools, facilitating their integration into clinical practice.

Goknur Selen Kocak, MD

President's Research Initiative Award Recipient

Disclosures:

Goknur Selen Kocak - The Myo-Guide project received grants from Muscular Dystrophy UK and The French Muscular Dystrophy Association (AFM-Téléthon). I do not have any financial interests or relationships to disclose.

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PLASMA EXOSOMES AS A POTENTIAL BIOMARKER FOR DIABETIC PERIPHERAL NEUROPATHY

Anza Memon (Detroit, MI), Lei Wang (Detroit, MI), Xuerong Lu (Detroit, MI), Michael Chopp (Detroit, MI), Zheng Gang Zhang (Detroit, MI), Xian Shuang Liu (Detroit, MI)

INTRODUCTION: Diabetic peripheral neuropathy (DPN) is one of the most common complications of diabetes. Although the NCS is the gold standard for DPN diagnosis, there is no blood biomarker for DPN. Exosomes(~50-200nm) vesicles that contain molecular cargo, including microRNAs(miRNAs), DNA, lipids, and proteins, show high potential as diagnostic biomarkers for various diseases.

OBJECTIVE: This study investigates the miRNA expression in plasma-derived exosomes from type 2 diabetes(T2D) patients with and without DPN as a potential biomarker for diagnosis of T2D-DPN.

METHODS: In this pilot translational biomarker study, plasma samples from T2D patients-with DPN, T2D -without DPN, and non-diabetic non-neuropathy(n=3/group) cohorts were collected. Plasma-derived exosomes were isolated using differential ultracentrifugation. Nanosight (NTA) and Western blot were used to determine exosome size distribution and markers, respectively. Twelve selected miRNA candidates reported or predicted to be correlated with diabetes were measured using real-time RT-PCR

RESULTS: NTA revealed that the number and size of plasma exosomes were 6.25x108/particles/ml with a mean size of 176.8±20.6 nm from DPN patients. Western blot analysis validated exosome marker proteins, including Alix, CD9, CD63, and CD81, in plasma-derived exosomes, but not Calnexin, negative control for exosome markers. Using RT-PCR, we demonstrated that compared to healthy subjects, expression of miR-21, miR-23a, miR-29a, and miR-451 was significantly increased in plasma-derived exosomes from T2D patients without DPN($p<0.05$). Notably, miR-29a and miR-206 were significantly increased in plasma-derived exosomes from DPN-T2D patients compared to T2D patients-without DPN($p<0.05$).

SUMMARY/CONCLUSION: These findings highlight the potential of plasma-derived exosome miRNAs as promising diagnostic markers for diabetes and its complication-DPN.

Anza Memon, MD

President's Research Initiative Award Recipient

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ACTIVITY AND MANUFACTURING OF KYV-101 ANTI-CD19 CHIMERIC ANTIGEN RECEPTOR T CELLS DERIVED FROM PATIENTS WITH NEUROLOGICAL AUTOIMMUNE DISEASES

Soo Park (Emeryville, CA), Simone N. Sandoval (Emeryville, CA), Jazmin Diana Bravo (Emeryville, CA), Hee Jin Kim (Emeryville, CA), Joseph K. Cheng (Emeryville, CA), Ranjita Sengupta (Emeryville, CA), Karen Walker (Emeryville, CA), Tom Van Blarcom (Emeryville, CA)

INTRODUCTION: B-cell targeting therapies demonstrate potential in neurological autoimmune diseases, but unmet needs remain, including treatment-free remission. KYV-101, a first-in-class, fully human autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, demonstrated promising early clinical results in myasthenia gravis (MG). KYV-101 has the potential to elicit B-cell depletion and immune reset with a single infusion.

OBJECTIVE: To investigate the activity and manufacturing of KYV-101 from patients with neurologic autoimmune diseases.

METHODS: Autologous T cells were collected and enriched from multiple sclerosis (MS) or MG patients. KYV-101 was generated by transducing T cells with a lentiviral vector encoding a fully human anti-CD19 CAR. Preclinical KYV-101 functional potency was assayed (cytokine release; cytotoxicity) in co-cultures with patient-derived CD19+ B cells, CD19+, or CD19– control cells. Manufacturing expansion and functional potency from a clinical cohort of KYV-101 treated patients were also assessed.

RESULTS: In preclinical assays, KYV-101 from MS patients induced greater dose-dependent cytotoxicity and IFN-gamma increases against CD19+ cells versus untransduced T cells, and negligible responses following co-culture with CD19– cells.

In the clinical cohort, KYV-101 manufactured from MS (n=2) and MG (n=6) patients displayed CD19-specific functional activity. Fold expansion ranges for KYV-101 from MS and MG patients were 32–61× and 15–50× (Day 8; pre-harvest), respectively, similar to previously observed expansion from non-neurologic autoimmune diseases.

SUMMARY/CONCLUSION: KYV-101 from neurologic autoimmune diseases shows activity specific for CD19+ cells. Manufacturing showed successful and consistent expansion across diseases. These data support further clinical investigation of KYV-101 as a novel therapy for neurologic autoimmune diseases.

Disclosures:

Soo Park - is an employee of Kyverna Therapeutics, Inc.

Simone N. Sandoval - is an employee of Kyverna Therapeutics, Inc.

Jazmin Diana Bravo - is an employee of Kyverna Therapeutics, Inc.

Hee Jin Kim - is an employee of Kyverna Therapeutics, Inc.

Joseph K. Cheng - is an employee of Kyverna Therapeutics, Inc.

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Karen Walker - is an employee of Kyverna Therapeutics, Inc.

Tom Van Blarcom - is an employee of Kyverna Therapeutics, Inc.

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EARLY GASTROSTOMY VERSUS LATE GASTROSTOMY TUBE PERFORMED IN ALS PATIENTS ADMITTED WITH ASPIRATION PNEUMONIA IN THE UNITED STATES

Baljinder Singh (New York, NY), Elina Zakin (New York, NY)

INTRODUCTION: Aspiration pneumonia is one of the common complications in patients with progressive ALS. We performed analysis to evaluate the clinical outcome as well as in-hospital complications with early (<7 days) and late (>7 days) gastrostomy tube placement among patients with ALS.

OBJECTIVE: To determine the rate and pattern of utilization and associated in-hospital outcomes of gastrostomy tube placement among patients with ALS.

METHODS: We obtained data for patients admitted to hospitals in the United States from 2017 to 2019 with a primary diagnosis of aspiration pneumonia in ALS patients using a large national database.

RESULTS: A total of 934 patients underwent gastrostomy tube out of which 548 (58.7%) had early gastrostomy and 386 (41.3%) had late gastrostomy tube. The racial differences in white, black, Hispanics, and others in early versus late gastrostomy tubes were: (73.9% vs. 63.5%, p<0.001), (8.5% versus 16.6% p< 0.100), (8.2% vs. 11.9%, p>0.05), (9.5% vs 8.03% p>0.05) respectively. Patients who underwent late gastrostomy tubes had more in-hospital complications: Sepsis and deep vein thrombosis (p<0.05). Teaching hospitals performed early gastrostomy 1.4 times more than non-teaching hospitals (p<0.001). Length of stay during hospitalization was significantly lower in the early gastrostomy tube group in comparison to the late gastrostomy tube (3.7% vs. 16.4%, p<0.01).

SUMMARY/CONCLUSION: Conclusion: The length of stay hence the cost of hospitalization is less in ALS patients who were admitted with aspiration pneumonia and were offered an early gastrostomy tube. More patients were discharged to home and assisted living facilities after early gastrostomy.

Baljinder Singh, MD

Resident and Fellow Member Award Recipient

President's Research Initiative Award Recipient

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ASSESSMENT OF THE EFFECTIVENESS OF TRANSCUTANEOUS VAGUS NERVE STIMULATION ON NEUROPATHIC PAIN IN KNEE OSTEOARTHRITIS PATIENTS

Gehad Elsehrawy (Ismailia, Egypt), Maha Ibrahim (Ismailia, Egypt), Nermeen A.moneim (Ismailia, Egypt), Mohamed Hefny (Ismailia, Egypt), Nashwa Elshaarawy (Ismailia, Egypt)

INTRODUCTION: Transcutaneous vagus nerve stimulation (tVNS) has been shown in recent human and animal studies to have strong analgesic effects in addition to its anti-inflammatory properties. Osteoarthritis (OA), headaches, fibromyalgia, and other chronic pain disorders may all benefit from inhibition of spinal nociceptive reflexes through vagal afferents. Furthermore, data suggests that osteoarthritis pain originates from sensitization of the peripheral and central neural systems.

OBJECTIVE: Taking this into account, our goal was to evaluate the effectiveness of tVNS on neuropathic pain in knee OA.

METHODS: The afferents of the vagus nerve's auricular branch were stimulated using a tVNS device. For a duration of 12 weeks, stimulation was administered to both groups once a day for 30 minutes, 3 days a week. The active and sham groups, comprising 34 patients each, were randomly allocated to a total of 68 patients suffering from chronic knee OA.

RESULTS: Compared to baseline, the immediate post-intervention PainDETECT (PD-Q) score was significantly improved in both the active (P <0.001) and sham groups (P =0.006). Additionally, this improvement was maintained until 4 weeks post-intervention in the active tVNS (P <0.001) but not in the sham tVNS (P =0.102). The immediate post-intervention Douleur Neuropathique 4 (DN4) score was significantly reduced compared to the baseline in active tVNS (P <0.001). Moreover, this reduction was maintained until 4 weeks post-intervention. However, in the sham tVNS, there was no significant difference in the DN4 score during the study period (P =1.000).

SUMMARY/CONCLUSION: This data points to the beneficial role of tVNS in treating neuropathic pain of OA.

Gehad Elsehrawy, PhD

President's Research Initiative Award Recipient

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REMOTE MONITORING OF MYASTHENIA GRAVIS USING WEARABLE SENSORS AND DIGITAL ASSESSMENTS

Amanda Guidon (Boston, MA), Ana Enriquez (Newton, MA), Ram Kinker Mishra (Newton, MA), Adonay Sastre (Newton, MA), Carina Stafstrom (Boston, MA), Petra Duda (Cambridge, MA), Ashkan Vaziri (Newton, MA)

INTRODUCTION: Myasthenia gravis (MG) causes fluctuating weakness which can impair activities of daily living (ADLs), vision, speech, mobility, and breathing. Remote monitoring technologies could overcome limitations of current outcome measures by assessing more disease domains with greater precision and reliability.

OBJECTIVES: 1) To describe the digital health platform we developed for MG which consists of a tablet application for gathering electronic patient-reported outcomes (ePROs), speech recordings and facial videos, paired with 1-week physical activity data via a wearable sensor (PAMSys,™ BioSensics). 2) To report study results from 20 adult participants with generalized MG.

METHODS: Physical activity parameters (e.g step counts, cadence, bouts of walking, steps per bout), and postural transitions are extracted from sensor data. Primary outcome is correlation of sensor-based measures to total score and sub-scores of the Quantitative MG, MG Composite, MG Quality of Life 15 Revised (QOL15r), MG Activities of Daily Living (MGADL) and Neuro-QOL Fatigue scales using linear regression (Spearman's coefficient). A pipeline for analyzing speech and video data has been developed. Participants are interviewed to determine perceived ease of use and utility based on the technology acceptance model (TAM) questionnaire.

RESULTS: Preliminary results from five participants (mean age 57.2 ± 11.4 years) show that median steps per walking bout are highly correlated with disease severity based on MG specific scale total scores (0.60 to 0.80). Participants without dysarthria demonstrated 81.9% higher speech clarity than patients with severe dysarthria on the MGADL.

SUMMARY/CONCLUSION: Preliminary results demonstrate feasibility of this platform for remote monitoring in MG. Enrollment is ongoing and full cohort data will be presented.

Amanda Guidon, MD, MPH

President's Research Initiative Award Recipient

Disclosures:

Amanda Guidon - consulting and/or Medical Advisory Board: Argenx, Alexion/Janseen, Ra Pharma/UCB Publishing Royalties: Oakstone Publications Other research funding support: MG Net Rare Disease Network MG Net Scholar Award, NIH Rare Disease Clinical and Research Training Program, Project Data Sphere, Dysimmune Disease Foundation, NINDS with Biosensics: 1R44NS122672-01A1

Ana Enriquez - is an employee of Biosensics.

Ram Kinker Mishra - is an employee of Biosensics.

Adonay Sastre - is an employee of Biosensics.

Petra Duda - is an employee of UCB.

Ashkan Vaziri - is an employee of Biosensics.

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UTILIZING ARTIFICIAL INTELLIGENCE TO DIFFERENTIATE NEUROGENIC AND MYOGENIC CHANGES IN ULTRASOUND IMAGING

Abdullah Al Qahtani (Bethesda, MD), Simon Liu (Bethesda, MD), Dat Duong (Bethesda, MD), Amna Othman (Bethesda, MD), Rebekah Waikel (Bethesda, MD), Caroline Donahue (Bethesda, MD), Angela Kokkinis (Bethesda, MD), Katharine Alter (University Park, MD), Ben Solomon (Bethesda, MD), Christopher Grunseich (Bethesda, MD)

INTRODUCTION: Differentiating between neurogenic and myogenic changes is instrumental in the field of neuromuscular medicine. This distinction is characterized on clinical exams, EDX, and biopsies. Over the past few years, the use of ultrasound has been expanding. Artificial Intelligence (AI) is revolutionizing the field of imaging analysis. Utilizing advanced algorithms and deep learning (DL) techniques to identify complex and subtle patterns holds promise to provide standardized and efficient means for patterns recognition on imaging

OBJECTIVE: To develop and test a model capable of differentiating neurogenic and myogenic changes in muscle ultrasound

METHODS: Two investigators independently labeled neuromuscular ultrasound images from patients and healthy controls enrolled under a natural history study of spinal and bulbar muscular atrophy (NCT04944940). They first categorized the images as normal or abnormal. If abnormal, the changes were then categorized as neurogenic or myogenic. Only images with an interrater agreement from 1 to 0.8 were included. Each image was then segmented into six equal boxes. A SEResNet34 classification model was trained to identify each subimage.

RESULTS: Our model achieved impressive performance with an overall accuracy of 86%. Identifying control from abnormal yielded 92% accuracy, 94.4% precision, 85% recall, 96.7% specificity, and 89.5% F1-score. For abnormal classification, the model produced 94% accuracy, 81.8% precision, 90% recall, 95% specificity, and 85.7% F1-score for myogenic changes and 86% accuracy, 81% precision, 85% recall, 86.7% specificity, and 82.9% F1-score for neurogenic chances.

SUMMARY/CONCLUSION: The current DL classifier is showing promising results. This highlights the potential of AI in enhancing diagnostic imaging analysis.

Abdullah Al Qahtani, MD, MPH

President's Research Initiative Award Recipient

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JUVENILE MYASTHENIA GRAVIS WITH RESPONSE TO RAVULIZUMAB-CWVZ

Reena Bastin (Chicago, IL), Joshua Chang (Chicago, IL), Danesh Reza (Chicago, IL), Henry David (Chicago, IL), Emily Doll (Chicago, IL), Helene Rubeiz (Burr Ridge, IL), Betty Soliven (Chicago, IL), Kourosh Rezania (Chicago, IL)

INTRODUCTION/BACKGROUND: Myasthenia gravis (MG) is a rare complication of allogenic stem cell transplantation (ASCT), associated with manifestations of graft versus host disease (GVHD). C5 complement inhibitors are FDA-approved for treating anti-acetylcholine receptor (AChR) generalized MG in adults.

CASE REPORT: A 14-year-old Middle Eastern male with HbS beta thalassemia underwent a ASCT complicated by GVHD, presented with a two-month history of intermittent ptosis, ophthalmoplegia, facial weakness, dysphagia, arm weakness, and progressive respiratory failure. Exam revealed intubated status, bilateral ptosis (R>L), facial diplegia, reduced muscle bulk with proximal more than distal upper and lower extremity weakness. Repetitive nerve stimulation (3 Hz) showed 16% electrodecremental response in the left nasalis. Needle study showed fibrillations and positive waves in right iliopsoas with myopathic recruitment. The MG panel was positive for AChR Binding Ab 21.1 (normal < 0.02 nmol/L). He received prednisone 30 mg and IVIG 2g/kg over 5 days with minimal improvement and developed hemolysis (likely secondary to IVIG). He received five sessions of plasmapheresis, resulting in transient improvement of weakness and extubation but was re-intubated after five days. Ravulizumab-cwvz was initiated at 900 mg (loading dose) followed by 2100 mg every 8 weeks (weight was 28.5 kg). After the second dose of ravulizumab-cwvz, the weakness dramatically improved leading to extubation. Six weeks post-initiation of ravulizumab, he regained full extraocular muscle function and normal strength in appendicular and limb muscles. Prednisonolone was tapered to 21 mg.

SUMMARY/CONCLUSION: This is the first report of successful management of a pediatric case of treatment refractory post-ASCT MG with C5 complement inhibitor therapy.

Reena Bastin, MD

Pediatric Award Recipient

Resident and Fellow Member Award Recipient

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CONGENITAL ONSET PRESYNAPTIC MYASTHENIC SYNDROME: SPECIFIC MUTATION, PHENOTYPE, AND ANALYSIS OF STIMULATION POTENTIAL WITH CONCENTRIC ELECTRODES

Wilmer Santiago Herrera Malpica (Bogotá, Colombia), Fernando Ortiz-Corredor (Bogotá, Colombia), Sandra Milena Castellar Leones (Bogotá, Colombia), Paula Vannesa Muñetones Hernandez (Bogotá, Colombia)

INTRODUCTION/BACKGROUND: Congenital myasthenic syndromes (CMS) can be classified according to their presynaptic, synaptic, or postsynaptic origin, their pattern of autosomal dominant or recessive inheritance, and the specific mutation type. Presynaptic forms represent around 5% to 10% of all CMS cases. The Synaptotagmin 2 (SYT2) gene encodes a protein of the synaptic vesicle membrane that acts as a calcium sensor in vesicular trafficking and exocytosis.

CASE REPORT: A 9-year-old girl presented with a history of perinatal hypoxia, predominant motor neurodevelopmental delay, behavioral disorder, mild borderline cognitive impairment, bilateral congenital hip dysplasia, flat feet, hyperlaxity, strabismus, and bilateral ptosis. Stimulation potential analysis with concentric electrode (SPACE) study in the frontalis muscle shows jitter with a minimum mean consecutive difference (MCD) of 27, maximum 122, average 69, abnormal. Consistent with a neuromuscular junction disease, trio exome sequencing was performed, which reported a variant in the SYT2 gene (NM_177402.5) c.1022T>C; (pPhe341Ser) missense type, with autosomal recessive inheritance pattern in compound heterozygosity compatible with congenital onset presynaptic myasthenic syndrome (CMS7B). Management with pyridostigmine was initiated with symptomatic improvement.

SUMMARY/CONCLUSION: Congenital onset presynaptic myasthenic syndrome (CMS7B) is a rare disease, secondary to homozygous or compound heterozygous mutation in the SYT2 gene on chromosome 1q32. This case describes the abnormal finding in the SPACE study and outlines the phenotypic characteristics of this rare disease, highlighting the importance of genetic sequencing, which is crucial for confirming the diagnosis.

Wilmer Santiago Herrera Malpica, MD

Pediatric Award Recipient

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ORBICULARIS OCULI MUSCLE STIMULATED JITTER ANALYSIS REVISED REFERENCE VALUES IN CHILDREN

Vishva Natarajan (Peachtree Corners, GA), Sumit Verma (Johns Creek, GA)

INTRODUCTION: The use of single fiber EMG (SFEMG) in children is limited due to difficulty maintaining constant voluntary activation, therefore, jitter estimation using electric stimulation i.e., stimulated jitter analysis (stim-JA) has emerged as an acceptable alternative. Stim-JA involves analyzing the variation in time intervals between pairs of consecutive potentials, known as the jitter or mean consecutive difference (MCD). There is a paucity of literature on the sensitivity, specificity, and MCD upper limits of pediatric stim-JA.

OBJECTIVE: To derive MCD upper limits and increase the specificity of pediatric stim-JA.

METHODS: Retrospective chart review of orbicularis oculi stim-JA on children over 2 years between January 2014 and December 2021. Clinical profile, acetylcholine receptor and muscle-specific kinase antibody status, and stim-JA results were retrieved for each patient. E-ref and bootstrapping were applied to stim-JA studies to derive de novo MCD upper limits.

RESULTS: Twenty-seven orbicularis oculi muscle (19 right, 8 left) stim-JA studies were performed on patients either definite neuromuscular junction (NMJ) defect (n=19, 17 AChR+, 2 MuSK+) or normal neurological examination and seronegative (n=8). Five hundred three apparent single fiber action potentials (ASFAPs) were analyzed with individual (41 µs) and mean MCD (46.8 µs) significantly higher in children with autoimmune myasthenia ($p<0.05$). Bootstrapping and E-ref showed revised MCD upper limits of 39 µs for individual and 24 µs for mean MCD significantly improved specificity while maintaining sensitivity of stim-JA ($p<0.05$).

SUMMARY/CONCLUSION: Orbicularis oculi muscle stim-JA revised individual (39 µs) and mean (24 µs) MCD upper limits improve specificity in diagnosis of NMJ disorders in children over 2 years.

Vishva Natarajan, MS

Pediatric Award Recipient

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DUAL SRP / SCLERODERMA MYOSITIS PRESENTING AS AN ASYMMETRIC SHOULDER GIRDLE WEAKNESS

Shanmitha Arun (Richmond, VA), Mathula Thangarajh (Glen Allen, VA)

INTRODUCTION/BACKGROUND: We present a challenging clinical case of a young girl who presented with asymmetric shoulder girdle weakness who was mistakenly diagnosed to have brachial plexus injury but was subsequently noted to have antibodies to both signal recognition particle (SRP) and scleroderma.

CASE REPORT: A 12-year-old was seen for painless left shoulder girdle weakness over 6 weeks. A shoulder girdle MRI found diffuse muscle edema and she was therefore sent for an EMG to our institution to rule out Parsonage-Turner syndrome. She had no facial or lower limb proximal muscle weakness. She denied fever, joint pain, and rash. NCS/EMG were normal. Creatine kinase was very high (>10,000) as was her aldolase (>100). A serum muscle antibody panel showed positive anti-SRP and anti-PM-Scl75 antibodies. She underwent an MRI which was negative for any malignancies. Her repeat shoulder MRI showed severe atrophy of all muscles of the rotator cuff, edema as well as fatty infiltration is most notable in the supraspinatus and superior aspects of the subscapularis muscle. MRI changes were also noted in posterior compartment muscles of the thighs, obturator internus and externus muscles, lumbosacral paraspinal muscles. A muscle biopsy of the paraspinal muscle showed mild myopathic changes. On follow-up visit 2 months later, she endorsed leg weakness and difficulty climbing stairs. A final diagnosis of overlap SRP/polymyositis was made, and she began treatment with intravenous immunoglobulin.

SUMMARY/CONCLUSION: This case illustrates an unusual presentation of a dual overlap myositis in a young child.

Shanmitha Arun, BS

Pediatric Award Recipient

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CASE REPORT: ISOLATED DYSARTHRIA AS THE PRIMARY MANIFESTATION OF MYASTHENIA GRAVIS

Carlos Rodriguez-Alarcon (Playas, Guayas, Ecuador), Daniella Bustamante-Mieles (Guayaquil, Ecuador), Rocio Santibanez-Vasquez (Guayaquil, Ecuador)

BACKGROUND: Myasthenia gravis (MG) is an autoimmune disorder characterized by ptosis, diplopia, dysarthria, dysphagia, limb weakness, and, in severe instances, respiratory muscle involvement. Dysarthria as an exclusive initial and primary complaint in MG is infrequent and seldom reported.

CASE REPORT: A 60-year-old male presented to the clinic with persistent dysarthria for a few months. He reported two prior episodes that had resolved spontaneously. Speech was clear upon awakening but deteriorated progressively throughout the day. Physical examination revealed dysarthria and dysphonia. Muscle strength, reflexes, and gait were normal. Additionally, the patient described coughing episodes previously attributed to gastroesophageal reflux disease. A non-contrast head MRI and video-electroencephalograph monitoring were unremarkable. Nasopharynx endoscopy revealed inadequate vocal cord adduction. Fiberoptic endoscopic evaluation of swallowing identified moderate pharyngeal dysphagia, characterized by diminished lingual agility, imprecise articulation, and intermittent weakness in voice quality. Single-fiber electromyography demonstrated variability in 30 muscle fibers of the left orbicularis oris upon facial nerve stimulation. Ten fibers exhibited individual Jitter values exceeding 31.8 msec, with an average Jitter surpassing the normal range (N 21.2 µs), indicative of neuromuscular junction dysfunction. Additionally, a chest CT scan revealed thymic involution. Laboratory tests revealed positive IgG anti-acetylcholine receptor levels (10.6 nmol/l) and negative anti-musk antibodies. Initiation of pyridostigmine therapy resulted in a notable improvement in symptoms, including enhanced speech velocity, modulation, and articulation.

CONCLUSION: EMG and autoantibody profiling played a crucial role in diagnosing MG, particularly with dysarthria as the sole initial symptom. The rarity of laryngeal MG emphasizes the need for heightened clinical suspicion and interdisciplinary collaboration.

Carlos Rodriguez-Alarcon, MD

Medical Student Research Award Recipient

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CASE REPORT: MOTOR-PREDOMINANT GUILLAIN-BARRE SYNDROME FOLLOWING COVID-19 INFECTION

Carlos Rodriguez-Alarcon (Playas, Guayas, Ecuador), Linker Viñan-Paucar (Guayaquil, Guayas, Ecuador), Michelle Avecillas-Zeas (Siegen, Germany), Oscar Del Brutto (Samborondon, Ecuador), Rocio Santibanez-Vasquez (Guayaquil, Ecuador)

BACKGROUND: Guillain-Barre syndrome (GBS) is a rapidly progressive, symmetric peripheral inflammatory disease that has been linked to infections. A post-COVID-19 GBS association has been reported, and here a case of a motor-predominant GBS is presented.

CASE REPORT: A 23-year-old male with a COVID-19 history 4 weeks prior developed extremity paresthesias, thigh weakness, and a deteriorating gait. 3 days before, he experienced cervicalgia and right facial palsy. His condition rapidly deteriorated, leading to paraparesis and facial diplegia. Physical examination showed facial diplegia, right VI palsy, flaccid quadriparesis, areflexia, normal sensation, no dysphagia, dysphonia, or hemodynamic instability, and preserved respiratory capacity. EDX studies on day 5 revealed an absent H reflex and a delay of distal motor latencies in both posterior tibial nerves, with reduced motor amplitude in the left common peroneal nerve. F waves were absent in the common peroneal nerves and prolonged in the posterior tibial nerves. Sensory latencies in the median, ulnar, radial, superficial peroneal, and sural nerves were normal. The concentric needle study showed no abnormal activity at rest, with a poor recruitment pattern of motor units of normal morphology. The patient was hospitalized, and a lumbar puncture on day 6 exhibited albumin-cytologic dissociation. The symptoms improved with intravenous immunoglobulin, exhibiting significant motor recovery upon discharge.

CONCLUSION: This case underscores the paramount significance of maintaining a heightened clinical suspicion for neurologic symptoms among individuals convalescing from COVID-19, emphasizing the importance of prompt evaluation and immunomodulatory therapy for managing post-COVID-19 neuromuscular complications.

Carlos Rodriguez-Alarcon, MD

Medical Student Research Award Recipient

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ASSOCIATION BETWEEN HYPERGLYCEMIC CRISIS SEVERITY AND NEUROPATHIC MANIFESTATIONS IN HISPANIC PATIENTS WITH DE NOVO HYPERGLYCEMIA: A CROSS-SECTIONAL STUDY

Carlos Rodriguez-Alarcon (Guayaquil, Ecuador), Danny Japon-Cueva (Guayaquil, Ecuador), Aldo Carofilis (Manta, Ecuador), Linker Viñan-Paucar (Guayaquil, Ecuador), María Cueva-Espinoza (Guayaquil, Ecuador), Presley Gruezo-Realpe (Esmeraldas, Ecuador), Rocio Santibanez-Vasquez (Guayaquil, Ecuador)

INTRODUCTION: Hyperglycemic crisis (HC) involves a rapid and significant rise in blood glucose, resulting in systemic manifestations. Neuropathy in de novo hyperglycemia (DNH) crises strongly signals additional microvascular complications, highlighting the necessity for comprehensive but often neglected screening and examination. Despite its prevalence, research on the Hispanic population is significantly lacking.

OBJECTIVE: Assess the relationship between HC severity and neuropathic manifestations in Hispanic patients with DNH.

METHODS: A cross-sectional study on Hispanic patients with DNH crises was conducted at a tertiary hospital's emergency department. Data collected from clinical records included neuropathic symptoms upon admission and glycemia classified by Sliding Scale Insulin Therapy (SSIT). The association between SSIT and neuropathic manifestations was determined via the χ^2 test.

RESULTS: The study comprised 273 Hispanic patients (average age: 65±13 years; 53.5% female). The HC was categorized by SSIT as follows: >300 mg/dL (47.6%), 250-300 mg/dL (8.8%), 200-250 mg/dL (6.6%), 150-200 mg/dL (4.8%), and <150 mg/dL (32.2%). Neuropathic manifestations were observed in 3.30% of the cohort, including lower extremity symmetric polyneuropathy (1.8%) marked by allodynia and paresthesias, lower extremity mononeuropathy (0.7%) characterized by a burning sensation, and trigeminal mononeuropathy (0.4%) featuring asymmetric facial numbness. The χ^2 test indicated no statistically significant association between hyperglycemia classification according to the SSIT and neuropathic manifestation in our sample (χ^2=4.28, p<0.368).

CONCLUSION: Stratifying HC severity by SSIT did not reveal a significant association with neuropathic manifestations. Caution is warranted due to variations in examination methods. Future research should refine screening protocols for HC neuropathic manifestations in Hispanic populations and explore additional contributing factors.

Carlos Rodriguez-Alarcon, MD

Medical Student Research Award Recipient

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MICHIGAN NEUROPATHY SCREENING INSTRUMENT IN PRIMARY CARE HISPANIC LOW-INCOME COMMUNITIES: DETECTING DIABETIC PERIPHERAL NEUROPATHY AND THE INFLUENCE OF EDUCATION

Carlos Rodriguez-Alarcon (Guayaquil, Ecuador), Daniella Bustamante (Guayaquil, Ecuador), Danny Japon (Guayaquil, Ecuador), Rocio Santibanez-Vasquez (Guayaquil, Ecuador)

INTRODUCTION: Diabetic peripheral neuropathy (DPN) is a prevalent complication of diabetes, necessitating prompt identification and intervention to mitigate grave consequences. The Michigan Neuropathy Screening Instrument (MNSI) serves as a promising assessment method for DPN, with potential usefulness in low-resource settings or rural areas where access to advanced diagnostic tools may be limited.

OBJECTIVE: Assess MNSI's efficacy in detecting DPN in rural Ecuadorian diabetic patients, considering education's influence.

METHODS: A cross-sectional study was conducted involving diabetic patients from rural Ecuadorian primary care centers, classified by their education level, who underwent MSNI. Statistical analysis, employing T-tests and ANOVA, was utilized to assess test sensitivity and determine the influence of education level on the outcomes.

RESULTS: This study included 50 patients (52% male, mean age 64±11.56 years) with varying education levels: 26% illiterate, 46% basic education, 12% bachelor's degrees, and 16% advanced degrees. Neuropathy was identified in 84% of participants using Test B (mean score: 4±2/10), whereas only 48% were detected using Test A (mean score: 7±3/15). The T-value (T=-4.85, p<0,001) exhibits a notable difference in neuropathy detection between subtests. Additionally, the ANOVA showed no significant differences in neuropathy detection by education level for either test (both p>0,05).

CONCLUSION: Integrating patient questionnaires with physician examinations is crucial for thorough neuropathy detection in diabetic patients. Test B surpasses Test A, improving diagnostic accuracy when used together. Education does not impact MNSI's neuropathy detection, emphasizing its broad suitability across diverse patients and its value for DPN screening, particularly in resource-limited settings, due to its simplicity and efficacy in facilitating clinical examinations.

Carlos Rodriguez-Alarcon, MD

President's Research Initiative Award Recipient

Medical Student Research Award Recipient

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DISABILITY AND MORTALITY IN LONG HAUL COVID-19 PATIENTS WITH RHABDOMYOLYSIS DURING THE ACUTE PHASE OF COVID-19 INFECTION

Kazim Jaffry (Colonia, NJ), Justin Matos (Edison, NJ), Narjis Jaffry (Edison, NJ), Suhayb Islam (Edison, NJ), Scott Karpenos (Edison, NJ), Daniel Menkes (Birmingham, MI), Nizar Souayah (Westfield, NJ)

INTRODUCTION: Early reports suggested an association between rhabdomyolysis (RM) after COVID-19 and an increased risk of morbidity and mortality during the acute phase of the illness. However, the effect of RM on post-acute sequelae of COVID-19 (PASC) prognosis was not investigated.

OBJECTIVE: To investigate the association of RM during the acute phase of COVID-19 infection and the outcomes of PASC.

METHODS: We retrospectively reviewed Epic Cosmos EMR data. PASC patients with and without RM during the acute phase of COVID-19 were identified for the time interval 2020-2023. SNOMED classification was used to identify patients with significant disability. A sample of non-PASC patients was used as a control to compare the prevalence of RM.

RESULTS: We identified 2,643 PASC patients with RM and 407,930 PASC patients without RM. There was a higher proportion of patients who developed PASC in the COVID group who developed RM during the acute infection as compared to the COVID group without RM (3.0% vs 1.8%; $p<0.05$). The prevalence of rhabdomyolysis among PASC patients was significantly higher than the non-PASC control cohort (0.644% vs 0.184%; $p<0.05$). PASC patients with RM had a higher mortality rate (8.4% vs 1.7%; $p<0.05$), a higher rate of hospice discharge (4.0% vs 0.9%; $p<0.05$), a higher proportion of placement on mechanical ventilation (23.6% vs 4.4%; $p<0.05$), and a higher rate of disability (20.8% vs 6.1%; $p<0.05$).

SUMMARY/CONCLUSION: There was significantly higher morbidity, mortality, and disability in PASC patients who developed RM as compared to PASC patients without rhabdomyolysis.

Kazim Jaffry, BA

Medical Student Research Award Recipient

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MORTALITY AND MORBIDITY OF POST-ACUTE SEQUELAE OF COVID-19 PATIENTS WITH CRANIAL NEUROPATHIES

Kazim Jaffry (Colonia, NJ), Narjis Jaffry (Edison, NJ), Justin Matos (Edison, NJ), Scott Karpenos (Edison, NJ), Suhayb Islam (Edison, NJ), Kranthi Mandava (Highland Park, NJ), Daniel Menkes (Birmingham, MI), Nizar Souayah (Westfield, NJ)

INTRODUCTION: We previously reported that patients with COVID-19 and cranial neuropathies are usually mild. However, the association and severity of post-acute sequelae (PASC) in COVID-19 patients with cranial neuropathy is unknown.

OBJECTIVE: To determine the association of cranial neuropathies with the clinical outcomes of patients with PASC of COVID-19.

METHODS: We conducted a retrospective analysis from 2020 -2023 using Epic Cosmos EMR data. We identified 7,438 patients with PASC with cranial neuropathy (PWCN) and 403,135 patients with PASC without cranial neuropathy (PNCN. Systematized Nomenclature of Medicine (SNOMED) classification was used to collect information regarding the disability status of patients.

RESULTS: The mortality rate was similar in the PWCN and PNCN groups (PWCN/PNCN: 1.8% vs 1.7%), as was the hospice discharge rate (PWCN/PNCN: 1.1% vs 0.9%), and length of hospitalization stay (PWCN/PNCN: 7.0±0.42 days vs 7.4±0.07 days). PWCN patients were more likely to be placed in a specialized nursing facility (SNF) (PWCN/PNCN: 6.7% vs 4.7%; $p<0.05$), had a higher requirement for mechanical ventilation (PWCN/PNCN: 4.0% vs 3.4%; $p<0.05$), were more likely to have a higher body mass index (BMI) (PWCN/PNCN: 63.1% vs 55.6%; $p<0.05$), were more likely to be disabled (9.8% vs 6.1%; $p<0.05$).

SUMMARY/CONCLUSION: Patients with PASC experiencing cranial neuropathies do not face higher mortality rates or longer hospital stays compared to patients with PNCN. However, those with cranial neuropathies in the context of PASC present with higher BMI and exhibit significantly more complications, including increased disability, higher rate of SNF discharge, and a greater necessity for mechanical ventilation. Ongoing research aims to elucidate the role of comorbid conditions and socioeconomic factors in these outcomes.

Kazim Jaffry, BA

Medical Student Research Award Recipient

23

UNVEILING DEMYELINATION IN DIABETIC NEUROPATHY: REVOLUTIONIZING CONDUCTION SLOWING DETECTION WITH AN INTUITIVE APPLICATION TOOL

Kazim Jaffry (Colonia, NJ), Ankit Pahwa (Newark, NJ), Nizar Souayah (Westfield, NJ)

INTRODUCTION: Previously, in a study of 114 chronic inflammatory demyelinating polyneuropathy (CIDP) patients meeting American Academy of Neurology criteria, regression analysis defined the conduction slowing range for a specific compound muscle action potential (CMAP) amplitude. Among 95 ALS patients, none exceeded two motor nerves with slowing in the regression equations range. Conversely, 47% and 23.3% of 219 diabetic neuropathy (DSP) and 219 non-diabetic neuropathy (NDSP) patients met the criteria, with reduced overlap (30.6% vs. 7.3%, $p<0.001$) when one nerve showed an F response in the demyelination range. This overlap was neutralized in two DSP groups by combining systemic sPLA2 activity with regression analysis, identifying a subgroup of diabetic patients with significant demyelination.

OBJECTIVE: To develop an EDX testing application utilizing regression analysis to identify conduction slowing in the demyelinating range not detected by conventional EDX testing.

METHODS: An Excel app inputs conduction velocity (CV), distal latency (DL), F wave (F), and CMAP amplitude, categorizing output as "in" (within demyelination range) or "out." Transformation starts by converting nerve data to percentages of upper and lower limits of normal for DL, F, CMAP amplitude, and CV. CMAP amplitude is the independent variable, while DL, CV, and F are dependent variables in regression equations. If the current transformed value falls within the identified range in columns 1 and 2, input is "in" (column 5), indicating demyelination.

RESULTS: The Excel app efficiently identifies conduction slowing beyond axonal loss expectations.

SUMMARY/CONCLUSION: Work is in progress to integrate a neuroinflammation biomarker, incorporate the app into EMG machines and electronic medical records, and estimate the likelihood of CMAP independent conduction slowing in DSP and NDSP groups.

Kazim Jaffry, BA

Medical Student Research Award Recipient

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IMPACT OF ELEVATED INTERLEUKIN-6 (IL-6) IN PATIENTS WITH COVID-19 AND ACUTE MUSCLE INJURY: A RETROSPECTIVE ANALYSIS

Kazim Jaffry (Colonia, NJ), Justin Matos (Edison, NJ), Narjis Jaffry (Edison, NJ), Kranthi Mandava (Highland Park, NJ), Suhayb Islam (Edison, NJ), Scott Karpenos (Edison, NJ), Roopa Sharma (Harrison, NJ), Howard Sander (New York, NY), Nizar Souayah (Westfield, NJ)

INTRODUCTION: Previously, we observed an association between poor outcome of encephalopathy in acute COVID-19 and elevated IL-6. However, the association between IL-6 and acute muscle injury during acute COVID-19 was not investigated.

OBJECTIVE: To investigate the impact on clinical outcomes of elevated Interleukin-6 (IL-6) in patients with COVID-19 and acute muscle injury.

METHODS: We retrospectively reviewed Epic Cosmos electronic medical record data of 17,641 patients with acute COVID-19 that had acute muscle injury based on rhabdomyolysis or elevated creatine phosphokinase (CK). We compared the following demographic and clinical outcomes of patients with and without elevated IL-6 levels: age, sex, body mass index (BMI), underlying disability, hospital stay duration, mechanical ventilation, skilled nursing facility (SNF) and hospice admissions, and mortality.

RESULTS: Among 17,641 patients with acute COVID-19 and acute muscle injury, 79.4% had increased IL-6. Patients with elevated IL-6 levels had statistically ($p<0.05$) greater: hospital stay duration (10.6±0.3 vs 8.7±1.3 days), use of mechanical ventilation (41.8% vs 21.6%), SNF admission rate (21.2% vs 17.7%), hospice admission rate (4.9% vs 3.1%), and mortality rate (33.3% vs 15.6%) compared to patients with normal IL-6. Patients with elevated IL-6 were significantly older (64±0.3 vs 60±0.6 years). Male predominance was observed in both groups (54.4% and 61.2%). BMI and underlying disability were not statistically different between the two groups.

SUMMARY/CONCLUSION: In patients with COVID-19 and acute muscle injury, elevated IL-6 levels are associated with greater hospital stay duration, use of mechanical ventilation, SNF admission, hospice admission, and mortality.

Kazim Jaffry, BA

Medical Student Research Award Recipient

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HUMAN-DERIVED NEURAL PROGENITOR CELL IMPLANTATION RESCUES MOTOR ENDPLATES FOLLOWING PERIPHERAL NERVE INJURY

Luigi Gonzales (Irvine, CA), Vivian Chen (Irvine, CA), Amanda Tedesco (Irvine, CA), Saman Andalib (Irvine, CA), David Wright (Irvine, CA), Tyler Johnston (Irvine, CA), Ali Habib (Irvine, CA), Robert Hunt (Irvine, CA), Oswald Steward (Irvine, CA), Ranjan Gupta (Irvine, CA)

INTRODUCTION: The degradation of motor endplates (MEPs) following peripheral nerve injury (PNI) plays a major role in determining the prognosis and extent of recovery for patients. Previous studies have demonstrated the effects of stem cells in providing neurotrophic support following PNI but its effects on the MEPs have not been studied.

OBJECTIVE: We hypothesize that human induced pluripotent stem cells (hiPSC) differentiated into motor neuron precursors would provide trophic support that prevents or limits MEP degradation following peripheral nerve injury.

METHODS: Under IACUC approval, chronic denervation injury models in mice were created via sciatic nerve transection. After 4 months of denervation, the denervated tibialis anterior (TA) of mice were injected with PBS (negative control), low dose hiPSC (10,000 cells), or high dose hiPSC (500,000 cells). Differentiation of hiPSC into functional motor neuron progenitors were performed based on a previously published protocol. At select time points post-injection, the TA were harvested and stained with the appropriate antibodies to confirm hiPSC survivability and detect the presence of MEPs.

RESULTS: Analysis of the muscles revealed viability and survivability of implanted hiPSC. No MEPs were found in muscle injected with PBS. The low-dose group demonstrated low density of MEPs with minimal complexity while the high-dose group revealed increased MEP density with increased morphology complexity. The contralateral, uninjured TA demonstrated high-density, healthy MEPs.

SUMMARY/CONCLUSION: Implantation of motor neuron precursor cells from hiPSC demonstrated a dose-dependent efficacy in rescuing MEPs following PNI and could serve as an adjunct to current treatment modalities for PNI.

Luigi Gonzales, BS

Medical Student Research Award Recipient

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AGING ACCELERATES DEGRADATION OF HUMAN NEUROMUSCULAR JUNCTION FOLLOWING PERIPHERAL NERVE INJURY

Luigi Gonzales (Artesia, CA), David Wright (Irvine, CA), Vivian Chen (Irvine, CA), Amanda Tedesco (Irvine, CA), Saman Andalib (Irvine, CA), Ali Habib (Irvine, CA), Tyler Johnston (Irvine, CA), Oswald Steward (Irvine, CA), Ranjan Gupta (Irvine, CA)

INTRODUCTION: While it is widely recognized that there is a difference in how adult and pediatric patients respond and recover after peripheral nerve injuries (PNI), the reasons for variability in outcomes between young adults and elderly adults remains unclear.

OBJECTIVE: We hypothesize that motor endplate (MEP) denervation occurs more rapidly in the elderly population, resulting in poorer prognosis compared to the younger adults.

METHODS: After receiving internal review board approval, denervated and healthy muscle biopsies were collected from post-PNI patients during standard-of-care procedures. The muscle samples underwent tissue clearing using a previously published protocol. Samples were stained before undergoing 3-D imaging using the Keyence BZ-X810. MEPs were assessed for morphology and innervation status.

RESULTS: Analysis of the MEPs revealed no significant difference in the percentage of healthy (pretzel) and unhealthy (intermediate and plaque) morphology between the two groups. Young muscle samples revealed an average of 48.78% innervated MEPs, more than double the percentage found in elderly samples (18.81%). The elderly had a lower percentage of MEP innervation (30.77%) at the earliest timepoint of three months post-injury while the young group still had MEP innervation (50.00%) at 7 months post-injury. Beyond that time, patients undergo a similar rate of loss of MEP innervation as the time from injury increases.

SUMMARY/CONCLUSION: Following PNI, elderly patients experience a much faster rate of initial MEP innervation loss. Our findings suggest that elderly patients reach the threshold percentage of MEP denervation sooner than their younger counterparts, suggesting potential benefit from earlier intervention.

Luigi Gonzales, BS

Medical Student Research Award Recipient

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COMPLEX REPETITIVE DISCHARGES AND MYOPATHIC ELECTROMYOGRAPHIC CHANGES IN LAMBERT-EATON MYASTHENIC SYNDROME

Olivia Ault (Lexington, KY), Nakul Katyal (Lexington, KY)

INTRODUCTION/BACKGROUND: EMG abnormalities mimicking myopathy can be seen in Lambert-Eaton myasthenic syndrome (LEMS). However, complex repetitive discharges (CRDs) have never been described in LEMS. We present a case of a LEMS with this rare electrophysiological phenomenon.

CASE REPORT: A 72-year-old woman presented to our clinic with a 1-year history of progressive weakness, orthostatic lightheadedness, and intermittent difficulties with chewing and swallowing. Ten years prior to these symptoms, she was diagnosed with multiple myeloma and treated with chemotherapy and stem cell therapy. She remained in remission afterwards. Neurological exam showed bilateral ptosis and weakness in proximal upper and lower extremities and neck flexion. Her patellar reflexes were initially absent but were obtainable and 2+ after brief exercise. On NCS, ulnar compound motor action potential (CMAP) amplitude improved from 2.5 mV to 6.4 mV after brief exercise. A 3 Hz repetitive nerve stimulation study showed low baseline CMAP amplitude with >10% decrement at rest. After brief exercise, a significant (>100%) improvement in CMAP amplitude was noted, suggesting a presynaptic neuromuscular junction defect. Her EMG was notable for CRDs in pronator teres and iliopsoas muscles, and myopathic changes in deltoid, triceps, pronator teres, and iliopsoas muscles. Paraneoplastic panel was positive for P/Q-type calcium channel antibodies with titer 0.32 nmol/l. Extensive cancer screening including repeat bone marrow biopsy did not reveal any underlying malignancy. The patient was diagnosed with LEMS and is scheduled to receive 3,4-diaminopyridine.

SUMMARY/CONCLUSIONS: Our case highlights the rare electrophysiological phenomenon of CRD and myopathic changes in LEMS.

Olivia Ault, BS

Medical Student Research Award Recipient

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AN EXEMPLAR OF PERSON-CENTERED GENETIC TESTING TO ADVANCE DIAGNOSIS AND COUNSELING

Jialin Chen (Henrico, VA), Mathula Thangarajh (Glen Allen, VA)

INTRODUCTION/BACKGROUND: We present the second known case of ataxic cerebral palsy associated with a de novo R480W mutation of the SPTBN2 in a 3-year-old male child to highlight how person-centered genetic testing can help with diagnosis and clinical management. SPTBN2 is highly expressed in Purkinje cells, encodes Beta-III spectrin, a cytoskeletal protein crucial for neuronal stability. Mutations in spectrin genes have been implicated in various neurological abnormalities. The R480W variant of SPTBN2 is very rare, with only one previously documented case report, and manifests in early childhood with ataxia and intellectual disability.

CASE REPORT: The patient was seen as a second opinion following an established diagnosis of ataxic cerebral palsy. Inconsistencies in the patient's history and clinical exam prompted re-evaluation, including genetic testing. Genetic testing revealed a de novo R480W mutation of the SPTBN2. MRI findings revealed cerebellar hypoplasia, consistent with previous reports of dominant SPTBN2 R480W de novo mutations. One notable feature of this child was the lack of increase in paternal age typically associated with this de novo mutation. Our index patient's father was only 27 years old.

SUMMARY/CONCLUSION: This case underscores the importance of considering person-centered genetic testing in the diagnosis of ataxic cerebral palsy and highlights the phenotypic variability associated with SPTBN2 mutations.

Jialin Chen, BS

Medical Student Research Award Recipient

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MUSCULOSKELETAL ULTRASOUND POSITIONING FOR NEUROGENIC THORACIC OUTLET BOTULINUM TOXIN INJECTION

Michelle Tan (Bellaire, TX), Angela Cortez (Houston, TX), Paul Paily (Houston, TX), Jeffrey Strakowski (Powell, OH)

INTRODUCTION: Several potential target muscles are treated in the injection of neurogenic thoracic outlet syndrome (TOS). Anatomic references of the region are usually provided in anatomic neutral position; however, the injection position is often different. The goal of the project is to provide reference images at varying anatomic positions for diagnosis and injections.

OBJECTIVE: This study examines ultrasound imaging at varying positions of pertinent muscles for diagnostic assessment and guided injections in the treatment of TOS.

METHODS: This is an internal review board approved study at the host institution. An 8-12 MHz linear broadband transducer was used to examine a healthy adult female subject in both anatomic neutral and other positions to optimize dynamic diagnostic assessment and injection approach. The pertinent muscles and vascular structures were recorded with still images and cine loops.

RESULTS: Side by side comparison of anatomic neutral and injection position images are provided for each target muscle. Muscles that are commonly clinically injected for TOS are the anterior scalene, pectoralis minor, trapezius, and subclavius. Ultrasound was also used to identify the phrenic nerve and four pertinent vessels: jugular vein, internal carotid artery, subclavian artery, and subclavian vein.

SUMMARY/CONCLUSION: This project provides ultrasound reference images of target muscles in the position commonly injected for treatment of neurogenic TOS and well as positional changes often seen in dynamic assessment. Awareness of the relationship of the muscles and vessels with changes in cervical and limb movement, including their typical injection position, will enhance accuracy of toxin placement and avoid neurovascular complications.

Michelle Tan, BA

Medical Student Research Award Recipient

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A CROSS-SECTIONAL ASSESSMENT OF AANEM-ACCREDITED ELECTRODIAGNOSTIC LABORATORIES IN RESIDENCY TRAINING AND IMPLICATIONS FOR PURSUING FELLOWSHIP

Milan Oxspring (Phoenix, AZ), Ojas Deshpande (Phoenix, AZ), Nandita Keole (Scottsdale, AZ)

INTRODUCTION: Since 2010, the AANEM has played an important role in ensuring quality and integrity of EDX laboratories by offering lab accreditation. Obtaining accreditation for labs used in resident training reflects the program's commitment to high quality patient care and clinical education.

OBJECTIVE: To evaluate the prevalence of physical medicine and rehabilitation (PM&R) and neurology residency programs with AANEM-accredited EDX labs and determine the corresponding proportion of neuromuscular/clinical neurophysiology (NM/CNP) fellows from those programs.

METHODS: The AANEM database, comprising 202 AANEM-accredited labs plus additional satellite facilities, was compared with rotation sites from 366 residency programs across PM&R, adult neurology, and child neurology. Information regarding 2023-2024 academic year NM/CNP fellows originating from United States residency programs was obtained from websites of the 69 fellowship programs in the AANEM directory.

RESULTS: Among 366 residency programs analyzed, 119 (32.5%) had accredited EDX labs. The number of programs with accredited labs and corresponding proportion within each specialty consisted of 38 (34.8%) PM&R, 53 (29.8%) neurology, and 28 (35.4%) child neurology. Of 57 NM/CNP fellows identified, 21 (36.8%) graduated from programs with accredited labs, distributed as follows: 2 (4.1%) PM&R, 47 (82.5%) neurology, and 11 (19.3%) child neurology.

SUMMARY/CONCLUSION: Less than one-third of neurology and PM&R residency programs have accredited laboratories. The relative proportion of residents who pursue NM/CNP fellowships is significantly greatest in adult neurology. Accreditation enables a higher quality training environment for residents by incorporating elements of health systems science education and more residency programs should consider accrediting their EDX labs.

Milan Oxspring, BS

Medical Student Research Award Recipient

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HETEROTOPIC OSSIFICATION: A POTENTIALLY OVERLOOKED COMPLICATION OF ELECTROMYOGRAPHY

Katrina Muñoz (Atlanta, GA), Avi Landman (Decatur, GA), Prateek Gandiga (Atlanta, GA), Carolina Garcia Santibanez (Atlanta, GA)

INTRODUCTION/BACKGROUND: Heterotopic ossification (HO) is the abnormal formation of bone outside of the skeletal system, typically occurring in soft tissues (e.g., muscles, joints, ligaments, tendons) secondary to trauma. The focal muscle trauma caused by EMG may also lead to calcium deposition and HO formation. Frequently cited side effects of EMG include pain, bleeding, and electrical injury, but rarely is HO cited as a potential complication in literature. Little is known as to which patients may be more likely to this complication, but some evidence suggests that patients with inflammatory myositis can experience calcium deposition in soft tissues following trauma and inflammation.

CASE REPORT: A 49-year-old woman presented to clinic with subacute proximal limb and bulbar weakness. Laboratory workup was notable for an elevated creatine kinase (6,444 U/L), anti-scl100, anti-RNP, and anti-SSA antibodies. EMG was performed and demonstrated irritable myopathy. Immediately after testing, the patient developed persistent pain in the right deltoid, while pain in other tested muscles subsided. In the following weeks, the patient reported continued pain and growth of an indurated mass in her right arm. Subsequent shoulder x-ray and humerus CT scan obtained 2 and 3 months after onset, respectively, showed an ill-defined hyperdensity within the soft tissues of the right lateral upper arm, consistent with HO of the deltoid muscle.

SUMMARY/CONCLUSION: Iatrogenic HO, thus, may be an overlooked complication of EMG and begs the question of how to appropriately treat this complication. In this case, our patient positively responded to laser lithotripsy which improved both lesion size and pain.

Katrina Muñoz, MBE

Medical Student Research Award Recipient

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SMALL FIBER NEUROPATHY ASSOCIATED WITH ANTIPLEXIN-D1 ANTIBODY

Michael Limia (Winston-Salem, NC), Kajol Patel (Winston-Salem, NC), Rachana Gandhi Mehta (Winston-Salem, NC)

INTRODUCTION/BACKGROUND: Small fiber neuropathy (SFN) affects small myelinated Aδ and unmyelinated C fibers, which are essential for thermal perception, nociception, and autonomic functions. Some cases of SFN may exhibit antibodies to plexin-D1, which target small unmyelinated pain-conducting neurons in the dorsal root and trigeminal ganglia, potentially inducing neuropathic pain. We describe two cases of SFN associated with antiplexin-D1 antibodies.

CASE REPORT: Case 1: A 34-year-old woman presented with intermittent burning and numbness involving her cheeks, lips, and hands, which worsened with sun exposure. Her medical history included orthostatic hypotension during her teenage years and a diagnosis of mixed connective tissue disorder. Investigations revealed normal EDX studies, an abnormal skin biopsy, elevated antinuclear antibody (ANA), and positive antiplexin-D1 antibodies. She did not respond to prednisone but experienced partial relief with duloxetine.

Case 2: A 40-year-old woman developed burning pain in her right leg which progressed to her other limbs and torso. The burning was accompanied by generalized allodynia, postural orthostatic tachycardia, constipation, lethargy, and cognitive fog. Her medical history included Hashimoto's thyroiditis and a mast cell disorder. Investigations revealed a normal EDX study, abnormal skin biopsy, elevated ANA and serum amyloid A, and positive antiplexin-D1 antibodies. She did not respond to prednisone, but intravenous Immunoglobulin (IVIg) relieved her neuropathic flare-ups and improved her nerve fiber density. Nortriptyline also partially alleviated her neuropathic pain.

SUMMARY/CONCLUSION: Both cases depict burning pain and dysautonomia as predominant symptoms of antiplexin-D1 antibody-associated SFN. Steroids failed to alleviate symptoms in either case, but the second patient experienced improvement with IVIg, suggesting its potential efficacy in refractory cases.

Michael Limia, MS

Medical Student Research Award Recipient

Disclosures:

Rachana Gandhi Mehta - has received research support from Akcea (now Ionis Pharmaceuticals, Inc.), Graticule and UCB Pharma. She is a Site Investigator for the Rare Disease Network for Myasthenia Gravis (MGNet) National Institute of Neurological Disorders & Stroke. She has participated in advisory boards for UCB Pharma and has received speaker honoraria from UCB Pharma. She has also served as a NEJM Group Clinical Reasoning Contributing Editor for NEJM Healer.

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CASE REPORT: SCRAMBLER THERAPY REDUCES EFFECT OF PERIPHERAL NEUROPATHY

Nolan Abdelsayed (Washington, DC), Nathan Abdelsayed (Los Angeles, CA), Justin Barsoum (Redondo Beach, USA), Alanna Reddy (Redondo Beach, USA)

INTRODUCTION/BACKGROUND: Neuropathic pain presents a significant challenge in clinical practice, often proving refractory to conventional treatment modalities. Scrambler therapy, an electroanalgesia therapy, has emerged as a potential solution for managing chronic neuropathic pain that remains unresponsive to standard interventions.

CASE REPORT: We present the case of a 66-year-old male suffering from persistent bilateral hand and foot pain attributed to small fiber painful peripheral neuropathy. Despite undergoing an exhaustive 2-year trial of various treatments, including methotrexate, acupuncture, CBD oil, low level laser light therapy, topical lidocaine, compound cream, IV lidocaine drip, Qutenza patches, intravenous immunoglobulin (IVIg) home infusions, low-dose naltrexone, and transcranial magnetic stimulation he experienced no significant relief. The patient was initiated on scrambler therapy, which resulted in a remarkable 80% improvement in overall bilateral hand and foot pain.

SUMMARY/CONCLUSION: Scrambler therapy, operating on the principles of Melzack and Wall's gate control theory by activating C fiber surface receptors, presents a promising avenue for managing chronic neuropathic pain resistant to classical forms of relief. This case underscores the potential efficacy of scrambler therapy as a novel and effective intervention for patients with neuropathic pain refractory to conventional treatments. Further research and larger studies are warranted to validate the effectiveness of scrambler therapy.

Nolan Abdelsayed, BS

Medical Student Research Award Recipient

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FOCAL DYSTONIA FOLLOWING TRAUMA: CAN SURGERY MAKE IT BETTER?

Ian Ackers (Lansing, MI), Cheryl Craig (Berkley, MI), Michelle Andary (Grand Rapids, MI), Michael Andary (East Lansing, MI), Geoffrey Seidel (Troy, MI)

INTRODUCTION/BACKGROUND: Dysesthesias in complex regional pain syndrome (CRPS) are common and well described; whereas dystonia symptoms are common but poorly understood. We present a case of focal dystonia following trauma, initially diagnosed as CRPS Type-1, later classified as CRPS Type-2.

CASE REPORT: A 28-year-old male presents with right foot pain, dysesthesia, and muscle cramping following local traumatic injury 3 years prior and was previously diagnosed with CRPS-Type 1. Previous work-up demonstrated normal labs, bone scan, and prior EDX testing was normal but tibial nerve was not evaluated. Right ankle MRI demonstrated marrow edema in the talus and calcaneus. Exam revealed dystonic posturing of the long toe flexors/extensors and foot intrinsic muscles. Full strength and normal reflexes were noted. He walked on the lateral aspect of the foot with absent heel strike. Allodynia/hyperpathia was present in the medial plantar nerve distribution with sensory loss along the lateral plantar nerve. Tinel Sign was positive at the tarsal tunnel. Repeat EDX testing demonstrated tibial neuropathy in the tarsal tunnel without active denervation. A tibial nerve block resulted in temporary resolution of dystonia and dysesthesias. Tarsal tunnel release resulted in complete resolution of sensory dysesthesias and dystonic muscle contractions.

SUMMARY/CONCLUSION: Response of the central nervous system to peripheral nerve trauma is complex and poorly understood. Previously reported treatments for CRPS 1&2 related dystonia lack efficacy. We report resolution of CRPS, tibial neuropathy, and dystonia after surgical release of the tarsal tunnel. Further investigation into mechanisms of focal dystonia is warranted.

Ian Ackers, DO, PhD

Resident and Fellow Member Award Recipient

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EXACERBATION OF ANTI-MAG NEUROPATHY WITH IMMUNE CHECKPOINT INHIBITOR

Malak Alaboudi (Cleveland, OH), Bashar Katirji (Cleveland, OH)

INTRODUCTION/BACKGROUND: Immune checkpoint inhibitors (ICPI) are monoclonal antibodies that have emerged as treatment for various types of cancer. ICPIs bind to cytotoxic T lymphocytes, activating the immune system to target and destroy the tumor cells. Although ICPI therapy is effective, one of the most feared adverse events are immune-related adverse events (irAEs). Immune neuropathy associated with anti-myelin associated glycoprotein (MAG) antibodies is a well-known nodo-paranodopathies.

CASE REPORT: A 78-year-old man presented with 3-4 months history of numbness, tremors, and gait instability. Neurological examination revealed tremors, impaired vibration and position sense, and absent reflexes. NCS revealed slowed upper limb motor conduction velocities ranging from 17-25 m/s and neuromuscular US showed hypertrophic multifocal neuropathy, Serum anti-MAG IgM antibodies were significantly elevated (1/204,800; Normal <1/1600). He was diagnosed with stage 4 non-small lung cancer and started on Pembrolizumab. He responded well to pulse therapy. 2 days after treatment, he developed worsening severe sensory ataxia, became bedridden and was hospitalized. Anti-MAG IgM antibodies rose back to 1/204,800. Treatment with plasma exchanges and methylprednisolone led to improvement. Pembrolizumab was stopped and he died 6 months later.

SUMMARY/CONCLUSION To our knowledge, there have been no reports of induced or exacerbated anti MAG neuropathy with the use of ICPI therapy. This observation should be added to the existing knowledge on neuromuscular complications associated with ICPI therapy. This should be added to other neuromuscular autoimmune diseases reported including myasthenia gravis, myositis, chronic inflammatory demyelinating polyneuropathy, and concurrent myositis and myasthenia gravis.

Malak Alaboudi, MD

Resident and Fellow Member Award Recipient

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LATE-ONSET RIBOFLAVIN-RESPONSIVE MULTIPLE ACYL-COA DEHYDROGENASE DEFICIENCY MISDIAGNOSED AS POLYMYOSITIS

Gustavo Arce Gomez (Cincinnati, OH), Hani Kushlaf (Cincinnati, OH)

INTRODUCTION/BACKGROUND: Multiple acyl-CoA dehydrogenase deficiency (MADD) is a rare autosomal recessive disorder of fatty acid oxidation. The late onset forms are clinically heterogeneous with variable symptoms ranging from episodes of metabolic decompensation to chronic muscular symptoms. We report the clinical features and test results of a patient with late-onset riboflavin-responsive MADD (RR-MADD) misdiagnosed as polymyositis.

CASE REPORT: A 41-year-old man was referred by a rheumatologist for treatment-resistant polymyositis. Intermittent treatment with prednisone did not result in symptom resolution. The patient developed, at the age of 33 years, episodic muscle pain, leg weakness, shortness of breath, and palpitations. During the episodes, the creatine kinase is higher than a thousand and remains elevated between episodes. Walking for more than an hour on a mail delivery route with dehydration is the only potential trigger. The neurologic exam showed a left-winged scapula, and mild weakness of shoulder external rotation, hip extension, and hip flexion. EDX testing revealed myopathic changes in the gluteus maximus muscles and increased insertional activity in the lumbar paraspinal muscles. Muscle biopsy specimens from the gluteus maximus and quadriceps showed lipid accumulation in vacuolated type 1 fibers and necrotic fibers, consistent with lipid storage myopathy. The serum acylcarnitine profile showed elevated levels of fatty acids of all chain lengths. Genetic testing confirmed two homozygous (p.P456L) pathogenic ETFDH mutations. Riboflavin treatment resulted in immediate marked improvement in all symptoms.

SUMMARY/CONCLUSION: RR-MADD can be difficult to recognize. The episodic symptoms in our patient argue against polymyositis. Appropriate laboratory workup and genetic testing are essential in diagnosing this treatable disorder.

Gustavo Arce Gomez, MD

Resident and Fellow Member Award Recipient

Disclosures:

Hani Kushlaf - receives grant funding, paid to his institution, from the MDA, Sanofi, and Healey ALS platform trial.

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NEUROMUSCULAR ULTRASOUND OF NEUROLYMPHOMATOSIS IN B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

Adebola Awolesi (Bethesda, MD), Kyle Tse (Bethesda, MD), Sara Silbert (Bethesda, MD), Rafael Rojas (San Jose, Costa Rica), Atsede Akalu (Bethesda, MD), Nirali Shah (Bethesda, MD), Tanya Lehky (Bethesda, MD)

INTRODUCTION/BACKGROUND: Neuromuscular ultrasound (NMUS) is commonly employed to complement EDX studies in the diagnosis of mononeuropathies. Use of nerve ultrasound characteristics, of echogenicity, vascularity, and cross-sectional area can be used to identify specific nerve pathology, such as compressive lesions, nerve infiltration, and presence of masses such neurofibromas. NMUS has the distinct advantage of bedside convenience and no requirement for contrast media. We present a case of neurolymphomatosis followed by NMUS in a patient diagnosed with B-cell acute lymphoblastic leukemia (ALL).

CASE REPORT: A 27-year-old female with a diagnosis of B-cell ALL presented with 10 months of increasing left hand pain, numbness, and weakness. Biopsy showed relapse of ALL adjacent to the left median nerve. Symptoms partially improved with chemotherapy and steroid but then worsened. Examination revealed numbness of the thumb, index, and middle fingers along with weakness of left median-innervated hand muscles, with mild bilateral (left greater than right) proximal arm and left toe weakness. NMUS of the left median nerve showed diffuse enlargement and hypervascularity most prominently at the forearm segment. These findings correlated with MRI which showed contrast enhancement of the median nerve. NCS also showed left median neuropathy. Patient received chimeric antigen receptor T-cell therapy with transient worsening median nerve conduction velocity and slight increased size of nerve on NMUS during cytokine release syndrome. Subsequent NMUS which showed resolution of hypervascularity with continued enlarged median nerve. Median NCS improved but remained abnormal. There was clinical improvement in symptoms and strength.

SUMMARY/CONCLUSION: NMUS remains a valuable diagnostic tool for accessing pathological processes affecting nerves.

Adebola Awolesi, MB, BS

Resident and Fellow Member Award Recipient

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A CASE REPORT: COVID-19 ASSOCIATED MULTIFOCAL MOTOR NEUROPATHY

Alexander Bader (Chicago, IL), Qin-Li Jiang (Chicago, IL), Nida Gleveckas-Martens (Chicago, IL)

INTRODUCTION: Mutations in the gene encoding superoxide dismutase 1 (SOD1) have been associated with about 2% of sporadic cases of ALS and 20% of familial cases. Tofersen is an antisense oligonucleotide which reduces toxic SOD1 protein synthesis and prevents neuronal degeneration caused by gain of function of the mutant protein. In the phase 3 trial of tofersen for SOD1 ALS, although it resulted in reductions of SOD1 protein and neurofilament light chains in plasma, it was not associated with a significant improvement in the primary clinical endpoint quantified by the ALSFRS-R score.

OBJECTIVE: In this case report, we describe a 71-year-old male with a history of familial ALS, who presented to the neuromuscular clinic for 1 year of progressive right leg weakness and received tofersen for SOD1 ALS.

CASE REPORT: Exam findings of right lower extremity weakness and atrophy with cramping and fasciculations were indicative of lower motor neuron disease, while diffuse hyperreflexia and the release of primitive reflexes were indicative of upper motor neuron findings. Genetic testing for ALS revealed the missense SOD1 variant c.256G>C (p. Gly86Arg). We report a positive response to intrathecal tofersen, with stability of the ALSFRS-R score, at 41/48, as well as a sustained decrease in cerebrospinal fluid levels of neurofilament light chain.

SUMMARY/CONCLUSION: One consideration for our patient’s response is the early initiation of tofersen (ALSFRS-R 40/48 at time of initiation). Though further study is needed, our case suggests that early genetic evaluation for ALS patients and early enrollment for treatment with tofersen may be clinically beneficial.

Alexander Bader, MD

Resident and Fellow Member Award Recipient

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NEUROMUSCULAR ULTRASOUND TO TEACH PERIPHERAL NERVOUS SYSTEM ANATOMY FOR NERVE CONDUCTION STUDIES AND ELECTROMYOGRAPHY

Marie Beaudin (Redwood City, CA), Kenneth Leung (Mountain View, CA), Sarada Sakamuri (Palo Alto, CA)

INTRODUCTION: In-depth knowledge of peripheral nervous system (PNS) anatomy is essential for trainees who are learning to perform nerve conduction studies (NCS) and electromyography (EMG). Neuromuscular ultrasound (NMUS) is a potentially useful tool for teaching PNS anatomy via live visualization of nerves and muscles and their relationships to important adjacent structures.

OBJECTIVE: The objective of this study was to explore the impact and experience of two live NMUS-based PNS anatomy courses targeted towards neuromuscular/EMG fellows.

METHODS: A needs assessment survey was completed by graduating fellows. A subsequent group of five incoming fellows completed two 2-hour in-person, interactive NMUS-based teaching sessions covering basic and advanced PNS anatomy relevant to NCS/EMG. Pre- and post-course surveys were completed by the participants.

RESULTS: All graduating fellows reported they would have benefited from additional teaching on PNS anatomy. At baseline, three of five incoming fellows rated their knowledge of nerve trajectory and depth as poor or very poor; after the first session, this improved to zero fellows. After two sessions, five out of five participants were satisfied with the training and rated it as very or extremely useful. All participants reported the course improved their grasp of nerve and muscle anatomy and level of confidence in performing NCS and EMG.

SUMMARY/CONCLUSION: NMUS is a useful tool for teaching essential anatomy to fellows training in NCS and EMG. Such teaching may improve fellows' accuracy, safety, and confidence around these procedures. Future research could compare different modalities for teaching and evaluating fellows' knowledge of PNS anatomy.

Marie Beaudin, MD, MSc

Resident and Fellow Member Award Recipient

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ASSESSING GLUCOCORTICOID ASSOCIATED TOXICITY IN MYASTHENIA GRAVIS USING THE GLUCOCORTICOID TOXICITY INDEX

Marie Beaudin (Redwood City, CA), Amanda Yaworski (Ottawa, CA), Srikanth Muppidi (Palo Alto, CA), Neelam Goyal (Palo Alto, CA)

INTRODUCTION: Glucocorticoids (GC) are mainstay therapy for the treatment of myasthenia gravis (MG). However, treatment is linked to many short- and long-term side effects. There is lack of quantitative data measuring the level of GC-associated toxicity in MG.

OBJECTIVE: The glucocorticoid toxicity index (GTI) is a weighted, validated clinical outcome assessment tool designed to measure and quantify GC related toxicity. The objective of this study is to quantify the burden of GC related toxicity in patients with MG using the GTI. Additionally, we aim to explore correlation between GTI scores and cumulative prednisone exposure and MG outcome measures.

METHODS: This is a monocentric, prospective, observational, non-interventional study. We aim to enroll 50 MG patients on prednisone 10 mg daily or higher without a secondary autoimmune disease. Enrolled patients will be assessed during three visits over 1 year (baseline, 3 to 6 months, 9 to 12 months). At each visit, the GTI and adverse event unit (AEU) will be completed, as well as disease burden and severity with the MG-Activies of Daily Living (ADL), MG Composite, and MG-Quality of Life15R validated scales.

RESULTS: All adult patients presenting for initial evaluation or follow up of MG were systematically screened for eligibility starting in October 2023. As of March 8, 2024, 167 patient visits were screened for eligibility. There were 31 patients who met the eligibility criteria, of which 27 were enrolled. The main reasons for exclusion were GC equivalent prednisone dosing <10 mg daily and telemedicine appointments.

SUMMARY/CONCLUSION: This study will allow quantitative evaluation of GC adverse effect burden in a cohort of patients with MG.

Marie Beaudin, MD, MSc

Resident and Fellow Member Award Recipient

Disclosures:

Marie Beaudin - is a sub-investigator on this research project, which was funded through an investigator-initiated grant by Argenx Pharmaceutical.

Amanda Yaworski - consulting activities for Novartis. Sub-investigator on this research project, which was funded through an investigator-initiated grant by Argenx Pharmaceutical.

Srikanth Muppidi - consulting and advisory activities for Alexion, Argenx, UCB/Ra Pharma, and Amgen. Sub-investigator on this research project, which was funded through an investigator-initiated grant by Argenx Pharmaceutical.

Neelam Goyal - is a principal investigator on this research project, which was funded through an investigator-initiated grant by Argenx Pharmaceutical. Consulting and advisory activities for Alexion, Argenx, Janssen, Lycia Therapeutic, Inc, UCB/Ra Pharma, and Amgen.

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CHRONIC NEUROPATHY AND A SUPERIMPOSED NEUROMUSCULAR JUNCTION DISORDER IN A DIFFICULT TO WEAN PATIENT: A CASE REPORT

Miriam Bekhit (Brooklyn, NY), Lawrence Chan (Brooklyn, NY), Sanjeev Agarwal (Brooklyn, NY)

INTRODUCTION/BACKGROUND: Neuromuscular disorders are increasingly recognized as a complication in patients in the ICU and represent a common cause of prolonged ventilator dependency.

CASE REPORT: A 67-year-old female with chronic obstructive pulmonary disease presented with shortness of breath, diagnosed with hypercapnic respiratory failure, necessitating ICU admission and continuous positive airway pressure from which weaning was challenging. Physical examination revealed 4/5 shoulder abduction, 5/5 elbow flexion/extension, 5/5 wrist flexion/extension, 3/5 hip flexion, 5/5 knee extension, 4/5 knee flexion, and 4/5 ankle dorsiflexion/plantar flexion strength bilaterally. Reduced vibration in both feet, and absent ankle reflexes. EDX testing showed chronic neuropathy and a superimposed neuromuscular junction disorder. Patient received pulse steroids, intravenous immunoglobulin (IVIg), and plasmapheresis due to no clinical improvement. Acetylcholine receptor antibody testing returned positive. Hospital course was complicated by worsening respiratory status, leading to tracheostomy due to ventilator dependence. Pyridostigmine was discontinued due to side effects. Patient completed a cycle of rituximab and was started on steroids. Autoimmune panel revealed no significant findings. Repeat EDX testing for persistent proximal weakness and weaning trial failures showed chronic axonal neuropathy, resolution of the previously observed decrement on repetitive nerve stimulation (RNS), with no evidence of myopathy. Symptoms were likely attributed to superimposed critical illness neuropathy/myopathy.

SUMMARY/CONCLUSION: More than one neuromuscular syndrome may occur simultaneously in ICU patients. Distinguishing between these syndromes can be challenging. EDX studies including RNS can help clarify the diagnosis in most cases and are recommended for any ICU patient experiencing unexplained weakness.

Miriam Bekhit, MD

Resident and Fellow Member Award Recipient

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EXPLORING THE LINK BETWEEN GLOSSOPHARYNGEAL NERVE DISORDER AND DIABETES MELLITUS: A RETROSPECTIVE ANALYSIS OF THE COSMOS-EPIC DATABASE

Nicholas Bellacicco (Newark, NJ), Kazim Jaffry (Colonia, NJ), Roopa Sharma (Harrison, NJ), Yaqian Xu (Newark, NJ), Hariharan Venkataraman (Newark, NJ), Mustafa Jaffry (Edison, NJ), Justin Matos (Edison, NJ), Nizar Souayah (Westfield, NJ)

INTRODUCTION: The relationship between glossopharyngeal nerve dysfunction and diabetes has not been extensively studied.

OBJECTIVE: To examine the occurrence of glossopharyngeal nerve disorder (CNIXD) in patients with HbA1c levels below and equal to or above 6.5%. Additionally, the prevalence of CNIXD among diabetic patients was compared to that in the general population.

METHODS: A retrospective electronic medical records analysis was completed using EPIC Cosmos. Keywords utilized were “glossopharyngeal neuralgia,” “glossopharyngeal sensory disorder,” and “glossopharyngeal motor disorder.” Data was collected from 1/01/2017 to 01/01/2024.

RESULTS: A total of 2,962 patients were analyzed and two groups were compared (n=2,400, CNIXD+ HbA1C <6.5% vs n=562, CNIXD+ HbA1C ≥ 6.5%). When comparing the two groups, respectively, there was a significant difference ($p<0.05$) in skilled nursing facility (SNF) rate (5.1% vs 9.1%), BMI over 30 (56.6% vs 74.6%), Age (63 years +/- 0.61 years vs 68 years +/- 1.04 years), and disability (6.6% vs 10.5%). There was a significant difference in male and female groups with males (30.8% vs 38.3%) and females (69.2% vs 61.7%). There was no significant difference between mortality rate, mechanical ventilation, and length of stay between the two groups. The rate of CNIX disorder development in patients with diabetes compared to the general population was (0.006% vs 0.002%, OR 2.307 [2.166, 2.458].

SUMMARY/CONCLUSION: Patients with both glossopharyngeal nerve disorders and diabetes experienced higher morbidity compared to non-diabetic individuals. The incidence of CNIX disorder among diabetic patients exceeds that of the general population. Further research is required to explore the connection between diabetes and CNIX dysfunction.

Nicholas Bellacicco, DO

Resident and Fellow Member Award Recipient

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CASE REPORT: AN UNUSUAL PATTERN OF DIFFUSE COMPLEX REPETITIVE DISCHARGES ISOLATED TO ONE MYOTOME IN A PATIENT WITH SEVERE RADICULOPATHY AND ANTERIOR HORN CELLS INJURY

Abdalmalik Bin Khunayfir (Cleveland, OH), Soheil El-Azzouni (Cleveland, OH), Robert Adams (Cleveland, OH)

INTRODUCTION/BACKGROUND: Complex repetitive discharges (CRDs) are a type of spontaneous activity on EMG that is estimated to happen once in every 200 EMG studies. CRDs are most often seen in either myopathic processes where they can be diffuse, or neurogenic processes with grouped active denervation. Here, we report a unique finding of diffuse CRDs in one myotome due to severe chronic and active neuropathic injury.

CASE REPORT: A 62-year-old man presented with 40 years of right neck and shoulder pain, along with subjective right shoulder weakness, and no numbness in the right arm. His NCS was normal. EMG showed persistent CRDs at ~60 Hz in all C5 muscles examined: the biceps, deltoid, infraspinatus, and brachioradialis muscles. Chronic neuropathic changes were detected in all myotomes in the right arm. A cervical spine MRI showed an oval lesion consistent with myelomalacia at the right anterior horn cells at the C5 level, as well as severe multi-level spinal and neuroforaminal stenosis.

SUMMARY/CONCLUSION: CRDs almost always occur in only one muscle in a specific myotome. This case demonstrated a bizarre pattern of diffuse CRDs in all muscles of one myotome. We speculate that this is due to the unique combination of two neuropathic lesions: chronic MRI-proven anterior horn myelomalacia, that corresponds to the C5 myotome, and severe C5 neuroforaminal stenosis likely causing active denervation. This study highlights the importance of looking into other etiologies of CRDs when robust unusual findings are seen.

Abdalmalik Bin Khunayfir, MD

Resident and Fellow Member Award Recipient

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CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHYDUE TO NEUROBORRELIOSIS: A CAUSATION OR ASSOCIATION?

Abdalmalik Bin Khunayfir (Cleveland, OH), Anthony Zampino (Cleveland, OH), Yiyi Zhang (Cleveland, OH), Bashar Katirji (Cleveland, OH)

INTRODUCTION/BACKGROUND: Lyme disease, is caused by the Borrelia burgdorferi sensu lato complex. The neurological manifestation of Lyme disease, or Neuroborreliosis, usually appears within the first 2 months post-infection. Peripheral neuropathy associated with Lyme disease almost always involves axonal injury, with demyelinating pathophysiology being exceedingly rare. It is unclear which patients have monophasic illness, and which patients require long-term immunosuppression.

OBJECTIVE: This report highlights two unique cases consistent with chronic inflammatory demyelinating polyneuropathy (CIDP) in association with neuroborreliosis, and to propose a classification schema for demyelinating neuropathy in association to neuroborreliosis.

CASE REPORT: Case one describes a 54-year-old man who developed CIDP, requiring long-term intravenous immunoglobulin (IVIg) and immunosuppression. This occurred after recovering from two prior attacks of neuropathy in conjunction with tick bites and confirmed Lyme disease in the prior 20 years. Case two describes a 21-year-old woman who developed subacute onset of sensory neuropathy and was found to have demyelinating neuropathy by EDX and ultrasound. Her cerebrospinal fluid analysis confirmed the presence of Lyme antibodies. She has required long-term IVIg for CIDP.

SUMMARY/CONCLUSION: These cases underscore that Lyme disease may trigger a chronic demyelinating condition akin to CIDP and requiring long-term immunomodulation/immunosuppression. The term Borrelia associated demyelinating autoimmune neuropathy (BADAN) is proposed, to aid in awareness and to include evaluation for Lyme disease for demyelinating neuropathies.

Abdalmalik Bin Khunayfir, MD

Resident and Fellow Member Award Recipient

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NEUROMUSCULAR COMPLICATIONS OF IMMUNE CHECKPOINT INHIBITORS: A CASE SERIES

Abigail Bose (Worcester, MA), James Lanni (Worcester, MA), David Cachia (Worcester, MA)

INTRODUCTION: Immune checkpoint inhibitors (ICIs) have become a mainstay in the treatment of many solid tumors over the past 10 years. Rarely, the initiation of ICIs can lead to activation of the host immune system against another target, leading to unintended autoimmune inflammation of other end organs. When the neuromuscular system is affected, immune-related adverse events (ir-AEs) described in the literature include myositis, myasthenic syndromes, and acute sensory and motor neuropathies.

OBJECTIVE: To present three cases of ir-AEs affecting the neuromuscular system in individuals receiving ICIs.

METHODS: We describe three cases who presented to a tertiary care center from 2022-2024.

RESULTS: Two patients had lung adenocarcinoma and were treated with pembrolizumab. One patient had gastroesophageal junction adenocarcinoma treated with nivolumab. All three began experiencing symptoms within the first 3 months of therapy. Each patient was found to be seropositive (acetylcholine receptor antibody, MuSK antibody, and striated muscle antibody) for an autoantibody implicated in myasthenia gravis. All three patients came off immunotherapy, not pursuing further cancer-directed treatments and eventually transitioned to comfort care.

SUMMARY/CONCLUSION: Neuromuscular irAEs remain a rare complication of immune checkpoint inhibitor therapy. We hereby emphasize that though in general most cases described in the literature improve with treatment, in a subset of patients, including our patient cohort, NM ir-AEs lead to termination of their cancer-directed care and transition to comfort care. Better understanding of how to effectively treat NM ir-AEs or how to identify patients at higher risk of developing these complications are needed.

Abigail Bose, MD

Resident and Fellow Member Award Recipient

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PARTIAL MOTOR CONDUCTION BLOCK IN INHERITED NEUROPATHIES

Kelby Brown (Chapel Hill, NC), Vinay Chaudhry (Chapel Hill, NC), Charlotte Sumner (Baltimore, MD)

INTRODUCTION: Conduction block (CB) in peripheral nerve is reduction in proximally vs distally stimulated compound muscle action potential (CMAP) amplitude or area. CB represents failure of nerve impulse to propagate in some (partial) or all (complete) of the structurally intact motor axons. While commonly seen in acquired demyelinating neuropathies, CB is not considered a feature of inherited demyelinating neuropathies.

OBJECTIVE: To describe four patients with inherited demyelinating neuropathies that demonstrate partial motor conduction block (PMCB) on NCS.

METHODS: A retrospective chart review was done to identify CMT patients who showed PMCB on their NCS. PMCB was defined by ≥30% amplitude reduction of the proximal relative to distal negative peak CMAP amplitude (Eur J Neurol. 2021; 3556–3583). Sites of entrapment were excluded.

RESULTS: Four patients with confirmed CMT were found to have PMCB. Two patients (26M, 54M) had CMT1A, one (20F) had CMT1B, and one (50M) had CMTX. All presented with typical clinical features of CMT including slowly progressive length-dependent sensorimotor deficits, areflexia. CMT Neuropathy Scores ranged from 7-20 (Mean 12.75). PMCB was demonstrated in the wrist-elbow segment of median nerve in all patients; elbow-axilla segment of median nerve in one patient; wrist-elbow segment of ulnar nerves in two patients; and above elbow-axilla segment of ulnar nerve in one patient. NCS also demonstrated diffuse uniform slowing in the range of 10-20 m/s in patients with CMT1A/1B, versus 30-40 m/s in one patient with CMTX.

SUMMARY/CONCLUSION: Inherited demyelinating neuropathies can present with atypical NCS findings such as PMCB, mimicking acquired neuropathies.

Kelby Brown, MD, MA

Resident and Fellow Member Award Recipient

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A CASE OF GM1-ANTIBODY CIDP COMPLICATED BY RESPIRTAORY FAILURE RESPONSIVE TO RITUXIMAB

Andrew Chapman (Charlottesville, VA), Darayus Toorkey (Charlottesville, VA), Guillermo Solorzano (Charlottesville, VA)

INTRODUCTION/BACKGROUND: Anti-GM1 antibodies are classically associated with multifocal motor neuropathy, rather than chronic inflammatory demyelinating polyneuropathy (CIDP.) CIDP usually responds to intravenous immunoglobulin (IVIg), plasma exchange (PLEX), and corticosteroids, and typically does not result in neuromuscular respiratory failure.

CASE REPORT: A 55-year-old man presented with symmetric, progressive weakness of all extremities (upper extremity predominant) over 3 weeks. His Medical Research Council (MRC) score was 44. An MRI of the brain and C-spine with and without contrast was nonrevealing. His cerebrospinal fluid showed albuminocytologic dissociation. A motor NCS showed markedly prolonged latency of the ulnar and tibial nerves, and an absent F wave response in the ulnar nerve. Sensory NCS showed reduced amplitude of the median and ulnar nerves. He improved after five treatments of PLEX. His weakness progressed 3 weeks later. A serum demyelinating panel revealed IgM antibody against GM1. With 2x/week PLEX, his MRC score was 39. However, reduction to weekly PLEX resulted in decrease of MRC score to 18. Despite adjuvant cyclophosphamide monthly, the patient had a significant relapse, including of his respiratory status. He was hospitalized – with prolonged intubation - for 2 months, during which he failed to respond to IVIg, PLEX, and cyclophosphamide. However, after rituximab initiation he improved sufficiently for discharge. He has been maintained on rituximab every 6 months with sustained remission.

SUMMARY/CONCLUSION: This case represents GM1-associated CIDP which showed poor response to traditional therapies, culminating in neuromuscular respiratory failure. His course was subsequently salvaged with rituximab. This suggests a role for B-cell-depleting therapy in refractory CIDP.

Andrew Chapman, MD

Resident and Fellow Member Award Recipient

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MEDIAL PECTORALIS MAJOR MUSCLE ATROPHY WITH CLAVICULAR HEAD SPARRING IN A BODYBUILDER

Byron Cheon (Miramar, FL), Tyler Kendall (Miami, FL), Sydney Shaffer (Miami, FL), Karim Salame (Miami, FL)

INTRODUCTION/BACKGROUND: Continuous muscle innervation is crucial for muscle growth and viability, yet interruptions in nerve supply can lead to atrophy. While cases of muscle atrophy due to nerve damage and denervation atrophy have been documented, we present a rare instance of atrophy of the sternocostal head of the pectoralis major muscle, sparing the clavicular head. This phenomenon has been described as secondary to hypertrophy of the pectoralis minor muscle impinging on the medial branch of the pectoral nerve.

CASE REPORT: A 45-year-old bodybuilder with well-controlled HIV on Biktarvy presented with weakness and atrophy of the right pectoralis muscle, devoid of trauma or pain. Both pectoralis muscles exhibited medial atrophy, with the right side more affected than the left. No weakness was noted in his upper extremities, and there were no other atrophied muscles or myelopathic findings upon examination. MRI scans of his cervical, thoracic, and lumbar spines revealed mild degenerative changes but were largely unremarkable. EMG studies indicated severe medial pectoral branch neuropathy with active denervation, alongside moderate C5 and L5 radiculopathies. The patient was advised to avoid exercises that could exacerbate hypertrophy of the pectoralis minor muscle, emphasizing the importance of tailored physical therapy intervention.

SUMMARY/CONCLUSION: This case underscores the importance of recognizing atypical presentations of muscle atrophy, particularly in specialized populations like bodybuilders, where hypertrophy-related neuropathies may occur. It emphasizes the necessity of tailored physical therapy interventions and avoidance of exacerbating factors to manage such conditions effectively.

Byron Cheon, MD, MS

Resident and Fellow Member Award Recipient

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THE ROLE OF NEUROMUSCULAR ULTRASOUND IN COMPRESSION NEUROPATHIES: A CASE REPORT OF A TIBIO-FIBULAR GANGLION CYST

Lauren Cooper (Jefferson, LA), Evan Reuter (New Orleans, LA), Marc Raj (Mandeville, LA)

INTRODUCTION: A ganglion cyst is a benign tumor arising from a musculoskeletal structure. While these are commonly identified in the upper extremities, they are far less common in the lower extremities. Utilizing neuromuscular ultrasound (NMUS) as an adjunctive tool to EMG may be helpful to identify a cause for compressive neuropathies and directing appropriate treatment.

CASE REPORT: A 55-year-old man with a past medical history of diabetes mellitus presented to the EDX lab with a 3-month history of right great toe weakness and foot paresthesia. He described an inability to extend his great toe with gait instability. NCS showed intact amplitudes of both sural and superficial peroneal sensory nerve action potentials (SNAPs). Peroneal motor study to the extensor digitorum brevis (EDB) was unable to be obtained due to muscle atrophy, but conduction velocity was preserved when recording the peroneal response over the tibialis anterior (TA). EMG was significant for fibrillations in the TA and extensor hallucis longus (EHL). EMG of the short head of the biceps femoris and peroneus longus were both normal. The deep peroneal nerve was identified on NMUS. After passing the fibular head, an anechoic region arising from the proximal tibio-fibular joint and measuring 4 x 1.2 x 1.2 cm was found to be compressing the nerve along its path.

SUMMARY/CONCLUSION: Utilizing NMUS can be helpful to direct treatment recommendations for compressive neuropathies. Using EDX studies alone cannot always capture the full picture and may lead to unnecessary diagnostic testing or inappropriate treatment approaches.

Lauren Cooper, MD

Resident and Fellow Member Award Recipient

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ISOLATED EXTENSOR DIGITORUM COMMUNIS WEAKNESS AFTER A GOUT FLARE

Lauren Cooper (Jefferson, LA), Troy Sbisa (New Orleans, LA), Taylor Bosch (New Orleans, LA), Andrew Simoncini (Mandeville, LA), Robert Patrick Owens (New Orleans, LA)

INTRODUCTION/BACKGROUND: A gout flare is a result of monosodium urate crystal deposition in joints and soft tissues causing an inflammatory arthritis. Involvement of a single joint in the lower extremity, most often the first metatarsophalangeal joint or the knee, is typical of initial gout flares. However, the infrequent presentation of gout in the upper extremities, along with associated weakness and tendinopathy, can cause diagnostic confusion.

CASE REPORT: A 70-year-old man presented to the EDX lab with a history of 7 months of isolated weakness with extension of digits III-V of his right hand. Further history was significant for a severe gout flare in that hand, extending up to his mid-forearm. There were no sensory abnormalities or pain. Physical exam was significant for slight hypothenar atrophy on the right. Strength was intact except for 2/5 strength in extension of digits III-V on the right and 4/5 strength in right finger abduction. NCS showed a focal right ulnar mononeuropathy. Radial sensory and motor studies were within normal limits. EMG was normal aside from decreased muscle activation in the right extensor digitorum communis (EDC) due to fatigue. Diagnostic ultrasound was performed given suspicion for musculoskeletal etiology. The EDC tendons were enlarged with increased peritendinous fluid. MRI showed near complete tearing of the 3rd and 4th EDC tendons.

SUMMARY/CONCLUSION: It is always important to consider that weakness may be of musculoskeletal origin rather than neurologic. Although less common in the hands, gout may cause severe tendinopathy, which may manifest as weakness in a patient presenting to the EDX lab.

Lauren Cooper, MD

Resident and Fellow Member Award Recipient

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UTILITY OF BILATERAL VERSUS UNILATERAL ELECTRODIAGNOSTIC TESTING FOR LUMBOSACRAL RADICULOPATHY IN PATIENTS WITH NORMAL CLINICAL EXAMINATION

Jessica Creager (Jacksonville, FL), Christopher Lamb (Jacksonville, FL)

INTRODUCTION: Bilateral lumbosacral radiculopathy is a common EDX referral reason. It is unclear whether bilateral EDX studies add sufficient diagnostic utility to justify additional discomfort and expense.

OBJECTIVE: The aim of this study was to determine the number of bilateral lower limb EDX studies needed to diagnose (NND) one additional lumbosacral radiculopathy compared to unilateral examination in selected patients.

METHODS: In this pilot study, we retrospectively reviewed EDX data for patients referred for radiculopathy who had symptoms of back pain and leg symptoms (symmetric or asymmetric) and normal examination. EDX interpretations were considered concordant when the laterality of radiculopathy diagnoses aligned with subjective symptoms. The proportion of concordant studies represents the sensitivity of unilateral EDX studies with the reference standard of bilateral studies. Using this value, NND for bilateral studies along with 95% confidence intervals were calculated.

RESULTS: Two of 17 patients with lumbosacral radiculopathy would not have been diagnosed with unilateral studies alone (NND 8.5, 95% CI 2.5-91). Approximately 181 patients would be required to narrow the NND 95% CI to between 6 and 13 based on this initial estimate of sensitivity.

SUMMARY/CONCLUSION: While it is not always necessary to perform bilateral EDX studies in select patients referred for bilateral lumbosacral radiculopathy, our findings suggest that bilateral studies are reasonable to perform given the relatively low NND (8.5) of bilateral versus unilateral studies. This pilot study provides a method of comparing the diagnostic utility of unilateral and bilateral EDX studies that can be used by other laboratories to refine their standard approach.

Jessica Creager, MD

Resident and Fellow Member Award Recipient

Disclosures:

Christopher Lamb - received grant support from Immunovant, Inc.

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A CASE OF FACIAL ONSET SENSORY AND MOTOR NEURONOPATHY (FOSMN)

Cynthia De la Rosa Zapata (Greer, SC), Eduardo Cortez-Garcia (Taylors, SC)

INTRODUCTION/BACKGROUND: Facial onset sensory and motor neuronopathy (FOSMN) is an extremely rare disease, with about 100 cases reported worldwide. It is characterized by paresthesias, in a trigeminal nerve distribution, which spread from cranial to caudal regions, followed by bulbar weakness. Its pathogenesis is unclear; however, it is believed to be a TAR DNA-binding protein (TDP)-43 proteinopathy and resemble ALS.

OBJECTIVE: To highlight a rare neurological disease and prevent delay in diagnosis.

CASE REPORT: A 70-year-old male presented with subacute onset of left upper and middle facial numbness. Exam revealed sensory loss predominantly to left V2 distribution with patchy involvement of V1, V3, and anisocoria. MRI brain was unremarkable. Twenty-months later, dense numbness progressed to the entire left trigeminal nerve distribution. New dysarthria, dysphagia, and weakness to muscles innervated by the hypoglossal, glossopharyngeal, bilateral lower facial, bilateral posterior interosseus and ulnar nerves were noted. Interval development of generalized hyporeflexia or areflexia was present.
Initial and repeat EDX studies revealed generalized motor neuron disease affecting bulbar and both extremity segments, and sensory neuronopathy of the bulbar segment. Neurofilament light chain was elevated. Autonomic reflex screen revealed an unspecified autonomic neuropathy. Testing for hereditary/autoimmune polyneuropathies, ALS, Kennedy's disease, paraneoplastic, metabolic, and infectious etiologies was negative. Given the history, clinical exam, and workup, FOSMN was diagnosed.

SUMMARY/CONCLUSION: FOSMN is a rare neurological disease with a characteristic onset pattern leading to low clinical suspicion when presenting with facial paresthesias. Has a variable prognosis. Its insidious progression requires prolonged surveillance and early diagnosis is critical for expedited care at an ALS multidisciplinary clinic.

Cynthia De la Rosa Zapata, MD

Resident and Fellow Member Award Recipient

DIFFERENTIATING IMMUNE MEDIATED NECROTIZING MYOPATHY FROM OTHER AUTOIMMUNE MYOPATHIES

Brandon Desowitz-Leibell (Las Vegas, NV), Se Won Lee (Las Vegas, NV)

INTRODUCTION/BACKGROUND: Immune mediated necrotizing myopathy (IMNM) is a rare autoimmune disease that causes subacute moderate to severe proximal weakness. Early immunosuppressant therapy with intensive rehabilitation may provide best long-term prognosis. EMG can be beneficial to distinguish IMNM from other autoimmune myopathies.

CASE REPORT: A 56-year-old Caucasian female without past medical history developed gradual bilateral lower extremity weakness 1 year prior to the presentation. She later developed upper extremity weakness, dysmasesis, and dysphagia. 11 months after symptom onset, she was admitted to the acute care unit due to aphonia and severe bilateral upper and lower extremity weakness, worse proximally. Sensations were intact. Labs revealed creatine kinase (CK) of 12,000. She was treated with intravenous immunoglobulin (IVIg) and steroids for presumed myopathy vs. immune-mediated neuropathies. Myositis panel including anti-signal-recognition-particle (SRP) and anti-3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) was negative. EMG in her inpatient rehabilitation unit stay demonstrated abnormal spontaneous activity with early recruitment in bilateral rectus femoris and left deltoid muscles, suggesting irritative myopathy. Subsequent muscle biopsy revealed scattered regenerating and necrotic muscle fibers with limited chronic lymphoid inflammation, suggesting IMNM. She was started on mycophenolate mofetil and continued PT/OT/ST, which significantly improved her strength, mobility, and functionality.

SUMMARY/CONCLUSION: This is a case of idiopathic IMNM, and an attempt to diagnose and differentiate it from other autoimmune myopathies or neuropathies. Positive anti-SRP/HMGCR quickly confirms IMNM. If negative, diagnosis is often delayed due to the necessity of EMG and muscle biopsy, thus delaying treatment. Delay in diagnosis and treatment can lead to extended stays in rehabilitation and poor health outcomes, including quality of life.

Brandon Desowitz-Leibell, DO

Resident and Fellow Member Award Recipient

CAN UPPER MOTOR NEURON LESIONS CAUSE ASYMMETRIC H-REFLEXES?

Alexander Doubek (Lansing, MI), Amber Vocelle (Lansing, MI), Ryan O'Shaughnessy (Lansing, MI), Madeline Niblock (Lansing, MI), Michael Andary (East Lansing, MI), Mathew Saffarian (East Lansing, MI)

INTRODUCTION/BACKGROUND: We present two cases of asymmetric tibial H-wave amplitude in the setting of upper motor neuron (UMN) pathology.

CASE REPORT: Case one involved a 35-year-old male with a history of thoracic myelopathy (Incomplete Brown-Sequard) status post laminectomy prior to presentation. He presented with bilateral lower extremity pain and left lower extremity weakness. On exam, he had left weaker than right lower extremity weakness (Grade 2-3 on left and 4 on the right) and hyperreflexia. Reflexes showed: left patellar 4/4, right patellar 3/4, left Achilles 3/4, right Achilles 2/4 (NIH Scale). EDX testing demonstrated right tibial H-wave amplitude of 0.2mV and left tibial H-wave amplitude of 10 mV and the left tibial was 2.2 ms faster.

Case 2 involved a 20-year-old female with a history of Chiari malformation type II and C2-T11 syrinx status post decompression. She presented with left-sided hemi-body pain and no weakness. Manual muscle testing revealed grade 5 strength for bilateral upper and lower extremities. There was asymmetric lower extremity hyperreflexia, left greater than right. Her left Achilles reflex was 4/4 and right 3/4. EDX demonstrated right tibial H-wave amplitude of 6 mV and left 12.5 mV. The left latency was 3.7 ms faster.

SUMMARY/CONCLUSION: We present two rare cases of asymmetric H-wave amplitudes and latencies with prior upper motor neuron pathology. We propose that this could be misinterpreted as peripheral nerve disease in asymmetric UMN disorder.

Alexander Doubek, DO

Resident and Fellow Member Award Recipient

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A CASE OF SEVERE PROGRESSIVE WEAKNESS, CACHEXIA, AND ATAXIA FOUND TO BE CONCURRENT SCURVY AND COGAN'S SYNDROME

Nga Ying Eng (Providence, RI), Vincent LaBarbera (West Warwick, RI)

INTRODUCTION/BACKGROUND: Initial symptoms of scurvy include fatigue, anorexia, easy bleeding, and dermatologic signs, but later stages may involve the musculoskeletal system. Cogan's syndrome is an autoimmune vasculitis with ocular and audio-vestibular impairment.

CASE REPORT: A 56-year-old woman with a history of obsessive-compulsive disorder, bilateral idiopathic optic nerve atrophy, and 2-3 years of hearing loss presented with progressive bilateral leg weakness, loss of balance, and marked weight loss over several months. Her exam was notable for mild dysmetria and diffuse muscle wasting with normal reflexes. Initial EMG revealed probable mild, length-dependent, large fiber polyneuropathy without evidence of lower motor neuron dysfunction, lumbosacral plexopathy, or demyelinating neuropathy. MRI brain, cervical and lumbar spine and neuropathy/myopathy labs were unrevealing. Repeat EMG showed a motor predominant neuropathic process. Muscle biopsy was negative for mitochondrial disease and extensive genetic testing did not provide a definitive diagnosis. Further investigations revealed positive atypical perinuclear anti-neutrophil cytoplasmic antibodies (1:40), elevated tumor necrosis factor alpha, interleukin-10, and interleukin-2. Malnutrition labs noted an undetectable vitamin C level. Overall, her progressive weakness and muscle wasting were deemed to be secondary to severe micronutrient deficiency and scurvy. She continues to undergo genetic and rheumatologic evaluation for optic nerve atrophy and hearing loss with a leading diagnosis of Cogan's syndrome.

SUMMARY/CONCLUSION: The presence of progressive weakness and muscle wasting warrants a broad differential to include inflammatory, nutritional, genetic/mitochondrial, degenerative causes, and/or multiple concurrent conditions. In this case, extensive testing was unrevealing for lower motor neuronopathy, and a multidisciplinary approach identified scurvy and Cogan syndrome as the primary causes.

Nga Ying Eng, MD

Resident and Fellow Member Award Recipient

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ALTERNATIVE DIAGNOSIS OF PATIENT SUSPECTED WITH AMYOTROPHYC LATERAL SCLEROSIS

Nurul Fadli (Depok, Indonesia), Winnugroho Wiratman (Jakarta Selatan, Indonesia), Ahmad Yanuar Safri (central jakarta, Indonesia), Fitri Octaviana (Jakarta Timur, Indonesia), Manfaluthy Hakim (Jakarta, Indonesia), Luh Ari Indrawati (Bekasi, Indonesia), Adrian Ridski Harsono (Jakarta Pusat, Indonesia), Astri Budikayanti (Jakarta, Indonesia)

INTRODUCTION: ALS is an adult-onset progressive neurodegenerative disorder involving both upper and lower motor neurons. ALS is a clinically heterogeneous disease, with chameleon presentations and several mimics.

OBJECTIVE: The aim of this study to evaluate other possible diagnoses of patients with suspected ALS.

METHODS: A cross-sectional study was conducted by taking secondary data from suspected ALS patients who visited the neurology clinic in Cipto Mangunkusumo and Universitas Indonesia hospital from January 2018 to February 2023. Data collected included demographic, clinical characteristics, and final diagnosis.

RESULTS: There were 62 patients with suspected ALS from January 2018 to February 2023. Twenty-seven (43.55%) patients were not diagnosed with ALS. Most of them were male (59.3%) with mean age 41.96 years (± 14.308). The symptoms t found in this group are limb weakness (85.2%), dysarthria (25.9%), dysphagia (25.9%), and fasciculation (22.2%). The final diagnosis of non-ALS patients included compressive myelopathy (25.9%), polyneuropathy (18.5%), syringomyelia (14.8%), myopathy (14.8%), hereditary spastic paraplegia, benign fasciculation syndrome, multiple sclerosis, progressive supranuclear palsy, stroke, and space occupying lesion.

SUMMARY/CONCLUSION: Compressive myelopathy, polyneuropathy, myopathy or muscular dystrophy, hereditary spastic paraplegia, benign fasciculation syndrome, multiple sclerosis, progressive supranuclear palsy, stroke, and space occupying lesion, can be alternative diagnoses in patients with suspected ALS.

Nurul Fadli, MD

Resident and Fellow Member Award Recipient

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SMALL FIBER NEUROPATHY PROGRESSING TO CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

Andrew Feldman (New York City, NY), Ashwin Malhotra (Englewood Cliffs, NJ), Mary Vo (New York, NY), Norman Latov (New York, NY)

INTRODUCTION/BACKGROUND: Patients with small fiber neuropathy (SFN) typically present with paresthesias and pain, distal sensory loss examination, and normal EDX studies. The diagnosis is confirmed by skin punch biopsy demonstrating a reduction in the intraepidermal nerve fiber density (IENFD). Idiopathic SFN is most often non-progressive, but 10-36% subsequently develop large fiber neuropathy. Progression to chronic inflammatory demyelinating polyneuropathy (CIDP), has not previously been reported.

CASE REPORT: This 42-year-old, right-handed man presented with 1 year of numbness, burning thigh pains, and myalgias. Skin biopsy showed reduced IENFD, consistent with SFN. Initial EMG and serological tests were normal. Over 10 months he developed increased numbness, paresthesias, and mild proximal leg weakness. Repeat EMG/NCS revealed a sensory motor polyneuropathy with multiple demyelinating abnormalities fulfilling criteria for definite CIDP. Treatment with intravenous immunoglobulin (IVIg) lead to improvement in his leg weakness. He continued to have a relapsing remitting course, stabilized with multiple courses of IVIg.

SUMMARY/CONCLUSION: This patient presented with sensory symptoms and was diagnosed with idiopathic SFN. Repeat EMG/NCS for subsequent weakness confirmed the diagnosis of CIDP. The patient improved with IVIg treatment, with multiple relapsing symptoms responsive to IVIg. It is known that IENFD can be reduced in patients with CIDP. Previous cases have shown SFN can progress to large fiber neuropathy in patients with systemic illnesses. However, SFN progressing to CIDP has not been described. Clinicians should have a low threshold to repeat EDX testing in patients with progressive sensorimotor symptoms and consider additional treatment options. CIDP should be considered in patients with SFN with progressive symptoms.

Andrew Feldman, MD, MEd

Resident and Fellow Member Award Recipient

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NOVEL MISSENSE MUTATION IN MYH2 MYOPATHY ASSOCIATED WITH CONGENITAL EXOTROPIA AND ADULT-ONSET PROXIMAL WEAKNESS

Gabriela Figueiredo Pucci (Pittsburgh, PA), Jackson Mitzner (Pittsburgh, PA), Kunal Malik (Pittsburgh, PA), David Lacomis (Pittsburgh, PA)

INTRODUCTION/BACKGROUND: Myosin myopathies comprise a group of inherited diseases caused by mutations in myosin heavy chain (MyHC) gene isoforms. The associated phenotypes vary widely. We report a novel point mutation in a case of MYH2 myopathy and describe the interesting phenotype and associated features.

CASE REPORT: 32-year-old man with congenital left exotropia (s/p multiple strabismus surgeries in childhood), presents with 2 years of progressive proximal lower and then upper extremity weakness. A 38-year-old brother lost ambulation from an unspecified muscular dystrophy with onset at age 23. Examination showed gynecomastia, bifacial weakness, mild proximal arm and leg weakness, atrophy of humeral, quadriceps, and upper pectoralis muscles, Beevor sign, absent patellar/Achilles reflexes and a waddling gait. Serum creatine kinase 3236 IU/L, aldolase 26.3 U/L (<8.1), negative myasthenia gravis antibody panel, and normal TSH and lactic acid. EDX study showed evidence of a proximal-predominant irritable myopathy with the vastus lateralis and biceps brachii being most affected. Neuromuscular ultrasound revealed more involvement (hyperechogenicity) in the deltoid, vastus lateralis, and biceps brachii. Biceps brachii muscle biopsy revealed a chronic myopathy/dystrophy with autophagic vacuoles containing filamentous material. Invitae genetic panel showed a lysine-to-arginine point mutation on codon 599 of the MYH2 gene. Predictive modeling indicated this missense variant is expected to disrupt MYH2 protein function with a positive predictive value of 80%.

SUMMARY/CONCLUSION: This is the first report regarding this variant in the MYH2 gene causing an autosomal dominant form of myosin myopathy associated with congenital ophthalmoplegia followed by adult-onset proximal and axial weakness.

Gabriela Figueiredo Pucci, MD

Resident and Fellow Member Award Recipient

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DIABETIC AMYOTROPHY: REHABILITATION INTERVENTIONS AFTER ELECTRODIAGNOSTIC DIAGNOSIS

Ricardo Fuentes-Saavedra (New York, NY), Yolanda Pham (New York, NY), Sandeep Yerra (New York, NY), Eathar Saad (Tenafly, NJ)

INTRODUCTION/BACKGROUND: Diabetic amyotrophy also known as diabetic lumbosacral radiculoplexus neuropathy (DLRPN) is a rare complication of diabetes, that presents in patients with moderate disease and rapid weight loss. Asymmetrical progression of pain, motor weakness, and proximal muscle atrophy can lead to variable degrees of disability. Although self-limited in the majority of cases, it may lead to permanent damage and even paraplegia.

CASE REPORT: This is the case of a right-handed 55-year-old male with history of type II diabetes (diagnosed years prior) who was seen for 3 months of right leg pain that then progressed to the hip and groin area. He endorsed numbness in the right toes and right foot drop, leading to multiple near-fall events.

On evaluation, he had weakness in the right ankle dorsiflexor, hip flexor, and extensor hallucis, accompanied by a steppage gait and no use of an assistive device. An absent right quadriceps reflex was noted, but sensation for pain, light touch, and vibration remained intact. His A1c was 7% and an MRI of the lumbar spine showed no significant spinal stenosis. EDX testing was compatible with radiculoplexopathy and underlying symmetrical polyneuropathy.

Multidisciplinary management was required to address his pain, using a multidrug regimen including duloxetine, gabapentin, and NSAIDs. Physical therapy and a posterior leaf orthosis were needed to address his weakness and gait instability.

SUMMARY/CONCLUSION: Although multiple pharmacological treatments have been used in attempt to treat diabetic amyotrophy, the only effective intervention is a comprehensive rehabilitation that considers the self-limiting nature of the disease. Further evaluation should be done to determine the response to immunoprognosis factors through electrodiagnosis.

Ricardo Fuentes-Saavedra, MD

Resident and Fellow Member Award Recipient

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DEVELOPING AN INTEGRATIVE NCS/EMG RESIDENT CURRICULUM

Sonal Gagrani (Austin, TX), Hannah Machemehl (Austin, TX), Krishna Pokala (Austin, TX), John Jefferson (Austin, TX), Sara Austin (Austin, TX)

INTRODUCTION: A basic understanding of EDX studies and interpretation is vital to neurology resident education. Certain milestones required by the Accreditation Council for Graduate Medical Education (ACGME) are not addressed nor assessed thoroughly at our institution.

OBJECTIVE: We developed a novel NCS/EMG curriculum to provide a comprehensive educational experience that addresses expected milestones.

METHODS: Third-year residents complete a 1-month NCS/EMG rotation. The current pre-revised rotation model was evaluated for effectiveness. In the revised curriculum, residents will take a pre- and post-rotation self-assessment and survey on their comfort level with expected milestones. The curriculum includes weekly assigned readings, independent practice, and scheduled clinical time. Additionally, there is a set of longitudinal EDX lectures given throughout the year.

RESULTS: Resident In-service Training Exam (RITE) scores from our institution from 2019-2023 in the neuromuscular section and related subsections are at par with national averages. Resident evaluations of our current rotation expressed common themes including a desire for early hands-on learning, inconsistent amounts of clinical time, and need for additional educational resources during the rotation. In a survey of post-rotation residents (n=9), 66.7% were not comfortable recognizing NCS/EMG patterns of common peripheral nervous system pathology and 55.6% were not comfortable interpreting EMG summary tables.

SUMMARY/CONCLUSION: Initial data suggests that while our current model may be able to prepare residents for board exams, there remain gaps in knowledge that are crucial to any neurology subspecialty. The proposed curriculum incorporates several learning tools to address these gaps. Data will be collected over several years to determine its efficacy and approval.

Sonal Gagrani, MD

Resident and Fellow Member Award Recipient

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STERIOD-INDUCED MYOPATHY WITH IRRITABLE PATTERN ON EDX STUDY

Sukhraj Gill (Bloomsburg, PA), J. David Avila (Danville, PA)

INTRODUCTION: Irritable myopathies are characterized by abnormal spontaneous activity in EDX studies. Inflammatory myopathies are a common cause of irritable myopathy. Steroid-induced myopathy is usually non-irritable. We present an unusual case of steroid-induced myopathy with an irritable pattern which, to our knowledge, has not been reported in the literature.

CASE REPORT: Our patient is a 23-year-old man with a history of adrenocorticotropic hormone secreting pituitary adenoma and resultant Cushing disease. He had trans-sphenoidal resection of the pituitary adenoma and was placed on hydrocortisone 50 mg twice daily afterwards. One week after resection he developed progressive proximal lower extremity weakness. Examination 3 months after the onset demonstrated severe proximal lower extremity weakness and milder proximal upper extremity weakness. Creatine kinase level was normal. Myositis antibody panel was negative. EDX study showed 3+ fibrillation potentials and early recruitment of motor unit action potentials with normal morphology in proximal limb muscles, consistent with a myopathy. Muscle biopsy showed atrophy of type 2 muscle fibers, suggesting steroid-induced myopathy. There was no inflammation. The patient was switched to prednisone 5 mg daily. On follow up examination 4 months later, his strength had improved significantly

CONCLUSION: The absence of an alternative explanation and improvement after reduction in corticosteroid dose, suggest that our patient had steroid-induced myopathy. We propose that steroid-induced myopathy can rarely have an irritable pattern on EDX studies.

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Disclosures:

J. David Avila - speaker bureau and consulting for Alnylam Pharmaceuticals, speaker bureau for argenx, Alexion, AstraZeneca, Takeda Pharmaceuticals, and UCB.

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THE RELATIONSHIP BETWEEN DISORDERED SLEEP AND PAIN PERCEPTION IN PATIENTS WITH PERIPHERAL NEUROPATHY

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INTRODUCTION: The crucial role of sleep in the modulation of pain is well established, and there is evidence to suggest that the treatment of disordered sleep in patients with neuropathic pain improves pain perception.

OBJECTIVE: To assess the relationship between disordered sleep and pain perception in peripheral neuropathy.

METHODS: The associations between disordered sleep, pain perception, and neuropathic symptoms were examined cross-sectionally in 24 subjects with peripheral neuropathy. For each subject, validated scales assessing sleep quality (Neuro-QoL Sleep, Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS), and Pittsburgh Sleep Quality Index (PSQI)), pain perception (Brief Pain Inventory (BPI), Pain Catastrophizing Scale (PCS)), and neuropathic symptoms (Michigan Neuropathy Screening Instrument (MNSI)) were compared. Models were adjusted for age, sex, body mass index, pre-existing sleep disorder, and mood disorder.

RESULTS: 75% (18/24) of participants were female with a mean age of 66.9 years (SD ± 10.5). Pain severity measured by BPI was associated with higher ISI (p=0.020), PSQI (p=0.047), and Neuro QoL Sleep (p=0.01), but not ESS (p=0.241) or FOSQ-10 (p=0.824). Similarly, higher PCS was associated with higher ISI (p=0.003), PSQI (p=0.09) and Neuro-QoL Sleep (p=0.001), but not ESS (p=0.155) or FOSQ-10 (p=0.410). MNSI score ≥7 was associated with worse sleep outcomes on all scales - ISI (p=0.009), PSQI (p=.048), Neuro-QoL Sleep (p=0.01), FOSQ-10 (p=0.005), ESS (p=0.01), FOSQ-10 (p=0.005).

SUMMARY/CONCLUSION: We demonstrate associations between several measures of disordered sleep and elevated pain perception in patients with peripheral neuropathy. Disordered sleep is modifiable with targeted interventions. Characterizing this relationship therefore has important implications for approaches to management of neuropathic pain.

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PERCEIVED STRESS AND ITS ASSOCIATION WITH SLEEP QUALITY IN PATIENTS WITH NEUROPATHIC PAIN AND DISTAL SYMMETRIC POLYNEUROPATHY

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INTRODUCTION: The role of sleep in the modulation of pain is well established, and there is evidence to suggest that the treatment of disordered sleep, in patients with neuropathic pain may improve pain perception. However, studies examining the drivers of impaired sleep and social determinants of health in patients with peripheral neuropathy are limited.

OBJECTIVE: To assess the relationship between sleep quality and perceived stress in patients with peripheral neuropathy.

METHODS: The relationships between disordered sleep, pain perception, and neuropathic symptoms were examined cross-sectionally in 24 subjects with peripheral neuropathy diagnosed by a neurologist. For each subject validated scales assessing sleep (Pittsburgh Sleep Quality Index (PSQI)), pain perception ((Brief Pain Inventory (BPI), Pain Catastrophizing Scale (PCS)), and neuropathic symptoms (Michigan Neuropathy Screening Instrument (MNSI)) were compared to the Perceived Stress Scale (PSS).

RESULTS: 75% of participants were female (18/24) and 16.7% identified as non-white (4/24), with a mean age of 66.9 years (SD 10.5). Greater stress as measured by the PSS was associated with worse sleep quality in univariate analysis with the PSQI (p=0.017). Further analysis adjusting for age, sex, race, history of major depression, PCS, and PSS still demonstrated a cross-sectional association in these participants with distal symmetric polyneuropathy (p=0.009).

SUMMARY/CONCLUSION: We demonstrate a strong association between perceived stress and worse sleep quality in a cohort of participants with peripheral neuropathy. A better understanding of the drivers of impaired sleep examining social determinants of health has important implications for developing targeted interventions that treat sleep impairment and neuropathic pain.

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SERONEGATIVE IMMUNE MEDIATED NECROTIZING MYOPATHY IN YOUNG ADULT WITH CYSTIC FIBROSIS ON TRIKAFTA

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BACKGROUND: Immune mediated necrotizing myopathies (IMNM) often occur in the setting of toxin exposures (statins, immune check point inhibitors), autoimmune diseases, or paraneoplastic processes. Here, we report a case of a patient with cystic fibrosis, status-post liver transplant, on stable doses of immunosuppression and elexacaftor/tezacaftor/ivacaftor (Trikafta), who developed seronegative immune mediated necrotizing myopathy, confirmed on muscle biopsy.

CASE REPORT: A 31-year-old man with cystic fibrosis, status-post liver transplant in 2000, on Trifakta, tacrolimus, and mycophenolate, presented with proximal leg weakness and persistently elevated creatinine kinase (CK), despite stopping Trifakta for 3 months for elevated AST/ALT. Exam showed mild proximal leg weakness. Labs showed CK range 1350 – 5400 U/L, aldolase 34 – 99 U/L, AST 93 – 115, ALT 109 – 226, tacrolimus level 3.2 – 14ng/mL, negative myomarker 3 panel, negative HMGCR antibody, and negative Oklahoma Medical Research Foundation comprehensive myositis panel. EMG/nerve conduction study showed no evidence of myopathy. Right vastus lateralis muscle biopsy showed necrotizing myopathy with MHC-I upregulation in necrotic and non-necrotic fibers. There was no evidence of inflammatory infiltrate. He was diagnosed with a seronegative immune mediated necrotizing myopathy and treated with IVIg 2g/kg every 4 weeks. At 3 months, CK was 497 U/L and strength exam was normal.

SUMMARY/CONCLUSION: We report a rare case of IMNM, confirmed on muscle biopsy, which may be related to prior Trikafta exposure in a patient with cystic fibrosis, despite cessation of the drug. Such a side effect has not been previously reported and will need additional surveillance to establish an association.

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Disclosures:

Arjun Seth - consultant for Argenx, UCB and Takeda Pharmaceuticals

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SEVERE RHABDOMYOLYSIS FOLLOWING LEVETIRACETAM ADMINISTRATION: A CASE SERIES

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

INTRODUCTION: Severe rhabdomyolysis is a rare, but underrecognized side effect of levetiracetam. We describe three patients who developed severe rhabdomyolysis with significant creatine kinase (CK) elevation after initiation of levetiracetam, and CK improvement following discontinuation of levetiracetam.

CASE REPORT: Case 1: A 33-year-old male with a history of epilepsy on valproic acid presented to the emergency department (ED) after being found unconscious at home. He was loaded with intravenous (IV) levetiracetam (60mg/kg). His serum CK on arrival was 644 units(u)/L. His CK continued to rise to a peak of 21,063 u/L despite no further seizures; it improved with fluid resuscitation.
Case 2: A 17-year-old male without significant past medical history presented to the ED with a generalized tonic-clonic seizure. He was given 500mg IV levetiracetam followed by 500mg daily levetiracetam maintenance therapy. His initial CK in the ED was 3,198 u/L which increased to a maximum of 84,965 u/L despite no further seizures. Levetiracetam was discontinued and CK improved with fluid resuscitation.
Case 3: 27-year-old male with neurofibromatosis type 1 and depression presented to the ED following seizure-like activity. He received 1000mg IV levetiracetam. Valproic acid replaced levetiracetam due to agitation. His initial CK was 154 u/L and increased to 8,115 u/L. It improved with fluid resuscitation.

SUMMARY/CONCLUSION: Severe rhabdomyolysis can occur secondary to levetiracetam administration. This phenomenon is likely underreported in clinical practice and should be recognized to avoid unnecessary investigation and treatment.

Morgan Heber, MD

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Disclosures:

Yuebing Li - has consulted for Alexion, argenx, Catalyst, Immunovant and UCB Pharma, and has received grant support from argenx.

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INSULIN NEURITIS: A DEVASTATING COMPLICATION OF RAPID GLYCEMIC CORRECTION DIAGNOSED BY EMG/NCS

Gabriel Howard (Philadelphia, PA), Andrew Reish (North Wales, PA)

INTRODUCTION: Insulin neuritis (IN) or “treatment-induced neuropathy of diabetes” is a rare, underdiagnosed form of axonopathic polyneuropathy occurring as a result of rapid glycemic correction with either oral or injectable agents. IN is a reversible disorder characterized by acute peripheral nerve damage from microvascular hypoglycemia which can result in autonomic dysfunction and severe neuropathic pain of extremities, trunk, or abdomen.

OBJECTIVE: A 50-year-old male was referred by orthopedics for EMG/NCS of severe bilateral thoracic radicular burning pain prior to planned thoracic spinal decompression for a unilateral mild neuroforaminal stenosis with concurrent stocking-glove distribution paresthesias which developed rapidly after starting treatment for his newly diagnosed diabetes. Over 3 months, an initial hemoglobin A1c had been corrected from 13.8 to 5.9 using short and long-acting insulin with discontinuation of all medications after experiencing a 70lb weight loss, new bowel incontinence, and ambulatory dysfunction with falls. Extensive laboratory and imaging workup by neurology and neurosurgery resulted with only incidental findings.

METHODS: A case report of IN to discuss the importance of its proper diagnosis.

RESULTS: EMG/NCS evaluation revealed severe large fiber sensory motor axonopathic polyneuropathy with diffuse symmetric acute denervation across multiple myotomes involving bilateral lower extremities, midthoracic paraspinals, and lumbar paraspinals. The patient was diagnosed with IN, informed of the regressive nature of this disorder, conservatively maintained on neuropathic medications, and enrolled in land-based therapy without surgical decompression.

SUMMARY/CONCLUSION: IN is a rare and potentially devastating disorder which may lead to excessive testing, surgical intervention, and healthcare overutilization if not properly diagnosed by an informed EDX physician or provider.

Gabriel Howard, DO

Resident and Fellow Member Award Recipient

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AN UNUSUAL CASE OF EARLY ELECTRODIAGNOSIS OF ACUTE MOTOR SENSORY AXONAL NEUROPATHY IN AN 18-YEAR-OLD FEMALE

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INTRODUCTION/BACKGROUND: Acute motor sensory axonal neuropathy (AMSAN) is an uncommon variant of Guillain-Barré syndrome (GBS) characterized by acute flaccid paralysis and sensory disturbances. It is associated with a prolonged recovery and more severe outcomes, such as frequent ventilator-dependence. GBS and its variants are diagnosed with cerebrospinal fluid (CSF) and EDX findings on EMG/NCS.

CASE REPORT: An 18-year-old female with cholecystectomy 2 months prior complicated by post-operative colitis and cannabinoid hyperemesis presented with 2 days of progressive bilateral lower extremity (BLE) numbness, pain, and weakness resulting in gait instability, followed by numbness in the medial three fingers bilaterally. Her exam was limited due to pain, however she had BLE length dependent sensory loss and motor weakness with hyporeflexia. MRI brain and pan-spine with and without contrast did not reveal a structural or demyelinating process, and CSF studies were unremarkable. EMG/NCS revealed absent sensory nerve action potentials (SNAPs) in bilateral sural and superficial peroneal nerves and absent F-waves in right peroneal and tibial nerves, as well as severely reduced compound muscle action potential amplitudes of the bilateral peroneal and tibial nerves with no evidence of conduction block. These findings, consistent with moderately severe AMSAN, prompted 2 g/kg intravenous immunoglobulin (IVIg) over 5 days, which significantly improved her symptoms and mobility. She was discharged home, ambulatory with a rolling walker.

SUMMARY/CONCLUSION: Despite an inconsistent, pain-limited exam, no clear antecedent, and normal CSF, it is imperative to pursue EDX studies if GBS is clinically suspected, as CSF findings are disease duration dependent, and the risks of delaying treatment can be severe, especially in uncommon variants like AMSAN.

Sara Hubacek, MD

Resident and Fellow Member Award Recipient

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ROLE OF NERVE BIOPSY IN IMAGING NEGATIVE NEOPLASTIC BRACHIAL PLEXOPATHY IN A WOMAN WITH METASTATIC BREAST CANCER

Matthew Jacobson (Midvale, UT), Ligia Onofrei (North Salt Lake, UT)

INTRODUCTION/BACKGROUND: Neoplastic brachial plexopathy is a known complication of metastatic breast cancer and is clinically suspected in patients presenting with unilateral upper extremity pain, associated weakness, and muscle atrophy on neurologic examination, and EMG/NCS findings that localize to the brachial plexus. Imaging with MRI and FDG-PET is often performed to confirm the presence of metastatic lesions affecting the plexus thus confirming the diagnosis.

CASE REPORT: We report an unusual case of imaging negative, biopsy proven metastatic breast cancer causing brachial plexopathy in a 44-year-old female with a history of metastatic breast cancer. Our patient presented with a several week history of progressive left upper extremity pain, weakness, and dysesthesias after recent placement of pleural catheter for drainage of a malignant pleural effusion. She additionally had a history of radiation to the chest area which further confounded the clinical picture. EMG/NCS was performed with evidence of active denervation localizing the brachial plexus. Contrasted MRI of the brachial plexus and FDG-PET scan were both read as negative for metastatic involvement. A biopsy was pursued due to continued clinical worsening, which confirmed metastatic breast cancer infiltrating the brachial plexus.

SUMMARY/CONCLUSION: Our case illustrates the need for clinicians to maintain a high degree of clinical suspicion for neoplastic plexopathy even when available imaging is unrevealing and the importance of pursuing alternative diagnostic modalities such as nerve biopsy.

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Resident and Fellow Member Award Recipient

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EARLY-ONSET DEMYLINATING POLYNEUROPATHY AND UPPER MOTOR NEURON SIGNS: THINK X-LINED ADRENOMYELONEUROPATHY

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INTRODUCTION/BACKGROUND: X-linked adrenoleukodystrophy (X-ALD) is caused by ABCD1 gene pathogenic variants that result in neurologic and endocrine manifestations. Neurologic presentations include progressive leukodystrophy, myeloneuropathy, or a mixture of both. The primary symptoms of myeloneuropathy consist of spastic paraparesis, sensory ataxia, sphincter dysfunction, and/or polyneuropathy (PN). Patients are diagnosed based on their symptoms, very long chain fatty acid (VLCFA) levels, and ABCD1 gene analysis. EDX studies demonstrate a primary axonal PN with variable demyelinating features.

CASE REPORT: A 39-year-old man initially presented with a 3-year history of progressive bilateral lower extremity numbness, paresthesias, weakness, and ambulatory dysfunction. Exam demonstrated sensory loss and muscle atrophy in the lower extremities, weakness of foot dorsiflexion, and hyperreflexia in all limbs. An EDX study was interpreted as sensorimotor PN with demyelinating features. He was thought to have a hereditary PN but did not have genetic testing. He was re-evaluated 15 years after the onset of symptoms. He reported a history of nausea with eating and unintentional weight loss. VLFCA levels were elevated. Single gene analysis revealed a hemizygous variant of uncertain significance in ABCD1 [c.818C>T, (p.Ala273Val)]. This variant was recently reported in two related males with adrenal insufficiency.

SUMMARY/CONCLUSION: Based on the clinical syndrome and EDX findings, we propose that the ABCD1 A273V variant is likely pathogenic. This case illustrates the importance of recognizing upper motor neuron signs in patients with suspected hereditary PN, to prioritize the differential diagnosis and guide genetic testing.

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Disclosures:

J. David Avila - speaker bureau and consultant for Alnylam Pharmaceuticals, speaker bureau for argenx, Alexion, AstraZeneca, Takeda Pharmaceuticals, and UCB.

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ISOLATED SUBACUTE CAMPTOCORMIA IN ANTI-PL12 ASSOCIATED IMMUNE-MEDIATED NECROTIZING MYOPATHY

Muruj Jumah (Cleveland, OH), Bashar Katirji (Cleveland, OH), Gaurav Chenji (San Diego, CA)

INTRODUCTION/BACKGROUND: Immune-mediated necrotizing myopathy (IMNM) is a rare autoimmune muscle disease that predominantly affects proximal muscles and has heterogeneous clinical presentations. Approximately 20% of IMNM patients show elevated anti-signal recognition particle (anti-SRP) antibodies, while 50% show elevated anti-HMGCR antibodies. In addition, paraspinal myopathy presenting as camptocormia may be a manifestation of a wide spectrum of myopathic disorders.

CASE REPORT: A 69-year-old man presented with 2 months of bilateral forearm myalgia and camptocormia following a viral infection. The general and neurological examinations were normal except for mild camptocormia. Laboratory testing showed positive anti-PL12 antibody, elevated creatinine kinase (CK) (initial was 791), negative anti-HMGCR antibody, and negative connective tissue disease (CTD) markers. Brain MRI was unremarkable. Lumbar spine MRI showed enhancement of the thoracolumbar paraspinal muscles. EMG showed active denervation and myopathic motor unit potentials confined to the thoracic and lumbar paraspinal muscles. High-resolution chest CT showed no evidence of interstitial lung disease (ILD). Biopsy of the thoracic paraspinal and deltoid muscles showed endomysial fibrosis, scant perivascular lymphocytic infiltration, and myofibers necrosis and regeneration. The patient responded well to immunosuppression with mycophenolate mofetil and showed improvement in camptocormia.

SUMMARY/CONCLUSION: IMNM associated with PL12 antibody may present as an isolated paraspinal myopathy with the absence of interstitial lung disease and other extra-muscular features. Our case highlights the importance of early paraspinal muscle EMG and biopsy as well as myositis-specific antibody testing in investigating isolated camptocormia to reduce the diagnosis delay and improve care management.

Muruj Jumah, MD

Resident and Fellow Member Award Recipient

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

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INTRODUCTION: Rozanolixizumab is a subcutaneous neonatal Fc receptor (FcRn) antagonist approved for treatment of acetylcholine receptor antibody-positive generalized myasthenia gravis (AChR+ gMG).

OBJECTIVE: To describe the clinical experience with the use of rozanolixizumab in clinic practice.

METHODS: Retrospective review.

RESULTS: Three patients diagnosed with AChR+ gMG were treated with rozanolixizumab. Among them were two females and one male, with mean (SD) age of 62.33 (7.5) years. Prior to initiating rozanolixizumab treatment, the mean MG-ADL score (SD) was 10.66 (1.15). Two patients were transitioned from efgartigimod to rozanolixizumab. Both completed two cycles of efgartigimod without any change in their MG-ADL scores (12 and 10, respectively). Following the completion of six weekly infusions of rozanolixizumab, the mean MG-ADL score (SD) improved to 6.66 (1.15). All patients demonstrated clinically significant improvements in MG-ADL scores (>2 points). The second cycle of rozanolixizumab was initiated 10 weeks after the commencement of the first infusion in the initial cycle. Following the completion of the second cycle, the mean MG-ADL score (SD) remained stable at 5.66 (0.57). One patient experienced infusion-related side effects, including nausea and headache, after the first infusion of rozanolixizumab. Subsequently, this patient was premedicated with Tylenol, Benadryl, and famotidine before subsequent infusions, and did not experience similar side effects. Two other patients were premedicated prior to their infusions and did not experience any side effects.

SUMMARY/CONCLUSION: Patients with AChR+ gMG had clinically meaningful improvement in MG-ADL scores after treatment with rozanolixizumab including those who did not respond to efgartigimod.

Nakul Katyal, MD

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Disclosures:

Raghav Govindarajan - served on ad board for Argenx, UCB, Janssen, Roche, and speakers bureau for Argenx and Alexion.

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LATE ONSET, AUTOSOMAL RECESSIVE MYOSIN HEAVY CHAIN IIA - RELATED MYOPATHY AND OPHTHALMOPLEGIA: A CASE REPORT

Lydia Kauffman (Hershey, PA), Mansoureh Mamarabadi (Hummelstown, PA)

INTRODUCTION/BACKGROUND: Myosin heavy chain (MYH) IIa is one of several proteins associated with skeletal muscle contraction, particularly in type 2a cardiac muscle fibers. Several case studies of mutations have been reported, in which patients develop myopathy and ophthalmoplegia beginning in early childhood/adolescence. Other symptoms have been reported though but vary between cases. We present a case of late-onset MYH IIa-related myopathy that advances in genetic testing yielded to correct diagnosis after 2 decades of symptom onset.

CASE REPORT: Our case describes an 82-year-old gentleman who presented at age 58 with progressive proximal muscle weakness in arm and legs, and ophthalmoplegia. The patient had a sister who also was experiencing leg weakness. Presentation was felt to be consistent with a mitochondrial disorder. Muscle biopsy at onset showed chronic myopathic changes. Mitochondrial DNA testing including evaluation for oculopharyngeal muscular dystrophy was unrevealing. At age 81, the patient returned with worsening of weakness and dysphagia. Neurological examination revealed proximal muscle weakness in arms and legs, complete ophthalmoplegia bilaterally without fatigable ptosis. Repeat genetics testing following 23 years revealed autosomal recessive, homozygous mutation in MYH2- gene. The patient did not report cardiac symptoms and echocardiography was normal.

SUMMARY/CONCLUSION: Our case highlights a late onset phenotype of MYH IIa gene with proximal myopathy, ophthalmoplegia and dysphagia. The case also demonstrates the evolution of genetics over the past 20 years. As a consideration in clinical practice, it may be beneficial to re-test patients without a definite diagnosis with updated genetic panels over time.

Lydia Kauffman, MD

Resident and Fellow Member Award Recipient

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OBTURATOR NEUROPATHY SECONDARY TO MINIMALLY INVASIVE URO-GYNECOLOGICAL SURGERIES

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BACKGROUND: Post-surgical neuropathies are rare complications of minimally invasive uro-gynecological surgeries. Obturator neuropathies in the setting of hysterectomy or prostatectomy have not been extensively studied. We report a case series of iatrogenic obturator neuropathies and review the current literature.

CASES: We present a 45-year-old male with history of metastatic prostate cancer (Grade group 4) who underwent robotically assisted prostatectomy and presented with 1 month of left thigh weakness and a 40-year-old female with history of grade 1 endometrial cancer who underwent laparoscopic radical hysterectomy and presented with 1 month of right thigh weakness. In the immediate post-op period, both patients noted weakness associated with numbness in respective medial thighs. On neurological examination, there was evidence of thigh adductor weakness, grade 3 motor strength with intact hip flexion, knee extension, and flexion. There was numbness in the medial thigh upon sensory evaluation and intact and symmetric reflexes. MRI of the lumbar spine was unremarkable without evidence of compression or transection of the obturator nerve. EMG studies revealed EDX evidence of abnormal spontaneous activity and absent motor unit action potentials in thigh adductors respectively, evident of active obturator neuropathy. Both patients were referred to physical therapy. Upon re-evaluation at a 3-month interval post-op, patients endorsed complete resolution of symptoms.

DISCUSSION: Obturator neuropathy is rare, occurring in 1% of people after major pelvic surgery, such as hysterectomies. Nerve damage during surgery can result from stretch or compression of the nerve from patient positioning or contact with electrosurgical devices. Early diagnosis and intervention are key in improving patient outcomes.

Collette Kokikian, MD

Resident and Fellow Member Award Recipient

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EARLY-ONSET, BILATERAL HIRAYAMA DISEASE IN A YOUNG VIOLINIST: A CASE REPORT

Ryan Kollar (Decatur, GA), Ryan Nelson (Durham, NC), Akhil Shivaprasad (Durham, NC), Madiah Ashraf (Dallas, TX), Vern Juel (Durham, NC), Jonathan Morena (Durham, NC)

INTRODUCTION/BACKGROUND: Hirayama disease (HD) is a male-predominant, adolescent-onset, and largely self-limited focal motor axonopathy affecting the C7-T1 myotomes. The pathogenesis is hypothesized to be that of flexion-induced compressive ischemia of the cervical anterior horn cells or nerve roots, which may result from dysplasia of the dural sac, nerve roots, or venous plexus or spinal ligamentous abnormalities.

CASE REPORT: A previously healthy, 12-year-old, right-handed boy of Korean ancestry presented with 8 months of atraumatic, painless, and progressive right > left hand atrophy and weakness preceded by a 4-inch growth spurt over the prior 6 months. He was a violinist practicing for 30-60 minutes most days of the week with his head held in a flexed posture. He initially noted clawing of his hands followed by inability to grasp his bow, loss of fine finger movement, and cold paresis. He denied sensory disturbances. Examination demonstrated atrophy of the right > left intrinsic hand and medial forearm muscles with brachioradialis sparing and asymmetric weakness of elbow extension, wrist flexion, finger extension and flexion, finger abduction, and thumb abduction. EDX revealed a sub chronic, pre-ganglionic motor neuropathic process affecting the bilateral C7-T1 myotomes. Confirmatory flexion MRI of the cervical spine is pending at the time of abstract submission.

SUMMARY/CONCLUSION: There is a dearth of data regarding behavioral factors contributing to the progression of HD, such as activities involving prolonged neck flexion. Timely diagnosis leading to prompt initiation of cervical neck collar and prevention of activities involving neck flexion is crucial for recovery.

Ryan Kollar, DO

Resident and Fellow Member Award Recipient

ANTI-MAG ANTIBODY ASSOCIATED WALDENSTROM'S MACROGLOBULINEMIA WITH IMPROVEMENT FROM BENDAMUSTINE AND RITUXIMAB: A CASE REPORT

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INTRODUCTION/BACKGROUND: Waldenstrom's macroglobulinemia (WM) is a lymphoma defined by at least 10% bone marrow infiltration by lymphoplasmacytic cells and IgM monoclonal gammopathy. Neuropathy is common in patients with WM and can present with anti-MAG antibodies.

CASE REPORT: A 56-year-old woman presented with 20 years of gradually progressive symmetric, ascending numbness, severe painful dysesthesia, distal limb weakness, action tremors of the hands, gait instability/frequent falls, constipation, orthostatic intolerance, and tachycardia. Serologies revealed an IgM-kappa monoclonal protein and low-titer-positive anti-MAG antibody (3266 Buhlmann Titer Unit (BTU)). She was referred for treatment of demyelinating symmetric (DADS) neuropathy. Examination demonstrated mild distal weakness, intention tremor in the hands, diminished pin sensation throughout the entirety of the arms and legs, diminished vibratory sensation distally, and unstable tandem walk. EDX revealed a distal predominant demyelinating neuropathy with secondary axon loss. She was referred to hematology for further evaluation of her IgM monoclonal gammopathy. Bone marrow biopsy demonstrated a small B-cell lymphoma with positive MYD88 mutation consistent with WM. Sural nerve biopsy showed no evidence of amyloid or vasculitis. She started bendamustine and rituximab and experienced improved gait, neuropathic symptoms, and fine motor movements.

SUMMARY/CONCLUSION: MAG antibody levels less than 7500 BTU and atypical clinical features of DADS warrant diagnostic scrutiny. Close interdisciplinary collaboration with hematology is crucial in patients with IgM monoclonal gammopathy for further evaluation of WM and other plasma cell dyscrasias, as this impacts treatment. MYD88 variant can be seen in patients with WM and anti-MAG antibody neuropathy. Patients with anti-MAG antibody-associated WM can improve with bendamustine and rituximab therapy.

Ryan Kollar, DO

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MULTI-LESION COMPRESSIVE ULNAR NEUROPATHY DIAGNOSED BY NEUROMUSCULAR ULTRASOUND AND ELECTRODIAGNOSTIC TECHNIQUES

Haylie Kromer (Pittsburgh, PA), Michael Glicksman (Pittsburgh, PA), Michael Munin (Pittsburgh, PA)

INTRODUCTION/BACKGROUND: Ulnar mononeuropathy at the elbow is the second most common mononeuropathy, typically presenting as intrinsic hand weakness and fourth- and fifth-digit paresthesia. Less common, ulnar neuropathy also occurs at the wrist and proximally at the Arcade of Struthers. This unique case illustrates the diagnosis and treatment of ulnar neuropathy with three sites of compression: Arcade of Struthers, elbow, and wrist.

CASE REPORT: A 64-year-old male presented with 3 months of progressive paresthesia and weakness of the fourth and fifth digits of the right hand. The patient also had a history of bilateral ulnar neuropathies at the elbow status post bilateral decompression surgeries in addition to bilateral Dupuytren's contractures. Clinical examination was notable for 4/5 strength in the right abductor digiti minimi and first dorsal interosseous muscles. EDX examination revealed conduction block without axonal loss in the proximal arm and slowed conduction across the elbow. Diagnostic ultrasound localized these demyelinating lesions at sites of nerve enlargement at the level of Arcade of Struthers and the retroepicondylar groove with cross-sectional areas of 11.18 mm2 and 13.33 mm2, respectively. The patient underwent ulnar nerve neurolysis at the midshaft humerus and the elbow. Intraoperatively, there was also substantial ulnar nerve compression in the palm by Dupuytren's fascia for which complete release and fasciectomy was performed. At 2-months post-surgery, he is showing improvement after decompression at the three sites.

SUMMARY/CONCLUSION: This case highlights how a multimodal diagnostic approach with EDX, ultrasound, and surgical exploration aided in identification and treatment of three sites of compressive ulnar neuropathy.

Haylie Kromer, DO

Resident and Fellow Member Award Recipient

PEDIATRIC ONSET SPINOCEREBELLAR ATAXIA 17 IN THE SETTING OF SUSPECTED GLOBAL DEVELOPEMENTAL DELAY

Samantha Kultgen (Madison, WI), Deanna Jewell (Madison, WI)

INTRODUCTION/BACKGROUND: Spinocerebellar ataxia type 17 (SCA17) is a rare autosomal dominant cerebellar ataxia characterized by ataxia, psychiatric symptoms, chorea, and dystonia with onset ranging from ages 3 to 75. There are fewer than 100 reported families worldwide with SCA17. SCA17 is diagnosed by genetic testing, specifically identifying abnormal CAG/CAA repeat expansion in TATA-box binding protein (TBP). Normal alleles have 25-40 repeats. Two individuals with CAG/CAA repeats greater than 60 have been reported, both with presentation in early childhood.

CASE REPORT: A 12-year-old patient previously diagnosed with mild developmental delay presented with worsening coordination. MRI demonstrated diffuse cerebellar atrophy and subsequent genetic testing lead to a diagnosis of SCA17, with 60 repeats in TBP. She was referred to pediatric physical medicine and rehabilitation. Equipment, orthotics, and therapy were ordered to assist with ambulation, transfers, and upper extremity use. She progressed over the next 2 years, developing increased ataxia, weakness, dysarthria, dysphagia, psychiatric symptoms, and dystonia. Multiple equipment items and alternative bracing for upper and lower extremities were ordered to facilitate mobility and activities of daily living to meet functional needs. Adaptive sports were encouraged. As her tone became worse over the following 2 years, her physiatrist started her on tone management. A gastric-tube (g-tube) was placed, and an augmentative and alternative communication device ordered to manage dysphagia and dysarthria.

SUMMARY/CONCLUSION: SCA17 is a rare diagnosis necessitating multidisciplinary involvement to manage tone, orthotics to accommodate changes in function, adaptive equipment, and care coordination.

Samantha Kultgen, MD

Resident and Fellow Member Award Recipient

NEUROMUSCULAR MANIFESTATIONS OF ADULT-ONSET GM1 GANGLIOSIDOSIS

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INTRODUCTION/BACKGROUND: GM1 gangliosidosis is a lysosomal storage disorder caused by mutations in the GLB1 gene, which encodes the enzyme beta-galactosidase. Reduced beta-galactosidase activity causes accumulation of GM1-ganglioside which has numerous toxic effects on the nervous system.

CASE REPORT: A 54-year-old male presented with progressive weakness and gait issues beginning at age 14. He was previously treated with immunotherapy for presumed chronic inflammatory demyelinating polyneuropathy (CIDP) or multiple sclerosis (MS) with no clear response to immunotherapy. The neurological examination was notable for distal weakness and wasting, pes cavus, areflexia, and extensor plantar responses. Prior work-up included MRI brain with patchy periventricular white matter lesions. MRI spine revealed prominent nerve root thickening. NCSs were repeated and demonstrated uniformly reduced conduction velocities of approximately 30 m/s. Given his phenotype, early age at onset, and inconsistent response to immunotherapy, there was suspicion for a genetic disorder. Next generation sequencing yielded a previously reported pathogenic variant and a variant of uncertain significance in the GLB1 gene. Biochemical analysis revealed significantly reduced beta-galactosidase activity and abnormal urine oligosaccharides, supporting the diagnosis of GM1 gangliosidosis.

SUMMARY/CONCLUSION: More commonly reported features of adult-onset GM1 gangliosidosis include generalized dystonia, dysarthria, and cognitive dysfunction. This case instead highlights GM1 gangliosidosis presenting with prominent neuromuscular features of distal weakness and demyelinating neuropathy. This disease may mimic other neuromuscular conditions such as CIDP or Charcot-Marie-Tooth disease. Our case illustrates that a thoughtful approach combining clinical assessment, genetic testing, and biochemical testing may be needed to fully investigate complex, inherited neuromuscular diseases.

Brianne Lacy, MD

Resident and Fellow Member Award Recipient

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INFANTILE BOTULISM: CASE SERIES

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INTRODUCTION: Infant botulism is a rare but serious neuromuscular junction disorder that clinically presents with symptoms including acute weakness and severe respiratory difficulty, making prompt diagnosis and treatment necessary. However key exam findings can sometimes be non-specific, with conditions such as spinal muscular atrophy, myasthenia gravis, and metabolic disease also on the differential. (1) Thus, early EDX studies can assist supporting the clinical suspicion and timely administration of botulism immune globulin.

OBJECTIVE: We summarized six patients' clinical course and EDX findings. History, reflexes, range of motion, and strength tests were not always possible and thus pathognomonic findings were rarely present. However, our study plus clinical findings helped to facilitate proper treatment and management. Our goal is to better guide others in similar situations when such diagnostic uncertainty exists.

CASE REPORT: This case series describes six patients seen and treated at our center for infantile botulism with improvement in symptoms after botulism immune globulin. EMG testing was ordered during the acute phase of their illness while awaiting stool studies. High-rate repetitive nerve stimulation helps in confirming diagnosis but was technically difficult to perform in unsedated children in the ICU, and thus was deferred in two patients. Our full EMG/ NCS, EMG, and repetitive nerve stimulation results were described. We also detail each patients' clinical course, lab results, and response to big administration.

SUMMARY/CONCLUSION: Our center's experience is that EDX testing in conjunction with certain clinical findings has been successful in helping to confirm the clinical suspicion of botulism even in absence of pathognomonic repetitive stimulation findings that are not always possible in ICU settings.

Allan Lara, MD

Resident and Fellow Member Award Recipient

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UTILITY OF THE VAGUS NERVE ULTRASOUND IN PATIENTS WITH AUTONOMIC DYSFUNCTION

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INTRODUCTION: The vagus nerve (VN) holds considerable importance in the autonomic nervous system. Autonomic testing is frequently ordered for patients with vague neurological symptoms suggestive of autonomic dysfunction (AD). However, there is a lack in literature regarding sonographic appearance of the VN in patients with AD.

OBJECTIVE: To determine the ultrasonographic cross-sectional area (CSA) reference value of the VN in patients with AD and evaluate its potential as an alternative diagnostic method to autonomic testing.

METHODS: In this prospective study, 40 patients with autonomic symptoms (20 with positive and 20 with negative tilt table test) and 20 age-matched asymptomatic controls. Data includes demographic information, clinical symptoms, tilt table test results, and ultrasonographic CSA of VN.

RESULTS: Eight subjects (four patients and four controls) are enrolled. All subjects were female. Median age and body mass index of patients were 31.5 years (range 21-53) and 32.2 (23.9 -47.2) and for controls were 50.5 years (range: 25-61) and 24 (range: 19.4-25.3). No significant difference observed in mean right/left CSA between patients (2.2/1.89 mm2) and controls (2.09/1.68 mm2). All patients reported lightheadedness, 50% reported palpitation. The tilt table was abnormal in three patients: two with postural orthostatic tachycardia syndrome, one with orthostatic intolerance. Mean VN CSA of patients with abnormal autonomic testing was not statistically different from controls.

SUMMARY/CONCLUSION: Enrollment and data collection are ongoing. VN ultrasound measurement may have value for diagnosis of AD, especially in patients who are unable to tolerate tilt tables test or for whom discontinuation of medications, which could affect the interpretation of testing, is not safe.

Rachel LaRosa, MD

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CHARACTERIZING THE CLINICOPATHOLOGICAL FEATURES OF A COHORT OF IBM PATIENTS

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INTRODUCTION: Inclusion body myopathy (IBM) usually presents with prominent quadriceps and finger flexor weakness, but patients may present with atypical features. We analyzed a cohort of IBM patients to understand the prevalence of atypical presentations.

OBJECTIVE: To characterize the clinicopathological features of a cohort of IBM patients seen in the Emory neuromuscular clinic.

METHODS: A single-center retrospective cohort analysis identified 78 patients with IBM seen in the Emory neuromuscular clinic from January 2013 through December 2022. Charts were reviewed for patient demographics, disease characteristics, muscle biopsy histology, EDX features, and laboratory findings.

RESULTS: Sixty-two percent of patients were male and 58% were White. Median age at symptom onset was 62 (interquartile range [IQR] 12). Median delay to diagnosis was 49 months (IQR 52). At diagnosis, 83% of patients had finger flexor weakness and 64% had quadriceps weakness. Atypical presenting symptoms, defined as either proximal arm weakness, facial weakness, or respiratory dysfunction, were present in 6%. The median creatine kinase value was 389 (IQR 388). Serum CN1A antibodies were present in 65% of patients. Five of 78 patients had a hereditary form of disease. EMG/NCS revealed myopathic changes in 65% of patients, mixed myopathic and neuropathic features in 20%, and purely neuropathic features in 15%. Sixty-four percent of patients underwent muscle biopsy. Of those, 92% showed evidence of inflammation, 52% rimmed vacuoles, and 16% mitochondrial pathology.

SUMMARY/CONCLUSION: Most cases in our cohort showed clinicopathological features typical of IBM. A small proportion of patients presented with atypical clinical features, but nevertheless showed typical pathology and symptom progression.

Mark Levine, MD

Resident and Fellow Member Award Recipient

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BEHAVIORAL NEUROLOGY SYMPTOMS IN PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY

Dominique Low (Oak Brook, IL), Partha Ghosh (Newtonville, MA)

INTRODUCTION: Duchenne muscular dystrophy (DMD) is a genetic disorder causing muscle weakness due to a mutation in the dystrophin gene. This gene also produces brain-specific dystrophin isoforms, so mutations can impact brain function in some DMD patients, leading to learning, memory, concentration, and behavior problems.

OBJECTIVE: This retrospective chart review aimed to estimate the prevalence of behavioral neurology symptoms in a DMD clinic.

METHODS: We reviewed the medical records, particularly the neurology notes, of patients with DMD seen over a 3month time period at a tertiary referral center. Additionally, neuromuscular clinic investigators recorded their clinical observations.

RESULTS: We reviewed the charts of 30 male DMD patients (mean age 13.0 years, SD 5.7). Racial demographics included White (36.7%), Black/African American (10.0%), Asian (6.7%), Other (26.7%), and Declined or unable to answer (20.0%). Overall, 56.7% (17 of 30) exhibited behavioral neurology symptoms or disorders, such as attention problems, hyperactivity, anxiety, language/speech delays, autism spectrum disorder, or oppositional defiant disorder. Among these 17 patients, 8 were on pharmacotherapy for behavioral neurology symptoms or disorders, such as methylphenidate, guanfacine, dexmethylphenidate, fluoxetine, or duloxetine.

SUMMARY/CONCLUSION: Our findings support existing research on the high prevalence of behavioral neurology symptoms in patients with DMD. As DMD management improves and life expectancy rises, addressing these challenges becomes crucial for enhancing the quality of life for patients and their families. Further research is needed to better understand the complex link between DMD and behavioral neurology co-morbidities to develop effective interventions that will improve both the clinical outcomes and quality of life.

Dominique Low, MD, MPH

Resident and Fellow Member Award Recipient

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NAVIGATING THE COMPLEXITIES THROUGH CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY AND GENETIC NEUROPATHIES

Elia Malek (Houston, TX), Seon Kyung Nam (Houston, TX), Suur Biliciler (Houston, TX), Thy Nguyen (Houston, TX)

INTRODUCTION: Chronic inflammatory demyelinating polyneuropathy (CIDP) is a frequent diagnostic label given to patients presenting with subacute, symmetric, demyelinating polyneuropathy. Genetic neuropathies, such as Charcot-Marie-Tooth (CMT) disease, with atypical presentation, short time course, and atypical diagnostic findings can further complicate the diagnosis.

OBJECTIVE: Revisit the importance of considering hereditary neuropathies in CIDP-like presentations and provide clinical and diagnostic clues that can aid in diagnosing genetic polyneuropathies.

METHODS: A retrospective chart review was conducted on patients presenting to the neuromuscular clinic at the University of Texas Health Science Center at Houston. Data included medical history, presentation, EDX, laboratory findings, and immune therapy received.

RESULTS: Eight patients with genetic neuropathy confirmed on genetic testing (six with CMT and two with HNPP) with clinical features suggestive of CIDP were identified. Four patients had EDX evidence of acquired chronic demyelinating polyneuropathy, two with chronic demyelinating polyneuropathy without conduction blocks, one with chronic axonal polyneuropathy, and one with multiple entrapment mononeuropathies. Seven patients met EAN criteria strongly supportive of CIDP. None had a sural sparing. Six patients received intravenous immunoglobulin, mostly without objective improvement.

SUMMARY/CONCLUSION: The distinction between genetic and immune-mediated neuropathies are challenging due to a spectrum of manifestations of immune mediated demyelinating neuropathies, possibility of superimposed inflammatory process in a genetic neuropathy and the expanding possibility of genetic neuropathies with demyelinating features such as partial motor conduction block or temporal dispersion. This study highlights the need for delicate attention to the time course/clinical presentation, diagnostic clues that can aid in distinguishing between CIDP and genetic neuropathies while taking note that hereditary neuropathies may have acute/subacute presentation, with no family history and exhibit EDX findings of acquired demyelination. Poor treatment response should prompt consideration for exploring alternative diagnosis.

Elia Malek, MD

Resident and Fellow Member Award Recipient

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BENIGN CRURAL AMYOTROPHY: TWO CASES OF A RARE CAUSE OF ISOLATED CALF ATROPHY

James Meiling (Winston Salem, NC), Vanessa Baute Penry (Winston Salem, NC), James Caress (Winston Salem, NC)

INTRODUCTION/BACKGROUND: Calf atrophy commonly occurs in Achilles tendon ruptures, S1 radiculopathies, distal myopathies, or motor neuron diseases (MND). Rarely, it is caused by focal denervation in benign crural amyotrophy (BCA).

CASE REPORT: Two unrelated males (67 [P1] and 45 years old [P2]) presented separately with isolated left calf atrophy for at least 5 years. Neither reported sensory complaints, upper motor neuron signs, fasciculations, or bulbar symptoms. Creatine kinase serum levels and MR lumbar spines were normal. EMG showed (P1) denervation and small motor unit potentials (MUPs) in both gastrocnemius medial head (GMH) and left soleus muscles. EMG showed (P2) denervation and poor activation of normal MUPs limited to left GMH. Neuromuscular ultrasound revealed diffuse hyperechogenicity, atrophy, and loss of normal muscle architecture with left GMH fatty infiltration. The surrounding anterior compartment muscles were unremarkable. Genetic screening for distal myopathies and hereditary MND in both patients revealed no pathogenic mutations or variants of uncertain significance in genes linked to conditions with this clinical presentation. MR left leg demonstrated (P1) severe atrophy of superficial posterior compartment muscles of the leg and partially imaged semimembranosus and (P2) mild nonspecific atrophy of mid and distal portions of GMH muscle. Slow progression of neuropathic denervation without sensory involvement restricted to the posterior compartment muscles strongly suggests a diagnosis of BCA.

SUMMARY/CONCLUSION: Benign crural amyotrophy is a rare, focally-denervating neurogenic atrophy affecting the leg posterior compartment. Imaging shows fatty replacement with muscle atrophy with predilection to GMH. BCA is insidious and slowly progresses for several years before stabilization.

James Meiling, DO

Resident and Fellow Member Award Recipient

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SONOGRAPHIC AND ELECTROMYOGRAPHIC CORRELATION OF SCAPULAR WINGING

James Meiling (Winston Salem, NC), Benjamin Rardin (Portland, OR), James Caress (Winston Salem, NC)

INTRODUCTION: Evaluation for neurogenic scapular winging is common in EDX laboratories. With growing incorporation of neuromuscular ultrasound (NMUS), another modality can now be used alongside EMG to evaluate scapular winging, particularly the serratus anterior (SA), rhomboid major (RM), and all portions of the trapezius (upper [UT], middle [MT], and lower [LT]).

OBJECTIVE: To conduct a retrospective chart review to determine the correlation of NMUS and EMG in scapular winging.

METHODS: Cases were identified between 2018-2023. Data were extracted via retrospective chart review. Adults with the clinical diagnosis of scapular winging who underwent EMG and NMUS were included.

RESULTS: Thirteen patients (6 females, mean age 47.3 years [range 26-72]) with scapular winging were identified. Evaluated muscles varied by patient. EMG was performed on SA (n=12), RM (n=10), UT (n=5), MT (n=2), and LT (n=1). Side-to-side EMG comparison was performed rarely in the SA, RM, and MT (all n=1). EMG identified neuropathies in seven patients, including long thoracic (n=4), dorsal scapular (n=2), and spinal accessory (n=2) mononeuropathies. One patient had both dorsal scapular and long thoracic mononeuropathies. All EMG-confirmed neuropathies showed fibrillations in the correlating muscle. NMUS was performed on SA (n=12), RM (n=12), MT (n=10), and UT (n=2). Side-to-side NMUS comparison was performed more frequently than by EMG, including SA (n=10), RM (n=9), MT (n=7), and UT (n=2). All muscles showing fibrillations showed atrophy and hyperechogenicity on NMUS.

SUMMARY/CONCLUSION: NMUS is a painless, low-cost alternative to EMG that offers easy side-to-side muscle comparison and can aid in the diagnosis of neurogenic scapular winging.

James Meiling, DO

Resident and Fellow Member Award Recipient

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A CASE OF SPINAL ACCESSORY NEUROPATHY FROM LOCAL ANESTHETIC TRIGGER POINT INJECTIONS

Isaac Metzler (Madison, WI), Collin Kreple (Waunakee, WI)

INTRODUCTION/BACKGROUND: This case presents an unusual complication of myofascial trigger point injections (TPI), a widely used treatment for pain.

CASE REPORT: A 33-year-old man presented for EDX studies to evaluate the possible cause of acute left shoulder weakness and trapezius atrophy following local anesthetic TPI for headaches. He received bilateral TPI to multiple locations within the neck and shoulders. During the procedure he recalled an acute onset of sharp left shoulder pain. He subsequently developed severe left sided neck and shoulder pain with shoulder weakness the following day. EDX testing was ordered and occurred one month after TPI. Our exam revealed 4/5 left shoulder elevation strength and left trapezius atrophy. Our NCS, which included left upper extremity antidromic sensory studies of the median and radial nerves and motor studies of the median and ulnar nerves, were normal. Needle EMG showed increased insertional activity, fibrillations, and positive sharp waves throughout the trapezius muscle. The left upper trapezius showed decreased recruitment and long duration polyphasic motor unit potentials. The EDX findings appeared consistent with an active left-sided spinal accessory neuropathy with reinnervation-associated changes.

SUMMARY/CONCLUSION: Even the simplest procedures are not without risk. Direct damage to the spinal accessory nerve found on EDX presumably from local anesthetic TPI for headaches emphasizes the importance of a thorough pre-procedural risk discussion performed by the provider.

Isaac Metzler, DO

Resident and Fellow Member Award Recipient

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SURAL NEUROPATHY AFTER DRY NEEDLING

Nicholas Miller (Winston-Salem, NC), Vanessa Baute Penry (Winston Salem, NC)

INTRODUCTION/BACKGROUND: We present a case of right sural neuropathy following dry needling treatment, diagnosed with NCS and ultrasound imaging.

CASE REPORT: A 50-year-old male ultramarathon runner developed right plantar fasciitis. During dry needling therapy he noticed a “shock like” pain in the back of his leg. Subsequently, he continued to experience burning pain down the right calf into the lateral heel, which was exacerbated with calf stretching. He was referred for EDX testing 4 months later. Sural mononeuropathy was suspected as his examination revealed a mild sensory deficit in the right lateral heel but was otherwise normal. NCS demonstrated a reduced right sural nerve sensory nerve action potential (SNAP) amplitude of 3uV, compared to a left sural SNAP amplitude of 8 uV. Sural nerve conduction velocities were 40 m/s and 42 m/s respectively. Ultrasound evaluation using a 10-22MHz linear transducer was performed. Short axis imaging of the right sural nerve revealed a focal region of increased cross-sectional area and hypo echogenicity. At the region of focal enlargement, the cross-sectional area of the sural nerve measured 4mm, while the adjacent region measured 2mm. Results from NCS and ultrasound were consistent with right sural mononeuropathy.

SUMMARY/CONCLUSION: Sural mononeuropathy is uncommon. Traumatic sural neuropathy can occur with ankle trauma and Achilles tendon repair. Nerve injuries following procedures such as dry needling or acupuncture are not well described. In this case an iatrogenic injury was suspected based on the temporal pattern and ultrasound findings.

Nicholas Miller, MD

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BANNWARTH SYNDROME (LYME NEUROBORRELIOSIS) OCCURRING DURING THE WINTER

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INTRODUCTION/BACKGROUND: Lyme disease is a tick-borne spirochete that is endemic to the Northeast, Mid-Atlantic, and Great Lakes regions of the United States that most commonly occurs during the spring and summer months. We present a case of Bannwarth syndrome (Lyme Neuroborreliosis) that occurred during the winter.

CASE REPORT: We present a case of a healthy 49-year-old male with Bannwarth syndrome without identified tick bite. Symptoms started in December with left lower lip and left-sided tongue numbness. Approximately 2 months later he developed severe lower back pain, dysphonia, and dysphagia which prompted evaluation in the emergency department. Over the next 24-hours, he developed right-sided facial droop involving both the upper and lower face, intranuclear ophthalmoplegia, paralysis of the right soft palate, absent gag reflex, reduced sensation to temperature and vibration in the lower extremities, and right foot drop. On MRI, he was found to have enhancement of the bilateral cranial nerves III, V, VII, and VIII, lower cervical spine nerve roots, cauda equina, and conus. Cerebrospinal fluid (CSF) studies identified elevated protein and white blood cells. Additionally, enzyme-linked immunosorbent assay (ELISA) identified IgG antibodies to Borrelia burgdorferi in his CSF which confirmed the diagnosis. He was successfully treated with doxycycline with improvement in symptoms.

SUMMARY/CONCLUSION: With climate change, tick-borne diseases including Lyme disease can occur outside of the typical season and should remain on the differential even during winter, particularly if a deep freeze did not occur.

Jenifer Moceri, DO

Resident and Fellow Member Award Recipient

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A RARE CASE OF ELSBERG SYNDROME MIMICKING GUILLAIN-BARRE SYNDROME

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INTRODUCTION/BACKGROUND: Elsberg syndrome (ES) is a rare infectious myeloradiculitis caused by Herpes Simplex type 2 (HSV-2) that generally presents as a cauda equina syndrome. Guillain-Barré syndrome (GBS) is the commonest cause of acute areflexic flaccid paralysis. Here, we describe an extremely rare ES resembling a GBS.

OBJECTIVE: To describe an unusual case of ES mimicking GBS.

CASE REPORT: A 75-year-old male with hypertension, chronic kidney disease, and heart failure was admitted with somnolence and ascending symmetric areflexic quadriparesis 2 days after watery diarrhea. He was diagnosed with GBS hypersomnolent variant. Due to his atypical presentation extensive workup was performed. Serum protein electrophoresis/immunofixation, anti-GQ1B, anti-nuclear, anti-neutrophil cytoplasmic, and autoimmune neuropathy antibodies and infectious tests were negative. Spine-MRI was unremarkable. Brain-MRI revealed trace bright diffusion weighed imaging signal in the left ventricular occipital horn. Initial cerebrospinal fluid (CSF) analysis showed marked neutrophilic pleocytosis, and high-protein, antibiotics were started; infectious CSF-workup was negative. NCS revealed severe sensorimotor polyneuropathy with mixed demyelinating axonal features. Due to lack of clinical improvement, a second CSF analysis was performed 5 days later, having a normal cytochemical examination, yet positive for HSV-2. Acyclovir was started, achieving clinical improvement. During hospitalization, he suffered one seizure followed by severe post-ictal encephalopathy with occasional generalized sharps waves on electroencephalography, treated with levetiracetam and supportive care. Upon discharge, motor function had improved.

SUMMARY/CONCLUSION: Our case expands the spectrum of manifestations associated with HSV-2 nervous system infection, highlighting the importance of considering ES as a potential and treatable cause of acute areflexic flaccid paralysis, particularly if standard treatment is ineffective.

Daniel Moreno-Zambrano, MD

Resident and Fellow Member Award Recipient

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ELECTRODIAGNOSTIC FINDINGS IN ANTI-MYELIN ASSOCIATED GLYCOPROTEIN ANTIBODY POLYNEUROPATHY

Joshua Nardin (Chapel Hill, NC), Rebecca Traub (Chapel Hill, NC)

INTRODUCTION: Anti-myelin-associated glycoprotein (MAG) polyneuropathy is typically described as a progressive distal, sensorimotor, demyelinating polyneuropathy with an indolent clinical course. Commonly, EDX testing shows prolonged distal motor latencies and low terminal latency index (TLI). More aggressive presentations may look similar to chronic inflammatory demyelinating polyneuropathy (CIDP). We summarize the EDX features of 20 patients with MAG antibody neuropathy.

OBJECTIVE: Compare the EDX characteristics of MAG antibody neuropathy within an institutional cohort to those described in the literature.

METHODS: A retrospective search of the electronic medical records was conducted to identify patients with anti-MAG antibody neuropathy, including only patients with high titer MAG antibody (>7000 BTU) with IgM paraprotein. NCSs were reviewed for pattern of neuropathy (demyelinating or axonal). TLI was calculated for median, ulnar, fibular, and tibial nerves.

RESULTS: Mean age of symptom onset was 69 years (55-85). EDX pattern of neuropathy was demyelinating in 55% of patients, and axonal in 35%, using European Academy of Neurology/Peripheral Nerve Society criteria. Mean TLI for the median, ulnar, fibular, and tibial nerves was 0.33 (0.16-0.74), 0.40 (0.20-0.89), 0.35 (0.14-0.77), and 0.39 (0.23-0.63). Mean TLI for all nerves was 0.36 (0.19-0.67). Of the three patients that had repeat EDX testing after treatment, two showed improvements in overall NCS and TLI, whereas one showed worsening. The TLI values in this cohort were overall higher than those described in literature.

SUMMARY/CONCLUSION: This sample of MAG antibody neuropathy patients had greater EDX phenotypic variability than described in the neuromuscular literature.

Joshua Nardin, DO

Resident and Fellow Member Award Recipient

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A CASE OF RECURRENT UNPROVOKED RHABDOMYOLYSIS CAUSED BY PERIPHERAL NERVE HYPEREXCITABILITY SYNDROME.

Isabel Narvaez Correa (Glen Allen, VA), Xinli Du (Glen Allen, VA)

INTRODUCTION/BACKGROUND: When evaluating a patient with non-traumatic rhabdomyolysis, the main differentials include toxin exposure, myopathies (autoimmune & metabolic), and muscular dystrophies. Although motor nerve hyperexcitability can cause mild creatine kinase elevations, it is generally <1,000IU/L. We report a case of recurrent unprovoked severe rhabdomyolysis in a patient with clinical Isaacs syndrome.

CASE REPORT: A 46-year-old male presents with daily muscle cramps, generalized muscle pain, and recurrent episodes of unprovoked rhabdomyolysis associated acute renal failure that requires aggressive intravenous hydration since his early 30s. The patient does not have muscle weakness. He has prominent muscle bulk despite not doing regular exercises. His creatine kinase levels weret >140K for at least three different occasions which improved with IV fluids, in between his creatine kinase levels stayed around 300-1000K. He underwent years of undiagnosed symptoms despite an extensive workup, which included a normal EMG/NCS, an unrevealing comprehensive myopathy genetic panel, and a right vastus biopsy that showed mild variation in fiber size with rare degenerative and rare esterase positive angulated fibers. The muscle pain continued to worsen, easily triggered by minor physical activities and affecting his ability to work. His neurological exam was unremarkable. Patient has no other neurological symptoms. He was found to have high titers of LGI-1 and voltage gated K channel antibodies. Malignancy workup is initiated. Treatment trial with sodium channel blockers and immunomodulating agents is started.

SUMMARY/CONCLUSION: Neuromyotonia should be considered in patients with recurrent unprovoked rhabdomyolysis, especially in those without myopathic changes on EMG.

Isabel Narvaez Correa, MD

Resident and Fellow Member Award Recipient

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ULTRASOUND GUIDANCE AND NEUROMODULATION AS A COMPLEMENT TO ELECTRODIAGNOSTICS FOR THE TREATMENT OF NEUROMAS.

Shannon Norland (Columbia, MD), Yin-Ting Chen (Bethesda, MD)

INTRODUCTION/BACKGROUND: Neuromas of the palmar cutaneous branch of the median nerve (PCBMN) can occur following surgery and may be missed with EDX alone. Ultrasound is a useful adjunct for the localization of nerve lesions. Neuromodulation also offers an alternative to resection in neuromas refractory to treatment.

CASE REPORT: A 44-year-old female with post-traumatic right wrist pain and a history of a distal pole scaphoid excision with radial styloidectomy presented 6 months postoperatively with persistent dorsal and thenar radiocarpal joint pain and sensory deficits of the palm. EDX testing with comparison studies revealed concomitant mild CTS unrelated to patient's symptoms. However, ultrasound evaluation of the median nerve and its branches demonstrated a distal neuroma of the PCBMN. A successful block of the right posterior interosseous nerve (PIN) and PCBMN was performed, thus confirming the primary pain generators. The patient's symptoms were refractory despite multiple interventions including carpal tunnel corticosteroid injection, chemoneurolysis and cyroneurolysis of the PIN and PCBMN. A peripheral nerve stimulator (PNS) trial was ultimately performed targeting the right median and radial nerves resulting in 80% patient reported improvement in global symptoms and functional scores.

SUMMARY/CONCLUSION: While lesions of the PIN and median nerve from trauma or compression at common sites of entrapment are well described in the literature, lesions to the cutaneous sensory branches are less understood. Ultrasound has proved a useful diagnostic complement to EDX to pin-point distal peripheral nerve lesions. Furthermore, neuromodulation has provided an effective treatment option for distal sensory nerve pathologies unresponsive to other treatment modalities.

Shannon Norland, DO, MPH

Resident and Fellow Member Award Recipient

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AN UNUSUAL DIAGNOSIS IN A 28-YEAR-OLD MAN WITH WEAKNESS AND SLURRED SPEECH

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INTRODUCTION/BACKGROUND: Late onset Tay-Sachs disease (LOTS) is a rare autosomal-recessive disorder caused by reduced B-hexosaminidase A activity leading to ganglioside accumulation in the central nervous system. It is underdiagnosed and often misdiagnosed due to its delayed presentation and varied clinical manifestations including weakness, cerebellar dysfunction, and psychiatric disturbances.

CASE REPORT: A 28-year-old man presented with 2 years of progressive, painless proximal muscle weakness. He complained of difficulty getting up from a chair and walking up the stairs. He also developed twitching of his thighs, exacerbated by dehydration and physical activity. Though he had mild dysarthria at baseline, this worsened over several months. He did not have tongue fasciculations, dysphagia, dyspnea, diplopia, or fatigable symptoms. His sister had similar symptoms starting in childhood and underwent evaluation for spinal muscular atrophy, however genetic testing was negative. Neurological examination was notable for moderate dysarthria, weakness in iliopsoas and quadriceps muscles, and hyperreflexia. There was no evidence of nystagmus or ataxia; the remainder of his neurological examination was unremarkable. Basic laboratory workup was unrevealing, including normal creatine kinase. MRI brain revealed diffuse pontocerebellar atrophy. NCS/EMG showed evidence of a chronic and mostly inactive disorder of the motor neurons, roots or motor axons affecting the right upper cervical, and bilateral lumbosacral levels. Genetic testing revealed two heterozygous pathogenic variants in the HEXA gene consistent with LOTS disease.

SUMMARY/CONCLUSION: Appropriate enzymatic and genetic testing for LOTS should be performed in relevant cases presenting as a motor neuronopathy with no evidence of a deletion in the SMN1 gene.

Chineze Nwebube, MD, MSc

Resident and Fellow Member Award Recipient

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MYH2 MUTATION IN MONOZYGOTIC AFRICAN AMERICAN TWINS PRESENTING WITH PTOSIS, DIPLOPIA, OPHTHALMOPLEGIA AND PROXIMAL WEAKNESS

Peter Pacut (Richmond, VA), Nicholas Johnson (Glen Allen, VA)

INTRODUCTION/BACKGROUND: MYH2 (myosin heavy chain 2) mutations can lead to autosomal dominant or recessive proximal myopathy with ophthalmoplegia. We describe monozygotic twins that have this above presentation with a heterozygous pathogenic variant in MYH2 that has not been previously reported to cause autosomal dominant disease.

CASE REPORT: A 41-year-old African American woman initially presented with muscles aches in the setting of a urinary tract infection. Her creatinine kinase (CK) was elevated at 1665. She was on a statin at that time, and it was discontinued. She continued to have flares of similar symptoms of muscles aches and fatigue with fluctuating CK between 300 and 1200. EMG was notable for myopathic changes. Myositis antibody panel was negative. She underwent a muscle biopsy of her left biceps and deltoid which was interpreted as inclusion body myositis due to presence of rimmed vacuoles. At age 44 she began to develop symptoms of left eye ptosis and diplopia. Her exam also revealed mild symmetric proximal muscle weakness in the deltoids and hip flexors. There were no joint contractures. She had antibody testing for myasthenia which was negative. Her identical twin sister had very similar symptoms, otherwise there was no family history. They both underwent genetic testing which revealed heterozygosity in MYH2 gene with pathogenic variant of c.3697G>T (p. Glu1233). This variant had not been previously reported to confer risk in an autosomal dominant pattern. This variant was not sufficient to cause symptomatic carrier status. Both twins were diagnosed with autosomal dominant proximal myopathy with ophthalmoplegia due to MYH2 mutation.

SUMMARY/CONCLUSION: MYH2 myopathy should be considered in patients with asymmetric ptosis, diplopia, and ophthalmoplegia.

Peter Pacut, MD

Resident and Fellow Member Award Recipient

Disclosures:

Nicholas Johnson - grants or contracts NIND R01NS104010, U01NS124974FDA 2R01FD006071CDC U01DD001242 Grants to institution Dyne Therapeutics Wyck Foundation Coalition to Cure Calpain 3 Muscular Dystrophy Association Cure Rare Diseases Novartis Pfizer AMO PharmaML bioFulcrum Therapeutics PepGen Vertex Sarepta Askbio Takeda Arthex Avidity Biosciences Participation on a Data Safety Monitoring Board or Advisory Board Biogen DSMB member Fulcrum DSMB member Consulting fees Novartis Personal fee Sarept Personal fee Askbio Personal fee Vertex Personal fee Dyne Personal fee AMO Pharma Personal fee Rgenta Personal fee Kate Therapeutics Personal fee Stock or Stock Options Angle Therapeutics Personal options Juvena Therapeutics Personal options.

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UTILITY OF THE REVISED AMYOTROPHIC LATERAL SCLEROSIS FUNCTIONAL RATING SCALE RESPIRATORY SUBSCORES FOR PREDICTING THE NEED FOR BILEVEL POSITIVE AIRWAY PRESSURE

Tefani Perera (Calgary, Canada), Jamie Greenfield (Calgary, Canada), Gordon Jewett (Calgary, Canada)

INTRODUCTION: ALS is a debilitating motor neuron condition.

OBJECTIVE: We evaluated the utility of the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R) for predicting use of bilevel positive airway pressure (BiPAP) in people with ALS.

METHODS: We conducted a retrospective study using the Pooled Resource Open-Access ALS Clinical Trials Database. People with ALS, ≥2 ALSFRS-R assessments, and baseline ALSFRS-R respiratory insufficiency score (RiS) = 4 (no BiPAP) were included. Primary outcome was RiS ≤3 (BiPAP use). Exposures were ALSFRS-R dyspnea (DyS) and orthopnea (OS) subscore transitions. Survival analyses estimated time to outcome and cumulative probability of outcome within 91 days.

RESULTS: We included 3,838 people. Median time [95% CI] from first ALSFRS-R to respiratory outcome was 563 days [528, 624] with 3.4% [2.9, 4.0] reaching outcome within 91 days. People meeting respiratory outcome within 91 days were more likely to have baseline DyS and OS ≤3. Probability of respiratory outcome was significantly associated with baseline DyS and OS (log-rank test $p<0.0001$). Median time [95% CI] to outcome was 393 days [336, 448] with 9.8% [7.8, 12.3] reaching outcome within 91 days after DyS transition to 3, versus 282 days [242, 335] and 17.6% [15.0, 20.6] after DyS transition to 2. Median time to outcome was 594 days [538, 630] with 2.6% [2.1, 3.2] reaching outcome within 91 days after baseline OS = 4, versus 230 days [196, 261] and 20.8% [17.9, 24.1] after OS transition to 3.

SUMMARY/CONCLUSION: Orthopnea and dyspnea ALSFRS-R sub score thresholds may help identify people with ALS at risk of needing BiPAP.

Tefani Perera, MD

Resident and Fellow Member Award Recipient

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SEQUENTIAL DEVELOPMENT OF HERPES ZOSTER RADICULOPATHY FOLLWED BY BRACHIAL PLEXOPATHY IN A PATIENT WITH POORLY CONTROLLED DIABETES, EXHIBITING FAVORABLE RESPONSE TO STEROIDS

Saniya Pervin (Lexington, KY), Nakul Katyal (Lexington, KY)

INTRODUCTION/BACKGROUND: Herpes zoster infection typically results in a painful dermatomal vesicular rash. Brachial plexus involvement is rarely observed. We describe a challenging case of a patient with poorly controlled diabetes mellitus (DM) who developed herpes zoster radiculopathy followed by brachial plexopathy.

CASE REPORT: A 58-year-old man with poorly controlled type 2 DM (HbA1C 11.6%) was seen for right upper extremity pain and weakness of 4-month duration. Symptoms started with painful, vesicular rash along the right C5-C6 dermatome. Three weeks later, he noted weakness in right thumb and index finger. One week later, he developed difficulty raising right arm antigravity. He received Acyclovir but not steroids. The rash resolved but the pain and weakness continued to progress. Examination showed right proximal and distal upper extremity weakness, scapular winging, supra and infraspinatus and deltoid atrophy. EMG showed subacute, right brachial plexopathy with upper trunk involvement, right anterior interosseous neuropathy and right C5-C7 radiculopathy with active paraspinal denervation. MRI brachial plexus showed STIR hyperintensities involving C5, C6 nerve roots, lateral, posterior, and medial cords. The patient was diagnosed with right radiculo-plexopathy, likely related to VZV and or diabetic amyotrophy. Given persistent neuropathic pain, he was started on oral steroid therapy (60 mg oral prednisone for 7 days followed by 10 mg daily taper) with close endocrinology follow-up. He noted mild reduction in pain from 6/10 to 4/10.

SUMMARY/CONCLUSION: In cases with persistent pain with VZV and or diabetic plexopathy, oral steroids with close blood glucose monitoring may be a reasonable consideration even later in the course of disease.

Saniya Pervin, MBBS

Resident and Fellow Member Award Recipient

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SCIATIC NEUROPATHY WITH CLINICO-RADIOLOGICAL PATTERN CONSISTENT WITH INTRANEURAL PERINEURIOMA: AN UNDERRECOGNIZED CAUSE OF PROGRESSIVE MONONEUROPATHY

Saniya Pervin (Lexington, KY), Nakul Katyal (Lexington, KY)

INTRODUCTION/BACKGROUND: Intraneural perineurioma is a rare and highly underdiagnosed condition. We present a case of chronic right sciatic neuropathy in a young woman with clinical and radiological patterns consistent with this condition.

CASE REPORT: A 19-year-old female presented with slow progressive right foot weakness, right posterior thigh pain, and gait difficulties of over 7-year duration. She denied any preceding inciting events. Examination showed right foot (dorsiflexion>>plantarflexion) and knee flexion weakness with absent right ankle reflex. EMG study showed findings consistent with chronic right sciatic neuropathy with ongoing active denervation in tibialis anterior and peroneus longus muscles, interestingly sparing the short head of biceps femoris. MRI of pelvis/right thigh showed increased signal on T2-weighted images and thickening in the right sciatic nerve, more pronounced proximally without evidence of external compression. MRI leg showed denervation of the peroneal longus, brevis, tibialis anterior, tibialis posterior, and popliteus muscles but with normal appearance of peroneal and tibial nerves. MRI lumbar spine was normal. Review of MRI neurogram showed radiological pattern of T1 hypointensity, T2 hyperintensity with post-contrast enhancement of sciatic nerve, a pattern consistent with Intraneural perineurioma. Patient was diagnosed with intraneural perineuroma based on the Perineurioma Diagnostic Criteria meeting clinical and radiological features consistent with this condition.

SUMMARY/CONCLUSION: In patients presenting with slow, progressive mononeuropathy, intraneural perineurioma should be in the differential and a careful review of imaging studies must be conducted with close attention to T1, T2, and post contrast sequences. The use of Perineuroma diagnostic criteria may obviate the need for tissue biopsy in this condition.

Saniya Pervin, MBBS

Resident and Fellow Member Award Recipient

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UTILITY OF THE EARLY SJOGREN ANTIBODY PANEL AS A DIAGNOSTIC MARKER FOR SENSORY NEUROPATHY

Stephanie Phillips (Detroit, MI), Cherine Fawaz (Detroit, MI), Lawrence Zeidman (Detroit, MI), Katie Latack (Detroit, MI)

OBJECTIVE: To assess the utility of Carbonic Anhydrase-6 (CA-6), Parotid Secretory Protein (PSP), and Salivary Protein-1 (SP-1) antibodies (Early Sjögren antibodies (ESA)) in the diagnosis of sensory neuropathy and determine predictive features.

BACKGROUND: Primary Sjögren syndrome is a chronic autoimmune disease characterized by lymphocytic infiltration of exocrine glands, but also frequently sensory neuropathy. ESA were found in 45% of Sjögren patients who lacked traditional antibodies (Ro/La). No other study has examined the association of ESA with sensory neuropathy.

DESIGN/METHODS: All neuropathy patients tested for ESA from May 2023-January 2024 were retrospectively analyzed for clinical/pathological features. Seropositive/seronegative groups were separated for statistical analysis.

RESULTS: 12 patients (83% female) with cryptogenic sensory neuropathy had ESA testing. 4 had abnormal EMG and 8 had normal EMG but abnormal skin biopsies (67% pure small fiber neuropathy (SFN)). 5 (42%) had abnormal ESA. Of these 5, 4 (80%) had pure SFN vs. 4 (57%) seronegative patients (p=NS). 5 (100%) seropositive patients had sicca symptoms vs. 1 seronegative patient (14%) (p=0.02). Seropositive patients had a median Utah early neuropathy scale (UENS) score=7 vs. 2 for the seronegative group (p=0.15). 5 (100%) of seropositive patients had pathological non-length dependence (NLD)/vasculitis or acute onset vs. 5 (71%) seronegative (p=NS); 80% seropositive had clinical NLD vs. 43% seronegative patients (p=0.29).

CONCLUSIONS: ESA may be seen in 42% of cryptogenic sensory neuropathy patients. Seropositive patients have more sicca symptoms and trend toward higher UENS scores and clinical NLD than seronegative patients. Further work on a larger population should be done to confirm these findings.

Stephanie Phillips, MD

Resident and Fellow Member Award Recipient

TOOLS AND METHODS FOR THE REMOTE ASSESSMENT OF AMYOTROPHIC LATERAL SCLEROSIS PROGRESSION: A SCOPING REVIEW

Michael Potemkin (Calgary, Canada), Tefani Perera (Calgary, Canada), Gordon Jewett (Calgary, Canada)

INTRODUCTION: People with ALS experience progressive functional impairment that makes attending clinical care and research participation challenging. Remote assessments of symptoms and disease progression in ALS could reduce the burden on patients and their caregivers. However, remote assessment tools have not yet been integrated into routine clinical care or late-stage clinical trials. We aimed to assess the current landscape of tools for the remote assessment of ALS symptoms.

OBJECTIVE: To perform a scoping review of tools, devices, and methods for the remote assessment of people with ALS.

METHODS: We systematically searched EMBASE, OVID Medline and Web of Science databases. All primary literature concerning remote monitoring devices or methods in ALS were included.

RESULTS: A total of 32 articles met inclusion criteria. Tools included accelerometers, tele-nursing protocols, neural-network integrated speech analysis apps, and questionnaires. Studies assessed symptom progression in various domains including respiratory (16 studies), motor (12), speech (12) and others, such as psychiatric and bulbar (5). The majority of studies assessed feasibility or diagnostic accuracy, but five were methodological proposals for larger future studies. Risk of bias was high, with only 10 studies using a gold-standard to compare disease progression.

SUMMARY/CONCLUSION: Remote ALS assessment is an emerging field that includes a broad range of innovative tools and methods. Larger long-term studies comparing diagnostic tests to gold-standard references, such as the ALSFRS-R, are needed.

Michael Potemkin, BHSc

Resident and Fellow Member Award Recipient

RADIAL TUNNEL VISION: USE OF ULTRA-HIGH FREQUENCY ULTRASOUND TO DIAGNOSE NERVE SHEATH TUMORS

Syed Qadri (Washington, DC), Daniel Wido (Bethesda, MD), Matthew Miller (Potomac, MD)

INTRODUCTION/BACKGROUND: Ultra-high frequency ultrasound (UHFUS, defined as >50MHz) is a clinical diagnostic tool capable of up to 30- µm resolution. This method has been increasingly used to diagnose numerous peripheral neuropathies including nerve trauma, mononeuritis, and peripheral nerve sheath tumors. Here, we report a unique case of posterior interosseus nerve (PIN) neuropathy due to UFUHS-demonstrated schwannoma.

CASE REPORT: A 55-year-old male presented with complaints of right radial forearm pain that started 5 years prior after an IV infiltration in the right hand. The pain subsequently migrated ever-more proximally to just above the olecranon. He also reported some subjective weakness in wrist and finger extensors. Needling, acupuncture, and previous steroid injection provided minimal relief. Physical exam yielded no gross atrophy nor muscle weakness. EMG/NCS tests demonstrated mild, non-focal slowing of the right radial nerve but no signs of active or chronic denervation to radial/PIN-innervated muscles. UFUHS of right upper extremity revealed a 1.7 cm lesion of the PIN at the level of the supinator. MRI confirmed 1.8 cm mass adjacent to the proximal radius/intimately involved with the supinator muscle, deemed likely a peripheral nerve sheath tumor of the posterior interosseous nerve or radial nerve. Surgical excision of the mass was later performed, confirming PIN schwannoma.

SUMMARY/CONCLUSION: In conclusion, UFUHS is a powerful diagnostic modality capable of serving as a useful adjunct to EMG/NCS in the localization of nerve sheath tumors. In this instance, UFUHS demonstrated remarkable fidelity with MRI findings of a PIN schwannoma.

Syed Qadri, MD

Resident and Fellow Member Award Recipient

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ASSESSING NORMAL LATENCY CHANGES IN ULNAR NERVE SHORT-SEGMENT INCREMENTAL STUDIES USING 15 AND 25 MILLIMETER INCREMENTS

Sandra Reiter-Campeau (Rochester, MN), Deborah O. Setter (Rochester, MN), Christopher Hanson (Rochester, MN), Ruple S. Laughlin (Rochester, MN)

INTRODUCTION: Short-segment incremental studies (SSIS, “inching”) increase diagnostic sensitivity and can localize focal lesions in ulnar neuropathy. A stimulator is moved along the nerve in short increments looking for a decrease in amplitude or an increase in latency of the compound muscle action potential. Some laboratories use the stimulator head to measure stimulation distance, which can vary by manufacturer. Latency changes depend on stimulation distances, and AANEM practice parameters state that normal maximal latency changes are approximately 0.4 ms and 0.6 ms for 10 mm and 20 mm distances, respectively.

OBJECTIVE: The purpose of this study is to determine the upper limits of normal for latency changes in ulnar SSIS using stimulators with 15 and 25 mm probe distances.

METHODS: Healthy, asymptomatic adult volunteers were prospectively recruited and underwent bilateral ulnar nerve SSIS using 15 and 25 mm Cadwell® StimTroller Plus handheld stimulators. The cathode-to-anode distance was used to determine increments. Ulnar SSIS were excluded if an amplitude decrement of 10% or more was present.

RESULTS: The study included 87 ulnar nerve SSIS from 45 subjects. Cathode-to-cathode stimulation measurements were on average 15.8 mm using the 15 mm stimulator and 26.7 mm using the 25 mm stimulator. Mean latency changes were 0.31 ms (range: 0.1-0.9 ms) and 0.50 ms (range: 0.1-1.2 ms) for 15- and 25-mm increments respectively, and the 99th percentile for latency changes were 0.70 ms and 0.93 ms, respectively.

SUMMARY/CONCLUSION: We propose 0.7 ms and 0.9 ms as normal maximal latency changes when performing ulnar SSIS with 15 and 25 mm increments.

Sandra Reiter-Campeau, MD

Resident and Fellow Member Award Recipient

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PERSISTENT FEMORAL NEUROPATHY FOLLOWING NERVE BLOCK FOR KNEE SURGERY

Sophie Rengarajan (Palo Alto, CA), Sarada Sakamuri (Palo Alto, CA)

INTRODUCTION/BACKGROUND: Femoral nerve blocks (FNB) are widely utilized during knee surgery to reduce pain and length of hospitalization. Transient neuropathy is expected, but persistent femoral neuropathy is infrequently diagnosed. We describe three such cases.

CASE REPORT: Case 1: A 32-year-old man with medial meniscus tear underwent arthroscopic repair with FNB. Post-op he had new right thigh and medial leg numbness and 5 days of knee extension weakness. At 5 months, he had persistent numbness, subtle quadriceps weakness, quadriceps denervation and chronic reinnervation on EMG, and asymmetric saphenous sensory NCSs.

Case 2: A 29-year-old woman with anterior cruciate ligament and medial meniscus tears underwent arthroscopic repair with thigh tourniquet and 3 days of take-home FNB catheter. Afterwards she had new right anterior thigh numbness and 1 to 2/5 knee extension. At 7 months she had persistent numbness, 3/5 knee extension, quadriceps denervation and chronic reinnervation on EMG, and asymmetric saphenous NCSs.

Case 3: A 66-year-old woman with knee osteoarthritis underwent total knee arthroplasty with thigh tourniquet and FNB. Post-op she had new medial leg numbness and knee extension weakness. At 12 months she had persistent numbness, 4/5 knee extension, quadriceps reinnervation on EMG, and asymmetric saphenous NCSs.

SUMMARY/CONCLUSION: Femoral neuropathy can persist after FNB and impact patients’ quality of life. Axonal injury may be related to mechanical, neurotoxic, and ischemic factors. The impact of intraoperative thigh tourniquet use is unclear. Large cohort studies are needed to determine the true prevalence of and risk factors for this condition.

CHARACTERISTICS OF FAMILIAL AMYOTROPHIC LATERAL SCLEROSIS WITH A PHE20CYS MUTATION IN THE SOD1 GENE

Kassandra Reyes (Austin, TX), Hannah Machemehl (Austin, TX)

INTRODUCTION/BACKGROUND: ALS is a progressive, neurodegenerative condition that affects the upper and lower motor neurons. Though most cases of ALS are sporadic, approximately 10% of cases are inherited. Of those with familial amyotrophic lateral sclerosis (FALS), 15-20% of these cases are linked to mutations in the Cu/Zn Superoxide Dismutase (SOD1) gene. Over 200 mutations of SOD1 linked to development of ALS have been reported to date. In this case report, we describe the characteristics of a family with FALS found to have a Phe20Cys mutation in the SOD1 gene, a rarely described variant.

CASE REPORT: Our proband patient is a 65-year-old male who began developing symptoms of leg weakness and recurrent falls in October of 2022, closely followed by a diagnosis of ALS. The patient has a strong family history of ALS with his grandfather, father, aunt, and twin brothers all being affected. On genetic testing, the patient was found to have a pathogenic variant of the SOD1 mutation which consists of a missense replacement of phenylalanine with cysteine at codon 21. Family history was obtained to develop a pedigree representing 30 family members. In four generations, six family members were affected with ALS.

SUMMARY/CONCLUSION: Here we present characteristics of a family with FALS with a Phe20Cys SOD1 mutation. We seek to describe the phenotype of this rarely described pathogenic variant, which has previously been reported in one other family.

Kassandra Reyes, DO

Resident and Fellow Member Award Recipient

Disclosures:

Hannah Machemehl - has served as a consultant for UCB and Octapharma.

BLINK REFLEX IN DEMSILIENIZING POLYNEUROPATHY, IN THE TWINKLING OF AN EYE

Cristhian Rojas Beltran (Bogota, Colombia)

INTRODUCTION/BACKGROUND: NCSs are a tool for the diagnosis of acute polyradiucloneuropathies also known as Guillain Barré syndrome. In addition to confirming clinical suspicion, these studies provide information on the type of compromise that is occurring in the nerve fiber, differentiating axonal presentation from demyelinating, however in cases of severe neurophysiological compromise the differentiation of these can be difficult, in this case the usefulness of the blink reflex is presented to differentiate between these presentations.

CASE REPORT: A previously healthy 13-year-old boy who was admitted for 1 month of sensation of paresthesia, hypoesthesia in gloves and boots and altered gait, nerve conduction studies were performed that showed absence of sensory potentials in all four extremities as well as a marked decrease in motor potentials in the four extremities, a palpebral reflex study was performed that showed marked alteration of latencies in all responses, concluding that it was a case of demyelinating type polyneuropathy.

SUMMARY/CONCLUSION: In severe cases of demyelinating nerve involvement, neurophysiological studies may appear to be axonal involvement as motor potentials are absent or markedly decreased; however, the alteration in myelin may show a temporary dispersion event in motor and sensory potentials, with an apparent marked decrease. Or absence of electrophysiological response, it is in this case that the blink reflex shows its usefulness as there is no decrease in motor responses and the alteration in nervous latencies is clearly evident.

Cristhian Rojas Beltran, MD

Resident and Fellow Member Award Recipient

EXERCISE TEST FOR EATON LAMBERT SYNDROME, CAN WE REALLY TRUST IT? A CASE REPORT

Nicolas Ruan dos Santos Cavalcante (São Paulo, Brazil), Lucas Marenga de Arruda Buarque (São Paulo, Brazil), Ian Felipe Barbosa Souza (São Paulo, Brazil), Jose Pedro Soares Baima (São Paulo, Brazil), Carlos Heise (São Paulo, Brazil)

INTRODUCTION/BACKGROUND: There is consensus in the literature that exercise testing (ET) can be used instead of high-frequency stimulation (HFS) for presynaptic neuromuscular junction disorders, such as Lambert-Eaton myasthenic syndrome (LEMS). The case presented is an example in which ET was not sufficient for this diagnosis.

CASE REPORT: A 47-year-old female patient presented with symmetric weakness in the lower limbs. After 2 weeks she had hoarseness and eyelid ptosis, with progressive involvement of the upper limbs. Physical examination was consistent with 3/5 lower extremity and 4/5 upper extremity strength bilaterally, areflexia, and preserved sensation. She progressed to respiratory failure and was transferred to the ICU. Theoretically, patients with LEMS have an increase or even normalization of compound muscle action potential after maximum effort. In this clinical case, the EMG showed decrease in the low-frequency repetitive stimulation test (32%) and after maximum effort (10s) there was no significant increase in compound muscle action potential (only raised 25%), leading to the hypothesis of a post-synaptic junction disorder. An increase of 70% was observed with the 30 Hz HFS. Only stimulation at 50Hz (244% increment) led to criteria for presynaptic disorder. Autoimmunity tests showed abnormalities (Anti-Ro and FAN above the reference value). The diagnosis of LEMS was confirmed using voltage gated calcium channel antibodies.

SUMMARY/CONCLUSION: Due to the delay in antibody results, it is essential that the LEMS diagnosis be made by EMG. This case showed that ET with a normal result cannot always be used to rule out presynaptic junction disorders. Given clinical suspicion, high-frequency stimulation is necessary.

Nicolas Ruan dos Santos Cavalcante, MD

Resident and Fellow Member Award Recipient

PULSATING NERVE: INTRANEURAL VASCULARIZATION IN A PATIENT WITH LEPROSY REACTION

Nicolas Ruan dos Santos Cavalcante (São Paulo, Brazil), Lucas Buarque (São Paulo, Brazil), Ian Felipe Barbosa Souza (São Paulo, Brazil), Jose Pedro Soares Baima (São Paulo, Brazil), Carlos Heise (São Paulo, Brazil)

INTRODUCTION/BACKGROUND: Ultrasound (US) allows the static and dynamic evaluation of peripheral nerves, and it is even possible to look for signs of inflammation. Infection of peripheral nerves can be caused by mycobacterium leprae, which has Schwann cells as its main target. The neurological deficit occurs due to direct invasion, and also due to the inflammatory reaction.

CASE REPORT: A 39-year-old Brazilian female, presented with weakness and a change in sensitivity in the left upper limb for about 1 year. Her medical history showed treatment for leprosy. Her skin biopsy (2007) of the palmar region showed intense perivascular and perineural inflammatory infiltrate, with vacuolated histiocytes. She received a diagnosis of multibacillary leprosy and treated (completed a treatment in 2013). EMG showed focal demyelination of the ulnar nerve at the elbow, Ultrasound longitudinal with color doppler of ulnar nerve showed intraneural vascularization (below and adjacent at the epineurium), which is a pattern suggestive of neuritis. Transverse evaluation showed presence of an intraneural fibrosis in wrist. In addition to focal thickening at the elbow and above it and loss of fascicular pattern. Cross sectional areas of the ulnar nerve were 8 mm2 at the wrist, 14 mm2 at the epicondylar groove and 22 mm2 at 2-4 cm above the elbow. The findings are compatible with leprosy neuritis.

SUMMARY/CONCLUSION: This case was illustrative to show that ultrasound can, in addition to focal thickening of the nerve, lead to the diagnosis of leprosy neuropathy. So, when we find a "pulsating nerve", especially in endemic places, neural involvement by leprosy should be the first diagnostic hypothesis.

Nicolas Ruan dos Santos Cavalcante, MD

Resident and Fellow Member Award Recipient

EVALUATING EFGARTIGIMOD'S IMPACT ON MYASTHENIA GRAVIS: INSIGHTS FROM A COMPARATIVE STUDY AND COSMOS-EPIC DATA

Roopa Sharma (Harrison, NJ), Kazim Jaffry (Colonia, NJ), Ahmed Sabra (Newark, NJ), Justin Matos (Edison, NJ), Mustafa Jaffry (Edison, NJ), Amine Aboussalah (New York, NY), Nizar Souayah (Westfield, NJ)

INTRODUCTION: We observed significant short-term improvements in some myasthenia gravis (MG) patients transitioning to efgartigimod from conventional therapies (CTs). This. This study aims to evaluate both immediate and enduring impacts on patient outcomes.

OBJECTIVE: To conduct a comparative analysis of the short- and long-term benefits of efgartigimod treatment in MG against CT options.

METHODS: Retrospective observational study from Rutgers Clinics supplemented by data from COSMOS-EPIC.

RESULTS: Our study included eight patients who transitioned to efgartigimod treatment, while 57 remained on CTs. Patients on efgartigimod showed improvements in MG-ADL scores at 3 and 12 months, with statistical significance observed only at the 3-month mark (3.57 ± 2.14 vs. 6.64 ± 3.39, p = 0.049). The average MG-ADL score did not significantly differ between the efgartigimod group, intravenous immunoglobulin (IVIg), and non-IVIg groups. Hospitalization rates were also similar across all groups. From the COSMOS-EPIC database, we identified 658 patients on Efgartigimod and 8,323 on IVIg. Compared to IVIg patients, those on efgartigimod had significantly lower instances of mechanical ventilation (4.6% ± 1.6% vs. 13.1% ± 0.725%), Skilled Nursing Facility (SNF) discharges (3.0% ± 1.3% vs. 9.6% ± 0.634%), and disabilities (4.9% ± 1.6% vs. 10.0% ± 0.645%).

SUMMARY/CONCLUSION: The administration of efgartigimod in MG demonstrated significant improvement in MG-activities of daily living scores within the initial 3 months compared to CTs. However, its effects wane within 12 months of use. Furthermore, patients receiving efgartigimod showed fewer instances of mechanical ventilation, disabilities, and discharges to SNF. Larger studies are necessary to further explore the long-term efficacy and safety of efgartigimod.

Roopa Sharma, MD

Resident and Fellow Member Award Recipient

IMPACT OF DIABETES MELLITUS ON CLINICAL OUTCOMES IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

Roopa Sharma (Harrison, NJ), Kazim Jaffry (Colonia, NJ), Nizar Souayah (Westfield, NJ)

INTRODUCTION: To investigate the impact of diabetes mellitus (DM) on the outcomes of chronic inflammatory demyelinating polyneuropathy (CIDP) patients.

OBJECTIVE: DM and CIDP co-occurrence complicate diagnosis and treatment due to symptom overlap. The influence of DM on CIDP outcomes is poorly understood.

METHODS: We retrospectively reviewed Epic Cosmos electronic records, and 51,444 patients with CIDP were included. Patients were categorized into two groups based on the presence or absence of underlying DM. We compared demographic, laboratory markers and clinical outcomes between these two groups, including age, gender, body mass index (BMI), disability, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), disability levels, skilled nursing facility (SNF) admissions, and mortality.

RESULTS: Of 51,444 CIDP patients, 33.9% had DM, experiencing worse outcomes: higher mortality (7.4% vs. 3.3%), amputation rates (2.4% vs. 0.253%), disability (19% vs. 10.9%), and SNF admissions (21.2% vs. 9.4%). The DM group was older (average age 67 vs. 63 years), more obese (67.7% vs. 42.2%), and had elevated inflammatory markers, indicating increased systemic inflammation.

SUMMARY/CONCLUSION: Our study demonstrated that DM is associated with worse clinical outcomes in patients with CIDP. These adverse outcomes may be due to direct damage to the peripheral nerves by DM, exacerbating the nerve damage caused by CIDP, or the presence of diabetic neuropathy complicating the timely diagnosis and treatment of CIDP. The findings underscore the urgent need for specific biomarkers to improve the diagnosis of CIDP in patients with diabetes, aiming to enhance patient outcomes through earlier and more targeted.

Roopa Sharma, MD

Resident and Fellow Member Award Recipient

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PROXIMAL BERRETTINI ANASTOMOSIS AND THE BENEFIT OF PREOPERATIVE ULTRASOUND

Kareen Shaw (Bethesda, MD), Daniel Wido (Bethesda, MD), Marin Smith (Bethesda, MD), Matthew Miller (Potomac, MD)

INTRODUCTION/BACKGROUND: EDX studies and diagnostic ultrasound (US) evaluation are vital tools for the management of CTS. Aberrant anatomy is an important consideration for surgical disposition. Berrettini anastomosis is an interneural communication between common palmar digital sensory branches from the median and ulnar nerves. Here, we report a unique case of a patient with moderate CTS and concomitant Berrettini anastomosis, highlighting preoperative value of US in the EDX clinic in avoidance of iatrogenic injury.

CASE REPORT: A 43-year-old male with a history of left carpal tunnel release (CTR) presented to the EDX clinic with 8 months of right first and third finger paresthesia aggravated with yard work and driving. Exam notable for preserved strength and sensation. Positive Tinel's at the wrist. He was refractory to conservative management. NCS demonstrated right median motor and sensory prolonged distal latency with normal amplitudes and conduction velocity. Ulnar nerve studies were normal. US demonstrated enlarged median nerve at the carpal inlet measuring 13mm2 with a difference of 3 mm2 from pronator quadratus. Berrettini anastomosis visualized just proximal to the cross-over of the palmar arterial arch and median digital branch.

SUMMARY/CONCLUSION: US is an important adjunct to EDX in the preoperative stage of CTS management. Identification of aberrant anatomy via US has the potential to minimize complications from CTR. In this case, a Berrettini anastamosis was identified and rather than proceed with US guided CTR, the patient was referred to orthopedics for open CTR.

Kareen Shaw, DO

Resident and Fellow Member Award Recipient

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CLINICAL OUTCOME AND PROGNOSTICATION OF INFLAMMATORY AND IMMUNE MYOPATHIES PATIENTS WITH AND WITHOUT CHEMOTHERAPY IN THE UNITED STATES

Baljinder Singh (Jersey City, NJ), Elina Zakin (Albertson, NY)

INTRODUCTION: Inflammatory and immune myopathy (IIM) is an umbrella term that comprises various types of myopathies based on the result of autoantibodies and clinical presentation. Very limited data is available on patients who were diagnosed with IIM and required chemotherapy for underlying malignancies.

OBJECTIVE: To compare the clinical outcome and in-hospital complication risk with chemotherapy and without chemotherapy in patients with inflammatory and immune myopathies.

METHODS: We obtained data for IIM patients admitted to hospitals in the United States from 2017 to 2019 with a primary diagnosis of IIM using a large national database.

RESULTS: A total of 1072 patients had IIM out of which 63 (5.8%) received chemotherapy for the underlying malignancies. No racial differences were observed in both groups, however mean age for the patients who required chemotherapy was more than the non-chemotherapy group (72.7 vs 67, $p < 0.01$). Patients who received chemotherapy had more in-hospital complications including, sepsis (25.1% vs. 11.6%, $p<0.01$), and acute kidney injury (23.8%% vs. 13.2%, $p < 0.01$). No significant difference was noticed in the length of stay during hospitalization in both groups. The number of deaths were higher in the chemotherapy group. In a further study of the patients who died in the chemotherapy group, the risk of myocardial infarction (MI) was 16 times higher compared to the patients who survived. ($p<0.01$)

SUMMARY/CONCLUSION: In hospitalization complications such as sepsis and acute kidney injury were higher in the patients who received chemotherapy, in IIM patients and patients who died had 16 times more risk of having MI.

Baljinder Singh, MD

Resident and Fellow Member Award Recipient

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A RARE CASE OF RELAPSING REMITTING CRANIAL MONONEURITIS MULTIPLEX AS INITIAL PRESENTATION OF NEUROSARCOIDOSIS

Serena Soleimani (Lansing, MI), Dudley Campbell III (Lansing, MI), Krish Muralidhara (Okemos, MI), Swathi Beladakere Ramaswamy (Okemos, MI)

INTRODUCTION/BACKGROUND: Neurosarcoidosis constitutes 10% of sarcoidosis and presents as leptomeningitis, myelopathy, stroke, epilepsy, peripheral neuropathy, myopathy, hypothalamic-pituitary dysfunction, or cranial neuropathy.

CASE REPORT: A 51-year-old female with insidious onset complete right facial weakness and right taste sensation loss was treated as idiopathic facial palsy after MRI ruled out stroke with a brief course of prednisone. Symptoms improved over the next few weeks with mild residual right eye closure weakness. Months later, she insidiously developed complete left facial weakness with MRI revealing left facial nerve enhancement. Symptoms completely resolved after another brief prednisone course. She then returned with asymmetric minimally fluctuating bilateral ptosis, bilateral V1 and V3 facial numbness and difficulty puffing out her left cheek. This was clinically suggestive of bilateral oculomotor, bilateral trigeminal and left facial nerve involvement.

MRI brain, with thin brainstem sections, re-demonstrated left facial nerve enhancement. Total-body PET showed normal fluorodeoxyglucose uptake. Serum studies were positive for atypical antineutrophil cytoplasmic antibodies, elevated erythrocyte sedimentation rate and C-reactive protein, but negative for antinuclear antibodies, double-stranded DNA, rheumatoid factor, angiotensin-converting enzyme, Sjogren and myasthenia gravis antibodies. Repetitive nerve stimulation and single-fiber electromyography did not suggest neuromuscular junction dysfunction. Cerebral spinal fluid (CSF) analysis revealed elevated cell count with lymphocyte predominance and elevated angiotensin-converting enzyme. CSF cytology and flow cytometry from three separate lumbar punctures were negative for malignancy.

Immunomodulatory therapy with prednisone and mycophenolate was initiated with notable symptom improvement and no further relapses.

SUMMARY/CONCLUSION: The variable presentation and rarity of isolated neurosarcoidosis makes diagnosis difficult. There are reports of single or multiple concurrent cranial neuropathies, but relapsing-remitting cranial mononeuritis multiplex is rare and should be considered in the differential.

Serena Soleimani, DO

Resident and Fellow Member Award Recipient

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UTILITY OF BEDSIDE ICE PACK TEST FOR EARLY RECOGNITION OF IMMUNE CHECK POINT INHIBITOR MEDIATED MYASTHENIA GRAVIS AND MYOSITIS

Nithisha Thatikonda (Galveston, TX), Anza Zahid (Houston, TX), Amador Dalton (Galveston, TX), Mujtaba Saeed (Houston, TX), Ivo Tremont-Lukats (Houston, TX), Sudhakar Tummala (Houston, TX)

INTRODUCTION: Immune checkpoint inhibitors (ICI) are associated with neurological immune-related adverse events (NiArE) such as myasthenia gravis (MG) and myositis. These conditions often present with overlapping symptoms, notably ptosis, dyspnea, and extremity weakness. Early recognition is warranted for appropriate treatment.

OBJECTIVE: To test the utility of a simple bedside ice pack test (IPT) in early recognition and distinction of ICI-mediated MG and myositis.

METHODS: We administered IPT to 14 patients who had received ICI in the past 6 months and presented with ptosis and neuromuscular weakness. Improvement in ptosis was considered positive IPT (non-fixed, fatigable ptosis) was suggestive of an immune-mediated MG-predominant process. The workup included myasthenia antibodies, EMG, serum markers of muscle injury (creatine kinase (CK), aldolase), myositis panel and muscle biopsy. Statistical analyses employed were median for continuous and frequencies for categorical variables.

RESULTS: Positive IPT was found in two (14%) patients with positive myasthenia antibodies and neuromuscular junction dysfunction on EMG in one patient. These two patients had mildly elevated CK and negative myositis panel and muscle biopsy thus, was suggestive of an MG-predominant process. Twelve (86%) patients had negative IPT (fixed and non-fatigable ptosis) with significantly elevated CK, positive myositis panel and muscle biopsy and positive myasthenia antibodies in six (42%) patients, suggestive of myositis-predominant process.

SUMMARY/CONCLUSION: ICI-mediated neurotoxicity poses a diagnostic challenge. Overlap between myasthenia and myositis is commonly observed in immune-mediated toxicity that might be due to the cross-reactivity of antibodies. However, IPT was able to distinguish MG vs myositis-predominant process, thus helping guide management.

Nithisha Thatikonda, MD

Resident and Fellow Member Award Recipient

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CONCURRENT GUILLAIN BARRE SYNDROME AND SEVERE NUTRITIONAL DEFICIENCY: COINCIDENCE OR SHARED PATHOPHYSIOLOGY?

Nithisha Thatikonda (Galveston, TX), Awab Elnaeem (Galveston, TX), Mohammad Almomani (Galveston, TX), Xiang Fang (Galveston, TX)

INTRODUCTION/BACKGROUND: Nutritional deficiency of thiamine and folate is a known cause of acute axonal neuropathy which presents with ascending weakness, and areflexia of the lower extremities mimicking Guillain Barré syndrome (GBS). However, concurrent GBS and severe nutritional deficiency is rarely reported in the literature. We describe a patient with concurrent GBS and severe nutritional deficiency with persistent weakness despite intravenous immunoglobulin (IVIg) and nutritional replacement.

CASE REPORT: A 25-year-old female with recent history of poor oral intake due to incarceration presented with 2 weeks of ascending weakness and numbness of her lower extremities. Neurological examination demonstrated severe weakness, areflexia, and decreased sensation to pain, vibration, and light touch in his lower extremities. Cerebrospinal fluid studies showed cytoalbuminologic dissociation with cell count of 1/mcL and protein of 154 mg/dL. MRI of the spine showed anterior lumbosacral spinal nerve root enhancement. NCS showed axonal neuropathy involving bilateral median, ulnar, peroneal, tibial, and sural nerves suggestive of acute axonal sensory and motor neuropathy (AMSAN) variant GBS. Serum thiamine level was 36 nmol/L (normal= 70-180 nmol/L) and folate was 1 nmol/L (normal – 6-36 nmol/L). MRI brain showed radiological features of Wernicke's encephalopathy suggestive of concurrent severe nutritional deficiency. She was treated with intravenous immunoglobulin (IVIg) and appropriate nutritional supplementation with minimal improvement at 6-week follow-up.

SUMMARY/CONCLUSION: The coexistence of GBS and nutritional deficiencies may extend beyond mere coincidence. The present case underscores the importance of exploring the possible role of nutritional deficiency in GBS pathogenesis and prognosis through prospective studies.

Nithisha Thatikonda, MD

Resident and Fellow Member Award Recipient

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RESPIRATORY SYNKINESIS IN THE SETTING OF CHRONIC UPPER TRUNK BRACHIAL PLEXOPATHY

Alex Thibodeaux (New Orleans, LA), Mason Thibodeaux (Shreveport, LA), Zachary Richard (New Orleans, LA), Lauren Cooper (Jefferson, LA), Marc Raj (Mandeville, LA)

INTRODUCTION/BACKGROUND: Respiratory synkinesis, aka "breathing arm" is a rare phenomenon resulting from aberrant regeneration wherein phrenic nerve fibers innervate upper trunk muscles. This results in synkinesis, where some upper trunk muscles fire in a rhythmic pattern in synchrony with the patient's breathing.

CASE REPORT: A 30-year-old man presented to the EDX lab with reports of intermittent left arm muscle spasm in the setting of chronic Erb's palsy from shoulder dystocia. Physical exam was significant for 4/5 strength in shoulder abduction, elbow flexion, and supination. NCS revealed an incidental finding of left CTS. EMG was revealing for chronic denervation-reinnervation findings in the muscles supplied by the upper trunk of the brachial plexus consistent with history of Erb's palsy. Additionally, there was a consistent motor unit firing pattern in both the biceps brachii and deltoid at rest, which was reproducible with inspiration. Diagnostic ultrasound (US) of the left brachial plexus was performed and revealed anastomotic connection of the phrenic nerve to the C5 nerve root.

SUMMARY/CONCLUSION: Given these findings, phrenic nerve fibers traveling amongst the C5 nerve root are likely responsible for consistent motor unit contraction with inspiratory effort. EMG/NCS, and US provided complementary information that allowed for more precise diagnosis of respiratory synkinesis. Due to situations such as this, diagnostic US should be considered a skill worth incorporating as an EDX physician.

Alex Thibodeaux, MD

Resident and Fellow Member Award Recipient

NORMAL NEEDLE ELECTROMYOGRAPHY IN KENNEDY DISEASE

Hemani Ticku (Cleveland, OH), Bashar Katirji (Cleveland, OH)

INTRODUCTION/BACKGROUND: Kennedy disease, or spinal-bulbar muscular atrophy (SBMA), is an X-linked motor neuron disease due to CAG repeat expansion within the androgen receptor gene. This condition manifests in adulthood with gynecomastia, tremors, cramps, limb and bulbar weakness, and variable sensory loss due to degeneration of anterior horn and dorsal root ganglia cells.

CASE REPORT: A 38-year-old man presented with dysphagia, dyspnea, and progressive numbness and weakness in his legs and arms over 5 years, followed by gait imbalance and postural hand tremors. Examination revealed sensory loss up to the knees and forearms, with areflexia/hyporeflexia. He had mild distal weakness, although limited by giveaway. EDX studies showed low sensory nerve action potentials and normal compound muscle action potentials, with normal needle EMG of the right upper and lower extremities (except for few long-duration motor unit action potentials in the right triceps and pronator teres muscles) without active denervation. Forced vital capacity was 61% predicted. Creatine kinase, antinuclear antibodies, Vitamin-B6, and long-chain-fatty acids level were normal. Neurofascin antibodies were negative. Genetic panels for comprehensive neuromuscular disorders and hereditary sensory autonomic neuropathy were negative. Quadricep muscle biopsy showed mild neurogenic atrophy. Genetic testing for trinucleotide repeat expansion confirmed 42 CAG repeats on androgenic receptor gene, confirming the diagnosis of SBMA.

SUMMARY/CONCLUSION: SBMA's clinical phenotype varies based on CAG repeat length, typically with longer repeats (≥47) associated with motor-dominant and shorter repeats (<47) with sensory-dominant presentations. However, even in sensory-dominant cases, widespread neurogenic changes are usually observed on needle EMG. This case highlights a unique sensory-dominant presentation of SBMA potentially related to shorter repeat expansion and younger onset of symptoms.

Hemani Ticku, MD

Resident and Fellow Member Award Recipient

STUDY OF AN EXTERNAL VIBRATING AND COLD DEVICE TO REDUCE PAIN WITH NEEDLE ELECTROMYOGRAPHY

Andriana Tompary (Chapel Hill, NC), Nathaniel Wooten (Chapel Hill, NC), Rebecca Traub (Chapel Hill, NC)

INTRODUCTION: Pain during needle EMG (NEMG) is a common concern that can lead to incomplete tests and patient discomfort. Previous interventions that have been explored to reduce pain with NEMG have shown limited benefit. In pediatric populations, an external vibrating and cold device has been evaluated during vaccinations and venipuncture with improvement of pain perceptions.

OBJECTIVE: To assess if this device leads to significant pain reduction compared to controls during NEMG.

METHODS: This was a prospective, randomized study conducted at a large academic hospital-based EMG laboratory. Fifty participants undergoing NEMG testing of the upper extremity were randomized into the treatment group (vibrating device) vs. standard of care (no device). Pain was rated on a scale from 0-10 for the abductor pollicis brevis (APB), first dorsal interossei (FDI), and pronator teres (PT) muscles.

RESULTS: There were no sex or age differences between the treatment and control groups. The mean, median, and range of pain scores for each muscle tested were as follows for the intervention and control groups: APB 4.48, 4.0, 1-10 versus 4.3, 3.5, 1-10; FDI 3.76, 3.76, 0-9 versus 3.08, 3.0, 0-9; PT 3.88, 4.0, 1-8 versus 3.74, 4.0, 0-7.5. Two-tailed T-tests did not show significant differences in mean or median pain scores between the treatment and control groups ($p < .05$) for all three muscles.

SUMMARY/CONCLUSION: There was no significant difference between the treatment vs. control group in pain rating scores for the three tested muscles with NEMG. Limitations included small sample size and large variability of pain scores within each group.

Andriana Tompary, DO

Resident and Fellow Member Award Recipient

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REAL-LIFE EXPERIENCE USING EFGARTIGIMOD IN MYASTHENIA GRAVIS PATIENTS: ALTERNATIVE FREQUENCY OF ADMINISTRATION BASED ON INDIVIDUAL PATIENT RESPONSE

Andriana Tompary (Chapel Hill, NC), Stephanie Iyer (Chapel Hill, NC), Said Alhassan (Chapel HIll, NC), Anahit Mehrabyan (Chapel Hill, NC)

INTRODUCTION: Efgartigimod is the first FcRn inhibitor that has been approved for the treatment of generalized myasthenia gravis (MG). In ADPT trial Efgartigimod was prescribed as a weekly infusion in cycles of four with at least 4-week interval with adjustment of the frequency of cycles based on the individual patient's response. There is limited information regarding the real-life experience of alternative mode of efgartigimod administration.

OBJECTIVE: The study aimed to investigate the real-world utilization of efgartigimod in MG patients, focusing on alternative dosing intervals beyond clinical trial parameters.

METHODS: Medical records of 28 MG patients treated with efgartigimod from January 2022 to September 2023 were reviewed. Patient demographics, treatment continuation, dosing intervals, and clinical outcomes were analyzed.

RESULTS: Among the 29 patients receiving efgartigimod, 12 (41.3%) discontinued after the first cycle, primarily due to treatment ineffectiveness or adverse events. Of the 17 patients who continued, dosing intervals varied, with 6 (35.3%) receiving infusions every 2 weeks, 5 (29.4%) every 4 weeks, and 6 (35.3%) with variable intervals. Most patients experienced clinical improvement, with a significant reduction in IgG levels post-treatment. Mild infections were the most reported adverse events.

SUMMARY/CONCLUSION: Real-world usage of efgartigimod revealed varied dosing intervals, with a predominant administration pattern of a cycle of 2 weekly infusions with 2-week intervals. Despite diverse dosing regimens, patients generally exhibited clinical improvement and reduced IgG levels, indicating the efficacy of efgartigimod in managing MG.

Andriana Tompary, DO

Resident and Fellow Member Award Recipient

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TREATMENT OF ULNAR NEUROPATHY AT THE ELBOW USING A GEL STAND-OFF FOR ULTRASOUND-GUIDED PERINEURAL INJECTION

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INTRODUCTION: Ulnar neuropathy at the elbow (UNE) can be treated with ultrasound-guided perineural injection. The goal is to improve symptoms and decrease nerve cross-sectional area through mechanical decompression.

OBJECTIVE: To demonstrate an alternative approach to perineural injection for UNE using a gel stand-off.

CASE REPORT: A 41-year-old female with right greater-than left medial elbow pain and paraesthesia in the fourth and fifth digits. NCSs/EMG demonstrated bilateral UNE. She completed 4 months of physical therapy, used elbow splints, and started gabapentin – all with limited alleviation. On pre-procedural examination, she had several areas of enlarged ulnar nerve cross-sectional area and abnormal nerve echotexture.

METHODS: The procedure was performed with the patient supine, shoulder abducted to 90-degrees, and the forearm supinated. A 15-6 MHz linear array ultrasound transducer was used to localize the right ulnar nerve proximal to the retrocondylar groove at an area of focal hypoechogenicity and increased nerve cross-sectional area. Lidocaine and dexamethasone were injected using a sonographically-guided in-plane anterior-to-posterior technique. When performing an in-plane procedure, a gel stand-off under one side of the transducer can be combined with a heel-toe maneuver to facilitate entry of the needle at a steeper trajectory.

RESULTS: On evaluation 3 weeks after her injection, the patient had experienced temporary reduction in pain and paraesthesia.

SUMMARY/CONCLUSION: UNE is a common cause of focal neuropathy. Ultrasound-guided ulnar nerve injection is a minimally invasive option that can provide symptom relief. The use of a gel stand-off technique is helpful in maintaining adequate visualization of the needle with a steeper needle angle.

Nicholas Tranchitella, MD

Resident and Fellow Member Award Recipient

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IS MYASTHENIA GRAVIS A GENETIC CONDITION? A CASE SERIES OF TWO PATIENTS WITH FAMILIAL MG

Vijaya Valapara (Galveston, TX), Milena Lobaina (Galveston, TX), Luz Reiley (Galveston, TX), Elena Shanina (Houston, TX)

INTRODUCTION/BACKGROUND: Myasthenia gravis (MG) is by far known as a non-hereditary condition. Familial MG is a rare occurrence and is available as case reports. Co-morbid autoimmune conditions like rheumatoid arthritis and thyroid disease are commonly associated with MG. We report two cases of sero-positive MG that has a positive family history of MG in multiple family members, suggesting autosomal dominant pattern of inheritance.

CASE REPORT: The first patient is a 75-year-old Caucasian male with hereditary coagulopathy, initially presenting with myasthenic crisis in the setting of acute pulmonary embolism. He was treated with anticoagulation and plasmapharesis. His chronic symptoms were diplopia, ptosis, and proximal muscle weakness. He has a family history of uncle with ptosis, niece with ocular symptoms undergoing evaluation for MG, and daughter diagnosed with dermatomyositis. Patient was seropositive for acetylcholine receptor antibodies. He is currently being treated with eculizumab infusions and is being worked up for genetic causes of MG. The second patient is a 67-year-old Hispanic male with initial presentation of diplopia, generalized fatigue and weakness. His father and brother were both diagnosed with MG and died of complications. He was positive for acetylcholine receptor and anti-striated muscle antibodies and pending genetic work up. His disease is stable with monthly intravenous immunoglobulin and mycophenolate mofetil therapies.

SUMMARY/CONCLUSION: Although MG is known to be a sporadic condition, genetic etiologies cannot be completely ruled out. Association with co-morbid autoimmune conditions and presence of positive family history for MG warrant further studies to understand the genetic underpinnings and genetic predisposition to autoimmune conditions.

Vijaya Valapara, MD

Resident and Fellow Member Award Recipient

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SPINAL MUSCULAR ATROPHY & CHARCOT MARIE TOOTH DISEASE 1B IN ONE PATIENT: A CASE FOR COMPREHENSIVE GENETIC TESTING

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INTRODUCTION/BACKGROUND: Spinal muscular atrophy (SMA) is an autosomal recessive lower motor neuron disorder caused by survival motor neuron (SMN) gene mutations causing proximal muscle weakness. Charcot Marie Tooth disease (CMT), a genetically diverse disorder characterized by distal sensorimotor polyneuropathy is caused by various mutations. Most variants have demyelinating neuropathy on EDX studies except CMT2. Both disorders have significant phenotypic variability.

OBJECTIVE: We present a case of adolescent-onset SMA co-occurring with CMT1B to highlight the importance of genetic testing in overlapping neuromuscular cases.

CASE REPORT: Patient is a 42-year-old male with generalized muscle pain at ~10 years followed by progressive, proximal extremity weakness at ~17 years. He was diagnosed with limb-girdle muscular dystrophy without a muscle biopsy/genetic testing/EDX. He began requiring a wheelchair at ~33 years. His maternal nephew had Duchenne's muscular dystrophy. Examination revealed proximal muscular atrophy and weakness in all extremities with generalized areflexia except for hyporeflexic Achilles bilaterally. Reduced pinprick sensation extending up to the level of abdomen and shoulders was present.

RESULTS: EDX studies revealed demyelinating sensorimotor polyneuropathy. Muscular dystrophy panel was negative. Comprehensive neuropathy panel revealed homozygous whole-gene SMN1 deletions, SMN2 copy number 4 and heterozygous missense MPZ variant, suggestive of adolescent-onset SMA and CMT type 1B. He started risdiplam for treatment.

SUMMARY/CONCLUSION: This case demonstrates overlap of proximal SMA variant and demyelinating CMT variant. It emphasizes the role of targeted genetic panels in patients with mixed syndromic presentations and those with limited access to specialty medical care who may remain undiagnosed into later life while missing opportunities for disease-modifying treatment.

Darshana Vijaywargiya, MBBS

Resident and Fellow Member Award Recipient

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ASYMMETRIC SENSORY AND MOTOR DEFICITS AS PRESENTING SYMPTOMS OF LATE ONSET EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

Amber Vocelle (Lansing, MI), Pavel Volkov (East Lansing, MI), Harnoor Tokhie (Chicago, IL), Dominick Utrie (Lansing, MI), Michael Andary (East Lansing, MI), Rani Gebara (Okemos, MI)

INTRODUCTION/BACKGROUND: Eosinophilic granulomatosis with polyangiitis (EGPA) typically presents with non-specific multi-organ symptoms that frequently delay diagnosis and treatment. This can have a profound effect on remission rate and quality of life. The purpose of this case report is to illustrate to fellow learners the importance of careful physical examination, and by extension, EDX through its use to identify a case of late onset EGPA which led to early suspicion of EGPA and rapid treatment planning.

CASE REPORT: A 72-year-old male with chronic obstructive pulmonary disease presented with a 4-week history of myalgias, sensory deficits, and weakness. Labs were significant for leukocytosis, marked eosinophilia, and elevated creatine phosphokinase. Exam demonstrated asymmetric weakness involving the right wrist extensors, extensor indicis, intrinsic hand muscles; left triceps, intrinsics hand muscles; diffuse leg weakness worse the right, and lower extremity areflexia. EDX confirmed corresponding axonal nerve damage to the right ulnar and median nerves and left ulnar, median, fibular, tibial, and sural nerves without evidence of demyelination or conduction block—consistent with mononeuropathy multiplex (MNM). Subsequent labs were positive for C-ANCA, anti-MPO antibodies, and elevated inflammatory markers.

SUMMARY/CONCLUSION: EGPA can present with prominent neurological weakness and muscle breakdown resulting in myalgias. The pattern of the weakness on exam can raise suspicion for MNM. EDX can confirm axonal degeneration—a hallmark of EGPA with neurological involvement. Although EPGA is typically diagnosed between 30 and 50, patients with less severe phenotypes may present as late as their seventh decade and respiratory symptoms may be less prominent.

Amber Vocelle, DO

Resident and Fellow Member Award Recipient

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NUTRITIONAL DEFICITS IN POEMS SYNDROME: A LIKELY CONTRIBUTOR TO POLYNEUROPATHY

Amber Vocelle (Lansing, MI), Sarah Smith (Seattle, WA)

INTRODUCTION/BACKGROUND: POEMS syndrome is a paraneoplastic syndrome that presents with a constellation of symptoms including diarrhea. Persistent diarrhea can cause nutritional deficits, influencing the pattern of neuropathy and available treatment options.

CASE REPORT: A 49-year-old male with history of vitamin B12 deficiency and diarrhea presented to neuromuscular clinic with a 2-year history of progressive neuropathy. Exam was significant for edema, decreased strength in bilateral hip and ankle flexors, lower extremity sensory deficits, and diffuse areflexia. EDX studies revealed absent sural sensory nerve action potentials, prolonged onset latency and fibular nerve compound muscle action potentials amplitude loss, and evidence of denervation to the tibialis anterior and gastrocnemius, consistent with severe axonal length-dependent sensorimotor polyneuropathy. Neuromuscular ultrasound demonstrated diffuse enlargement of the right median nerve with patchy echotexture changes. Further multi-disciplinary evaluation confirmed POEMS syndrome diagnosis (two mandatory major, two other major, and four minor criteria met). Although recent B12 level normalized, B6 was less than five. We hypothesize that severe B6 deficiency may have contributed to the neuropathy pattern.

SUMMARY/CONCLUSION: Diarrhea and inflammation decrease transit time and reduce absorption of water-soluble vitamins. Although B12 deficiency is associated with POEMS syndrome, B6 deficiency is less well-documented. Indeed, this is second reported case study of B6 deficiency in POEMS syndrome. Both cases presented with axonal sensorimotor polyneuropathy-- common in B6 deficiency and less frequent in POEMS syndrome. Previous study illustrated marked symptom and function improvement with B6 supplementation. This raises the concern for concurrent nutritional neuropathy in POEMS syndrome and may suggest vitamin monitoring and supplementation may improve neuropathy severity.

Amber Vocelle, DO

Resident and Fellow Member Award Recipient

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A CASE OF ANTI-MDA5 MYOSITIS WITH A RAPID AND DEVASTATING PROGRESSION

Vedang Vyas (Houston, TX), Jorge Patino (Houston, TX), Omolara Kolawole (Houston, TX)

INTRODUCTION/BACKGROUND: Anti-melanoma differentiation-associated gene 5 (Anti-MDA-5) dermatomyositis is an inflammatory myopathy with unique skin lesions and is often associated with acute-to-subacute development of interstitial lung disease, with a catastrophic clinical course.

CASE REPORT: A 49-year-old Hispanic female was admitted to the ICU for a 1-week history of nonproductive cough and shortness of breath with progressive worsening respiratory failure, after unsuccessful treatment for community-acquired pneumonia. Neurology was consulted for concern of myasthenia gravis exacerbation. The examination revealed proximal muscle weakness, pronounced in bilateral shoulder abduction, hip flexion, and neck extension, with no evidence of fatigability. The patient reported a 1-month history of generalized body aches, a scaly rash at both elbows, and on the epigastrium. Imaging was remarkable for diffuse ground-glass opacities suggestive of interstitial lung disease. The patient was intubated due to worsening respiratory distress. Infectious and rheumatological work-up was nonrevealing; she had an elevated sedimentation rate, C-reactive protein, and aldolase, but normal creatine kinase. Dermatological evaluation of the epigastric rash was conclusive of dermatomyositis. A myositis panel revealed anti-MDA-5 myositis. Despite early treatment with intravenous steroids and immunotherapy, the patient had a complicated course with development of pancytopenia in the setting of cyclophosphamide, distributive shock requiring extracorporeal membrane oxygenation, and an intracerebral hemorrhage. Unfortunately, the patient expired due to her devastating neurological injury with multi-organ failure.

SUMMARY/CONCLUSION: Anti-MDA-5 dermatomyositis can have a rapidly progressive course with a high mortality due to pulmonary involvement; as such, it is imperative for any clinician to be cognizant of the presentation, to ensure early commencement of immunomodulating therapies.

Vedang Vyas, MD

Resident and Fellow Member Award Recipient

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PERISCOPING A PERINEURIOMA: ULTRASOUND WITH ELECTRODIAGNOSTICS TO EVLAUATE POSTERIOR INTEROSSEUS NERVE PALSY

Daniel Wido (Bethesda, MD), Syed Qadri (Washington, DC), Matthew Miller (Potomac, MD), J Banks Deal (Bethesda, MD), Yin-Ting Chen (Colorado Springs, CO)

INTRODUCTION/BACKGROUND: Posterior interosseous nerve (PIN) syndromes secondary to space-occupying lesions are relatively uncommon clinical entities in the EDX laboratory. Ultrasound (US) can often provide a more definitive etiology for neuropathies. Here, we present a case of PIN palsy caused by perineurioma visualized on US during EDX studies.

CASE REPORT: A 35-year-old right-handed male with a history of partially successful right long finger extensor tenolysis after hand trauma presented with progressive extensor weakness. Exam was notable for atrophy, intact sensation and 3/5 wrist and finger extension. EDX with extensor indicis proprius found compound muscle action potential reduced amplitude, and EMG of extensor digitorum communis with complex repetitive discharges and reduced recruitment. US showed marked PIN swelling and intraneural architecture loss proximal to the supinator and positive doppler signal around and within the nerve. MRI demonstrated T1 hypointense, T2 hyperintense, enhancing fusiform lesion along the deep branch of radial nerve as it crossed the supinator muscle fascia. The patient underwent incisional biopsy with nerve decompression -pathology later confirmed perineurioma with immunostains for S100 and epithelial membrane antigen. Patient had stable extensor motor function and was able to return to work. The lesion was not resected, and he will continue close follow up with possible tendon transfer if his function worsens.

SUMMARY/CONCLUSION: Perineuriomas are rare peripheral nerve sheath tumors that are not managed with surgical resection. This case reinforces ultrasound evaluation as a valuable adjunct to EDX studies to better localize and characterize pathology for expeditious diagnosis and treatment of nerve sheath tumors.

Daniel Wido, MD

Resident and Fellow Member Award Recipient

SMALL FIBER SENSORY NEUROPATHY/NEURONOPATHY PRESENTING AS NOTALGIA PARESTHETICA

Nathaniel Wooten (Chapel Hill, NC), Vinay Chaudhry (Chapel Hill, NC)

INTRODUCTION/BACKGROUND: Notalgia paresthetica (NP) is a condition of chronic pruritis and dysesthesia localized to upper-mid back. NP is not rare but is often under diagnosed and mistaken for a primary dermatologic condition, delaying treatment. While the T2-T6 dermatomes are most often affected, there is evidence of a high incidence of cervical spine pathology in patients with NP compared to the general population. Previous studies have reported both increased and decreased epidermal nerve fiber density (ENFD). We report a patient with refractory pruritis above the scapular region who had reduced ENFD and cervical spine pathology.

CASE REPORT: A 59-year-old female without significant medical history presented for 3 years of intense skin itching predominantly over the left posterior shoulder and neck in roughly the C6 and C7 dermatomes. Intermittent similar itching was noted in the left forearm. She had seen multiple dermatologists, a spine surgeon, physiatrist, and pain specialist among others, and tried multiple modalities of therapy without benefit. MRI of the cervical spine demonstrated moderate and moderate to severe C5-C6 and C6-C7 neural foraminal narrowing. ENFD demonstrated a nerve fibers/mm density of 12.36 (nml >10.7) and 4.77 (nml>6.5) at the proximal and distal left arm, respectively. She had minimal relief with topical capsaicin and tacrolimus, oral gabapentin, and lamictal. Dramatic relief was obtained with compounding cream of amitriptyline HCl 2%, ketamine HCl 1%, and lidocaine HCl 5%.

SUMMARY/CONCLUSION: Although our patient had cervical spine pathology, the reduced fiber density is indicative of non-length dependent small fiber neuropathy/neuronopathy (SFN) as the cause of her NP.

Nathaniel Wooten, MD

Resident and Fellow Member Award Recipient

CHARACTERIZATION OF LYMPHOCYTES IN AMYOTROPHIC LATERAL SCLEROSIS AND FRONTOTEMPORAL DEMENTIA BRAINS USING SINGLE NUCLEAR RNA SEQUENCING DATA

Mai Yamakawa (Los Angeles, CA), Jessica Rexach (Los Angeles, CA)

INTRODUCTION: ALS is a fatal neurodegenerative disorder involving upper and lower motor neurons without cure. Neuroinflammation is an attractive therapeutic target for ALS, however, knowledge of lymphocytes in ALS brains is lacking.

OBJECTIVE: To characterize lymphocytes in postmortem brains from ALS and frontotemporal dementia (FTD) patients.

METHODS: Four existing single nuclear RNA sequencing (snRNAseq) datasets of postmortem ALS/FTD brains are jointly analyzed with our cross-disorder snRNAseq dataset. After joint QC, integration, and cell type annotation, lymphocytes are identified as CD3-zeta-positive cells. Downstream analysis including cell compositional analysis, differential gene expression analysis, weighted gene co-expression network analysis, and gene regulatory network analysis are performed.

RESULTS: Among 2,370,527 cells from 238 donors after rigorous filtering, a total of 5,867 CD3-zeta positive lymphocytes from 212 donors were identified. There were 2623 CD8 (+) T cells from 143 donors, 1121 natural killer (NK) cells from 137 donors, and 1043 CD4 (+) T cells from 102 donors. One dataset showed increased CD4 (+) cells in the motor cortex from c9-ALS and c9-FTD patients compared to the control. Another dataset showed decreased NK cells in the frontal cortex from FTD-GRN patients compared to control. The remaining results will be presented at the conference.

SUMMARY/CONCLUSION: Characterizing rare populations in the brain cells poses unique technical and analytical challenges. Changes in CD4 (+) T cells and NK cells have been reported in blood and cerebrospinal fluid from ALS and FTD patients. Single-cell sequencing is a strong research tool that can advance deciphering intricate cellular cross-talk in diseased brains.

Mai Yamakawa, MD

Resident and Fellow Member Award Recipient

A CASE OF MILLER-FISHER PRESENTING WITH AN UNUSUAL TRIAD: HYPOPHONIA, DYSPHAGIA, OPHTHALMOPLEGIA

Jordan Yaukey (Hershey, PA), Bhavan Shah (Hershey, PA), Divpreet Kaur (Hummelstown, PA)

INTRODUCTION/BACKGROUND: Miller Fisher is most commonly diagnosed with having at least two of the following symptoms: ataxia, areflexia, and/or ophthalmoplegia. We report a novel case of a unique presentation of Miller Fisher syndrome after Influenza A. The patient initially presented with ophthalmoplegia and progression to hypophonia and dysphagia, but never experienced any ataxia or areflexia.

CASE REPORT: Patient is a 43-year-old healthy female with past medical history of hypothyroidism, anxiety, and depression who presented to the emergency department with right upper extremity parasthesia and right sided eye drooping. She noticed double, blurry vision with vertical and extreme horizontal movement. Patient had right cranial nerve 3rd, 4th deficit and bilateral 6th nerve deficit. Imaging including MRI/MRA/CT were unyielding. Patient tested positive for Influenza A without flu symptoms. Lumbar puncture was performed and was unremarkable. She subsequently developed hypophonia and difficulty swallowing approximately 2 days after initial presentation. Patient saw improvement after approximately 10 days and was discharged with close follow up. GQ1B antibody titer returned and revealed a titer of 1:3200 which is indicative of Miller Fisher variant of Guillain-Barré. EMG/NCS revealed no signs of demyelination although dids not exclude diagnosis. Patient symptoms completely resolved without treatment, but ontravenous immune globulin could be considered in the future.

SUMMARY/CONCLUSION: Although presenting with irregular symptoms, Miller Fisher syndrome cannot be fully excluded in the presence of negative Brighton criteria in the setting of recent viral illness. Extensive workup and retuned antibody titers revealed a classically elevated GQ1B antibody titer indicative of Miller Fisher variant of Guillain-Barré.

Jordan Yaukey, DO

Resident and Fellow Member Award Recipient

TRENDS OF AMYOTROPHIC LATERAL SCLEROSIS (ALS) CLINICAL TRIALS FROM 1999-2024 POSTED ON WWW.CLINICALTRIALS.GOV

Aaron Zelikovich (Philadelphia, PA), Eric Anderson (Reston, VA), Jinsy Andrews (New York, NY), Colin Quinn (Philadelphia, PA)

INTRODUCTION: ALS is a progressive neurodegenerative disease-causing substantial morbidity and early mortality. Multiple disease-modifying agents are now available with only a modest effect on functional outcomes and survival. There has been a substantial increase in the number of clinical trials in ALS over the past 20 years, which presents an opportunity to analyze trends in trial sponsorship, design, and performance.

OBJECTIVE: To create a database of amyotrophic lateral sclerosis (ALS) clinical trials on www.clinicaltrials.gov and analyze trends over the past 3 decades.

METHODS: “ALS” and “Amyotrophic Lateral Sclerosis” were searched on www.clinicaltrials.gov in January 2024. A database was created to capture the information provided.

RESULTS: A total of 1,091 unique trials were identified from the terms ALS and amyotrophic lateral sclerosis 1999 to 2024. Two hundred and eighty-six trials were removed due to non-ALS trials (other neurological disorders, drug name with ALS, or advanced life support) and 753 were analyzed. Drug trials had the largest representation (n=355) with the most common dosing regimen being oral (n=183) and daily (n=99). Thirty-four countries were represented with the United States (n=309) having the highest number. There were 40% of the studies that did not specify ALS diagnostic criteria for eligibility and 4.4% required genetic testing. A total of 181 unique drugs have been tested from 355 registered drug studies.

SUMMARY/CONCLUSION: Analyzing trends in ALS clinical trials will help guide future trial designs to optimize ALS outcomes and trials.

Aaron Zelikovich, MD

Resident and Fellow Member Award Recipient

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A CASE REPORT OF A PATIENT WITH CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY (CIDP) OR MULTIFOCAL MOTOR NEUROPATHY (MMN); CHALLENGES IN DIAGNOSIS AND TREATMENT.

Aaron Zelikovich (New York, NY), Norman Latov (New York, NY), Mary Vo (New York, NY)

INTRODUCTION/BACKGROUND: Multifocal motor neuropathy (MMN) is distinguished from chronic inflammatory demyelinating neuropathy (CIDP) by the absence of sensory symptoms clinically and on NCS. The presence of motor conduction block and elevated anti-GM1 antibodies are supportive of MMN, but not a requirement.

CASE REPORT: To present a case of predominantly motor neuropathy, highlighting the diagnostic challenge in differentiating between CIDP and MMN, and deciding on treatment. A 42-year-old man presented in 2015 with right leg weakness, mild finger numbness, and muscle cramps in his legs. Examination showed weakness in right extensor hallucis longus and hip flexion. NCS showed evidence of a multifocal predominantly motor demyelinating polyneuropathy without conduction block. He was diagnosed with CIDP and treated with intravenous immunoglobulin (IVIg) with a good response. In 2019 he had a worsening of his lower extremity strength. Repeat serum testing showed an increase IgMk monoclonal gammopathy from IgM 182 (nl 48-271) to 410 (nl 50-300) and an increase in IgM anti-GD1a from 1:1600 (nl < 1:800) to 1:102,400 (nl < 1:800), which has been associated with motor neuropathy. His symptoms progressed after IVIg treatment was denied by insurance. He trialed 1g solumedrol for 4 days with worsening of his symptoms requiring hospital admission for IVIg where he improved.

SUMMARY/CONCLUSION: The distinction between CIDP and MMN is clinically important as patients with MMN treated with corticosteroids may deteriorate clinically. This patient initially diagnosed with CIDP may have had MMN given the presence of high titer IgM anti-GD1A antibody and progression while on steroids despite no clear conduction block on NCS.

Aaron Zelikovich, MD

Resident and Fellow Member Award Recipient

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MYASTHENIA GRAVIS UNMASKED: INSIGHTS FROM POSTPARTUM CASE-SERIES ANALYSIS

Mrinal Acharya (Kharagpur, India)

INTRODUCTION: Myasthenia gravis (MG) is a neuromuscular disorder characterized by muscle weakness and fatigue, with a higher prevalence in women of childbearing age. Pregnancy and the postpartum period can influence the course of MG, potentially leading to exacerbations or onset of the disease. While the manifestation of myasthenic symptoms for the first time during the postpartum period is infrequently documented, it may be noteworthy that immune dysregulation plays a well-established role in such cases.

OBJECTIVE: This case series aims to report the clinical presentations, management, and outcomes of three females who developed MG within 1 year of giving birth.

METHODS: A retrospective analysis of medical records was conducted to identify females with MG onset within 1 year postpartum. Data regarding clinical features, antibody status, treatment modalities, and response to therapy were collected and analyzed.

RESULTS: All three patients presented with varying degrees of muscle weakness and fatigability, consistent with MG. One patient had limited ocular involvement, while the other had generalized MG affecting multiple muscle groups. Anti-AChR antibody testing was positive in all cases. Treatment with steroids resulted in significant improvement in symptoms and functional status in all patients.

SUMMARY/CONCLUSION: This case series underscores the link between pregnancy/postpartum phases and the onset of MG in women during the postpartum period. Additional investigations are imperative to elucidate the underlying mechanisms and identify optimal management approaches for this distinctive subset of MG patients.

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ULTRASOUND MEASURES AS A BIOMARKER FOR MUSCLE ATROPHY IN LATE ONSET TAY SACHS DISEASE

Euan Forrest (Bethesda, MD), Frances Gavelli (Bethesda, MD), Cyndi Tifft (Bethesda, MD), Camilo Toro (Bethesda, MD), Derek Day (Washington, DC), Jared Stowers (Washington, DC), Abdullah Al Qahtani (Baltimore, MD), Katharine Alter (Bethesda, MD)

INTRODUCTION: Late onset Tay Sachs disease (LOTS) is a rare, genetic, lysosomal storage disorder. Abnormal ganglioside accumulation results in progressive, neurogenic muscle weakness, dysphagia, tremors, etc. With promising emerging therapies, it becomes imperative to accurately quantify changes in muscle integrity, something currently lacking in LOTS literature.

OBJECTIVE: To determine if ultrasound (US) measures are biomarkers for changes in muscle integrity by comparing patients with LOTS to controls.

METHODS: Greyscale and shear-wave elastography US (Siemens Accuson 2000US; 9L4 linear probe) images were captured for the biceps, triceps, rectus femoris (RF) and semimembranosus in a cohort of 23 patients participating in a LOTS natural history study. Muscle thickness and Heckmatt scores were quantified in a subset of patients (n=10; 6/F; age=42.0±12.1 years; BMI=26.3±4.2) and compared to matched controls (n=10; 6/F; age=42.2±12.1 years; BMI=26.6±4.2).

RESULTS: Patients had higher Heckmatt scores for all muscles ($p<0.001$). The RF was atrophied (thickness Δ=-0.78±0.18 cm, $p<0.001$) and stiffer (stiffness Δ =1.26±1.40 m/s, $p=0.01$) in our patients. Differences in extensor-flexor thickness (Δ=-0.15±.09, $p<.001$) and stiffness (Δ=0.62±0.74, $p=0.048$) ratios were found in the patients' lower limbs, but not upper. Cross-cohort differences were not found for triceps, biceps, or semimembranosus thickness measures and triceps/biceps ratios.

SUMMARY/CONCLUSION: US measures of muscle integrity serve as key biomarkers reflective of muscle involvement in LOTS. The significant differences in lower, but not upper limb muscles, for all but the Heckmatt scores likely arises from earlier involvement of the lower limbs in LOTS and the progression variability within our patients, indicating US's ability to nuance fine differences in disease progression.

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DIAPHRAGM ULTRASOUND MEASUREMENTS IN PATIENTS WITH SHORTNESS OF BREATH IN A NEUROMUSCULAR TERTIARY CENTER

Monica Alcantara (Toronto, Canada), Hans Katzberg (Toronto, Canada), Vera Bril (Toronto, Canada)

INTRODUCTION: Diaphragm ultrasound (US) is a safe, sensitive, and reproducible method to investigate patients with neuromuscular diseases who present with shortness of breath (SOB) and are at risk of respiratory dysfunction. Measurements of thickness and thickening ratios have been shown to be superior to phrenic NCS, chest X-rays, and fluoroscopy to detect diaphragm involvement.

OBJECTIVE: To investigate the utility of diaphragm US in patients with neuromuscular diseases and SOB and to compare diaphragm measurements with forced vital capacity (FVC).

METHODS: We prospectively performed bilateral diaphragm US and portable supine/upright forced vital capacity (FVC) in adult patients with neuromuscular diseases and SOB and in a group of healthy individuals. Diaphragm thickness at maximal inspiration, end-expiration and thickening ratios were compared to FVC measurements.

RESULTS: Of 20 patients (11 neuropathies, 5 myopathies, 4 generalized MG, mean age 52±14.5Y) and 11 controls (46.63±17.64Y), 5 patients had SOB in the supine position and 7 had supine FVC fall>15%. Mean FVC upright/supine was 2.48±0.85L/ 2.17±0.78L in the neuropathy (group1), 2.60±1.06L/ 2.27±1.20L in the combined myopathy/generalized myasthenia gravis (group 2) and 3.32±0.89L/ 3.15±0.82L in controls ($p=0.09$ upright, $p=0.04$ supine). Patients showed bilateral reduced thickness at maximal inspiration as compared to controls (R/L from group 1; group 2; controls): (0.35±0.07cm/0.32±0.09cm; 0.33±0.10cm/0.33±0.06cm; 0.49±0.16cm/0.48±0.15cm; $p=0.009$) and reduced thickening ratios:(1.43±0.3/1.48±0.38; 1.46±0.15/1.29±0.22; 1.83±0.41cm/1.72±0.35cm; $p=0.01$/$p=0.02$). There were no correlations between thickening ratios or thickness measurements and supine FVC fall.

SUMMARY/CONCLUSION: Diaphragm US was useful to identify changes in thickness and thickening ratios in patients with neuromuscular diseases who present with SOB and may be at risk of respiratory insufficiency.

PHASE 3 TRIAL DESIGNS EVALUATING RILIPRUBART, A C1S-COMPLEMENT INHIBITOR, IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

Richard A. Lewis (Los Angeles, CA), Jeffrey Allen (Minneapolis, MN), Ingemar S.J. Merkies (Maastricht, The Netherlands, Netherlands), Pieter A. van Doorn (Rotterdam, The Netherlands, Netherlands), Claudia Sommer (Würzburg, Germany, Germany), Erik Wallstroem (Cambridge, MA), Xiaodong Luo (Bridgewater, NJ), Miguel Alonso-Alonso (Cambridge, MA), Nazem Atassi (Cambridge, MA), Luis Querol (Madrid, Spain)

INTRODUCTION: Standard-of-care (SOC) therapies (immunoglobulins/corticosteroids) for chronic inflammatory demyelinating polyneuropathy (CIDP) have variable efficacy, high treatment administration burden, and significant side-effects. Riliprubart, a first-in-class, humanized, IgG4-monoclonal antibody, selectively inhibits activated-C1s and has convenient subcutaneous route of administration. Phase 2 trial (NCT04658472) results indicated promising clinical benefits with favorable benefit-risk profile.

OBJECTIVE: To present two Phase 3 trial designs which will evaluate riliprubart in two different CIDP populations with high unmet needs: patients refractory to SOC therapies and responders to intravenous immunoglobulins (IVIg) with residual disability.

METHODS: Two global, multicenter, randomized, Phase 3 trials are planned: MOBILIZE, a placebo-controlled trial targeting SOC-refractory patients; VITALIZE, a double-dummy trial targeting IVIg-treated patients with residual disability. Treatment duration in both trials is 48 weeks (24-week double-blinded period [Part-A], plus 24-week open-label period [Part-B]). Participants will be randomized (1:1) to receive riliprubart or placebo (MOBILIZE; N≤140), and riliprubart plus IVIg-placebo or IVIg plus riliprubart-placebo (VITALIZE; N≤160). Sample sizes will be re-estimated based on pre-defined interim analysis during Part-A. Eligible adults with CIDP diagnosed based on 2021 European Academy of Neurology/Peripheral Nerve Society guidelines with Inflammatory Neuropathy Cause and Treatment (INCAT) score 2-9 (score 2 exclusively from legs) can be included. Primary endpoint is percentage of participants responding, defined as ≥1 point decrease from baseline in adjusted INCAT score at Week-24 (Part-A). Key secondary endpoints include change from baseline in additional disability/impairment measures (Part-A) and long-term efficacy (Part-B).

RESULTS: Both trials will begin enrollment in 2024.

SUMMARY/CONCLUSION: These Phase 3 trials aim to demonstrate riliprubart efficacy in CIDP, including patients with refractory disease or residual disability.

Disclosures:

Richard A. Lewis - consultant with CSL Behring, Grifols, Pfizer, Sanofi (Steering Committee), argenx, Pharnext, Roche, Johnson & Johnson, Takeda, Boehringer Ingelheim (DSMB), and Momenta. He is also part of scientific advisory boards, Alnylam and Akcea and medical advisory board - The GBS| CIDP Foundation International

Luis Querol - received research grants from Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), CIBERER, Fundació La Marató, GBS-CIDP Foundation International, UCB and Grifols. He received speaker or expert testimony honoraria from CSL Behring, Novartis, Sanofi, Merck, Annexon, Alnylam, Biogen, Janssen, Lundbeck, argenx, UCB, Dianthus, LFB, Avilar Therapeutics, Octapharma and Roche. He serves at Clinical Trial Steering Committee for Sanofi and was Principal Investigator for UCB's CIDP01 trial

Jeffrey Allen - consultant for Sanofi, Alexion, Alnylam, argenx, Annexon, CSL Behring, Johnson & Johnson, Grifols, Takeda, Immunovant, Immunopharma, and Pfizer

Ingemar S.J. Merkies - received grants from Talecris Talents program, GBS| CIDP Foundation International and FP7 EU program, outside the submitted work. A research foundation at the University of Maastricht received honoraria on behalf of him for participation in steering committees of the Talecris Immune Globulin Intravenous for Chronic Inflammatory Demyelinating Polyneuropathy Study, Commonwealth Serum Laboratories, Behring, Octapharma, LFB, Novartis, Union Chimique Belge, Johnson & Johnson, argenx, outside the submitted work, and Octapharma during the conduct of the study

Pieter A. van Doorn - consultant with Annexon, argenx, Hansa Biopharma, Immunic, Octapharma, Roche, Sanofi, (Institutional research fund received all honoraria), and received grants from the Prinses Beatrix Spierfonds, Sanquin, and Grifols

Claudia Sommer - consultant for Alnylam, Air Liquide, Bayer, Immunic, Ipsen, LFB, Merz, Nevro, Pfizer, Roche and Takeda, and has received honoraria from Alnylam, CSL Behring, Grifols, Lilly, Merck, Novartis, Pfizer and TEVA

Erik Wallstroem - employees of Sanofi and may hold shares and/or stock options in the company

Xiaodong Luo - employees of Sanofi and may hold shares and/or stock options in the company

Miguel Alonso-Alonso - employees of Sanofi and may hold shares and/or stock options in the company

Nazem Atassi - employees of Sanofi and may hold shares and/or stock options in the company

VALUE OF HIGH-RESOLUTION ULTRASOUND IN DIAGNOSING MULTIFOCAL MOTOR NEUROPATHY IN A PATIENT WITH CERVICAL SPINAL STENOSIS

Amad Amedy (Nashville, TN), William Jones (Nashville, TN)

INTRODUCTION/BACKGROUND: We present a case of multifocal motor neuropathy (MMN) in the setting of severe cervical stenosis.

CASE REPORT: A 48-year-old man with Crohn's disease presented with a 1-year history of worsening bilateral upper extremity weakness, cramping, and occasional numbness and paresthesias. Patient noted a debilitating right wrist drop worsening for the past 3 months. Patient was referred by spine surgery to evaluate for cervical radiculopathy. Prior outside EDX studies suggested left-hand CTS. Left carpal tunnel release was performed with no improvement. Cervical spine MRI showed severe bilateral neuroforaminal stenosis from C4-C5 to C6-C7 levels. Physical exam demonstrated severe atrophy and weakness in the left shoulder girdle and right forearm muscles. Repeat EDX revealed motor conduction blocks of the left median motor at the forearm, right radial motor at the humerus, and left ulnar motor at the forearm (77%, 88%, 32% respectively). EMG showed denervation in C6-C8 innervated muscles bilaterally. High-resolution ultrasound (HRUS) of the left median and right radial nerves demonstrated fascicular enlargement, multifocal narrowing, and torsion. Median nerve cross sectional area (CSA) at the pronator teres and distal humerus were enlarged at 49 mm2 and 57 mm2, respectively. Radial nerve CSA at the mid-humerus and elbow were enlarged at 31 mm2 and 25 mm2 srespectively. Patient was referred to a neuromuscular specialist. Laboratory studies were positive for Anti-GM1 antibodies confirming MMN. Patient was started on intravenous immunoglobulin (IVIg) treatment.

SUMMARY/CONCLUSION: HRUS is a valuable, inexpensive tool to help confirm peripheral neuropathies such as MMN in settings where a patient may have multifactorial causes of their symptoms.

MANAGEMENT OF MYASTHENIA GRAVIS IN A PATIENT WITH PRE-EXISTING HYPOGAMMAGLOBULINEMIA

Albert Amran (Birmingham, AL), Kenkichi Nozaki (Birmingham, AL)

INTRODUCTION/BACKGROUND: Myasthenia gravis (MG) is an autoimmune disorder affecting post-synaptic neuromuscular junction transmission, in which pharyngeal and respiratory muscle involvement can precipitate life-threatening crises. While appropriate outpatient care in addition to emerging new therapies have drastically improved its management, various factors including medical comorbidities still make its management difficult.

CASE REPORT: We present a 72-year-old male with refractory MG associated with acetylcholine receptor (AchR) antibodies as well as pre-existing hypogammaglobulinemia. While his MG symptoms improved after switching subcutaneous immunoglobulin injections to intravenous infusions at higher doses, the patient continued to experience multiple crises. His pre-existing immunodeficiency presents a barrier to neonatal Fc receptor blockade as well as safely initiating complement inhibition due to a failure to respond to vaccination. Additionally, a strong history of allergic reactions to many medications including penicillin required allergic desensitization in a medical intensive care unit. Finally, eculizumab was successfully introduced with daily penicillin coverage which improved MG management. Prior immunoglobulin characterization revealed deficiencies in IgG1 and IgG2 with normal IgG3 and IgG4.

SUMMARY/CONCLUSION: Here we discuss the challenging management and interesting pathophysiology involved in this MG patient with pre-existing immunoglobulin deficiencies and how these are hypothetically related to the aberrant effector immune response in AchR-related myasthenia gravis. Ultimately, inhibition of complement 5 in conjunction with penicillin coverage and regular IVIg has proved sufficient for controlling this patient's symptoms. Consideration of the hypothesized pathophysiologic mechanisms of autoantibody effector responses in MGs may provide guidance for more specific, effective immunomodulation without making immunocompromised patients more vulnerable.

MOTOR END PLATE MORPHOMETRY FROM MUSCLE BIOPSY CORRELATED WITH ELECTROMYOGRAPHY DATA IN PATIENTS WITH BRACHIAL PLEXUS/PERIPHERAL NERVE INJURY

Saman Andalib (Irvine, CA), David Wright (Irvine, CA), Luigi Gonzales (Irvine, CA), Amanda Tedesco (Irvine, CA), Ali Habib (Irvine, CA), Oswald Steward (Irvine, CA), Ranjan Gupta (Irvine, CA)

INTRODUCTION: Optimal timing for surgical intervention after peripheral nerve or brachial plexus injuries remains controversial. Surgeons currently rely on serial physical examination and electromyography (EMG) to help guide decision-making. This study seeks to determine if there is a correlation between EMG data and muscle biopsy samples in patients undergoing nerve transfer.

METHODS: We performed a prospective analysis of 14 patients undergoing nerve transfer. Pre-operative EMG data was recorded in affected muscles by a board-certified neurologist. Fibrillation potentials/sharp waves were acquired and rated 0, 1+, 2+, or 3+. Muscle biopsies were obtained at the time of nerve transfer and were stained with acetylcholine receptor-alpha and neurofilament/synaptophysin to identify motor evoked potentials (MEPs) and innervating presynaptic axons. Visualized MEPs were morphologically categorized as pretzel (healthy) or intermediate/plaque (unhealthy). Healthy MEPs were quantified as a percentage of total MEPs present. Partial correlation analysis was utilized to control for time from injury. Pearson's correlations were used to define the relationship between the fibrillation potentials/sharp waves and MEP morphology.

RESULTS: A negative correlation ($r = -0.56$, $p = 0.035$) was observed between the fibrillation potentials/sharp waves and percentage of healthy pretzel MEPs. As fibrillations and sharp waves increased, the percentage of MEPs demonstrating healthy pretzel morphology decreased, suggesting an inverse relationship with neuromuscular junction health.

SUMMARY/CONCLUSION: The correlation between biopsy findings and EMG data while controlling for time from injury supports the use of muscle biopsy as an adjunct to electromyography. Integrated diagnostic approaches with objective data will help to refine management strategies for nerve injuries.

KNOWLEDGE OF MYASTHENIA GRAVIS AND NEUROMUSCULAR DISEASE AMONG NEUROLOGY RESIDENTS

Mao Liu (Brooklyn, NY), Kereisha Donegal (Brooklyn, NY), Yaacov Anziska (Brooklyn, NY)

INTRODUCTION: For decades, neurology program directors have believed training in outpatient subspecialty care for residents is insufficient.

OBJECTIVE: To assess the myasthenia gravis (MG) and neuromuscular knowledge of our adult and pediatric neurology residents (PGY 2-5).

METHODS: An anonymous survey with relevant questions was administered with answers ranging from 0 to 5 (0, not at all; 1, a bit; 2, less than average; 3, average; 4, above average; 5. very well).

RESULTS: We found that 54.6 % of residents could sufficiently (4 or 5) identify signs and symptoms of MG and 48.5% felt comfortable with performing MG exam. Only 18.2% of residents felt familiar (4) with treatment options in MG and 24.3% felt confident (4) in taking care of MG patients. While no resident felt fully knowledgeable about neuromuscular diseases or comfortable with neuromuscular encounters, 15.2% had knowledge and 18.2% expressed confidence in these encounters "above average". In terms of barriers to MG care, 66.7% mentioned lack of exposure, 24.2% denied any barriers, 6.1% mentioned lack of infrastructure, and 3% chose lack of education. The survey found that 87.9 % of residents felt a specialized electronic template would improve MG patient management. To improve neuromuscular education, 84.8% of residents chose biweekly case studies with self-learning, 63.6% recommended EMG electives with hands-on practice, 36.4% chose a journal club on recent neuromuscular advances, and 3% advocated for more outpatient neuromuscular clinic. Overall, two-thirds of residents foresaw taking care of both neuromuscular and MG patients in their future careers.

SUMMARY/CONCLUSION: Our findings highlight the need for MG and neuromuscular education among residents.

PHASE 3B STUDY MT-1186-A02 TO INVESTIGATE THE SUPERIORITY OF DAILY DOSING VS THE FDA-APPROVED ON/OFF REGIMEN OF ORAL EDARAVONE IN PATIENTS WITH AMYOTROPHIC LATER SCLEROSIS

Jeffrey Rothstein (Baltimore, MD), Angela Genge (Montreal, CA), Shari De Silva (Rogers, AR), Lorne Zinman (Toronto, CA), Marvin Chum (Ontario, CA), Adriano Chio (Torino, Italy), Gen Sobue (Aichi, Japan), Manabu Doyu (Aichi, Japan), Daniel Selness (Jersey City, NJ), Vesna Todorovic (London, United Kingdom), Nissim Sasson (Rehovot, Israel), Fumihiro Takahashi (Jersey City, NJ), Alejandro Salah (Jersey City, NJ), Art Wamil (Jersey City, NJ), Stephen Apple (Jersey City, NJ)

INTRODUCTION: An on/off dosing regimen of Radicava IV (edaravone) and Radicava ORS (edaravone) oral suspension was approved by the United States FDA for aALS treatment in 2017 and 2022, respectively. Clinical trials showed that edaravone slows the rate of physical functional decline.

OBJECTIVES: Evaluate whether investigational daily dosing displayed superior efficacy vs the approved on/off dosing regimen of oral edaravone in patients with ALS based on ALS Functional Rating Scale-Revised (ALSFRS-R) score changes, and assess safety and tolerability, over 48 weeks.

METHODS: Study MT-1186-A02 (NCT04569084) was a multi-center, phase 3b, double-blind, parallel group superiority study that randomized patients to oral edaravone (105-mg dose) administered once daily or the same oral edaravone dose administered according to the FDA-approved on/off regimen. Patients had definite or probable ALS, baseline forced vital capacity ≥70%, and baseline disease duration ≤2 years.

RESULTS: At week 48, combined assessment of function and survival (CAFS), including change in ALSFRS-R score and time to death, indicated daily dosing did not show a statistically significant difference vs on/off dosing. Oral edaravone was well tolerated and no new safety concerns were identified in either group in study MT-1186-A02.

CONCLUSION: Daily oral edaravone did not show a statistically significant difference, and therefore did not show superiority, to the FDA-approved on/off regimen in the CAFS, reinforcing the appropriateness of the FDA-approved regimen.

Disclosures:

Jeffrey Rothstein - is a consultant for Expansion Therapeutics, National Institutes of Health, Department of Defense, F Prime, The ALS Association.

Vesna Todorovic - is an employee of Mitsubishi Tanabe Pharma Europe Ltd.

Nissim Sasson - has served as a consultant for NeuroDerm and Mitsubishi Tanabe Pharma, Inc.

Fumihiro Takahashi - is an employee of Mitsubishi Tanabe Pharma America, Inc.

Alejandro Salah - is an employee of Mitsubishi Tanabe Pharma America, Inc.

Art Wamil - is an employee of Mitsubishi Tanabe Pharma America, Inc.

Stephen Apple - is an employee of Mitsubishi Tanabe Pharma America, Inc.

Angela Genge - has served as a consultant for Mitsubishi Tanabe Pharma, Inc.

Lorne Zinman - has received honoraria for consulting with MTP, Biogen, Amylyx and Cytokinetics.

Adriano Chio - serves on scientific advisory boards for Mitsubishi Tanabe, Roche, Biogen, Denali Pharma, AC Immune, Biogen, Lilly, and Cytokinetics and has received a research grant from Biogen.

Gen Sobue - has served as a medical advisor for Mitsubishi Tanabe Pharma Corporation.

Manabu Doyu - is a medical advisor for the MT-1186-A02 study.

Daniel Selness - is an employee of Mitsubishi Tanabe Pharma America, Inc.

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PHASE 3 OPEN-LABEL SAFETY EXTENSION STUDY OF ORAL EDARAVONE ADMINISTERED OVER 96 WEEKS IN PATIENTS WITH ALS (MT-1186-A03)

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INTRODUCTION: Radicava (intravenous [IV] edaravone) and Radicava ORS (oral suspension edaravone) were approved by the United States FDA for the treatment of ALS in 2017 and 2022, respectively, and studies have demonstrated these approved formulations have similar pharmacokinetics. Study MT-1186-A01 indicated that oral edaravone was well-tolerated over 48 weeks, with no new safety concerns identified.

OBJECTIVES: To evaluate the safety of oral edaravone in patients with ALS over 96 weeks.

METHODS: Study MT-1186-A03 (NCT04577404) was a phase 3, open-label, multi-center, extension study that evaluated the long-term safety of oral edaravone over an additional 96 weeks in patients who have completed the initial 48 weeks of Study MT-1186-A01. Participants received oral edaravone (105-mg dose) according to the FDA-approved dosing for IV edaravone. Patients had definite, probable, probable-laboratory-supported, or possible ALS; baseline forced vital capacity ≥70%; and baseline disease duration ≤3 years.

RESULTS: In study MT-1186-A03, oral edaravone was well tolerated with no new safety concerns. The most common treatment-emergent adverse events (TEAEs) were fall, muscular weakness, dyspnea, constipation, and dysphagia. These TEAEs were consistent with the safety profile for edaravone from previous clinical trials.

SUMMARY/CONCLUSION: Oral edaravone showed no new safety concerns and was well-tolerated during the 96-week study period.

Disclosures:

Angela Genge - has served as a consultant for Mitsubishi Tanabe Pharma, Inc.

Manabu Hirai - is an employee of Mitsubishi Tanabe Pharma Corporation.

Alejandro Salah - is an employee of Mitsubishi Tanabe Pharma America, Inc.

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Carlayne Jackson - serves on the Data and Safety Monitoring Board for Mitsubishi Tanabe Pharma America, Inc., and Anelixis.

Gary Pattee - has served as a consultant for Mitsubishi Tanabe Pharma, Inc.

Gen Sobue - has served as a medical advisor for Mitsubishi Tanabe Pharma Corporation.

Masashi Aoki - has served as medical advisor for Mitsubishi Tanabe Pharma Corporation.

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A CASE OF MYOCLONIC EPILEPSY WITH RAGGED RED FIBERS (MERRF) WITH UNIQUE BRAIN MRI FINDINGS

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INTRODUCTION: Myoclonus epilepsy with ragged-red fibers (MERRF) syndrome is a neurological disorder that is characterized by myoclonus, myopathy, peripheral neuropathy, and slow decline in intellectual ability. This mitochondrial syndrome is inherited maternally and most commonly is caused by m.8344A>G mutation in the mtDNA gene, MT-TK which encodes mitochondrial transfer (t)RNA lysine.

OBJECTIVE: We present a case of MERRF with unique MRI findings.

CASE REPORT: A 27-year-old Hispanic male born from biological parents with no family history of neurologic diseases who presented with progressive muscle weakness over the course of 5 months and increasing shortness of breath requiring intubation and mechanical ventilation. On examination, the patient had minor dysmorphic features including low-set ears and a small mandible, mild generalized muscle weakness compared to the muscle bulk, preserved reflexes, severe proprioception loss in both lower extremities and no signs of appendicular ataxia.

METHODS and RESULTS: Extensive workup, including electromyography (EMG), lumbar puncture, and autoimmune workup were negative. MRI brain showed bilateral T2/FLAIR hyperintensity at the medial thalamus, dorsal midbrain, bilateral facial colliculi, dorsal medulla and cervicomedullary junction with no contrast enhancement. Genetic testing was done and revealed mutation (m.8344 A>G) in the MTTK gene which is consistent with MERRF.

SUMMARY/CONCLUSION: MERRF is a mitochondrial disease that usually present with progressive weakness, ataxia, and epilepsy. Usual MRI findings include cerebellar atrophy, increased signal intensity in the periaqueductal gray matter or cerebellar peduncles. Here, we report a new pattern of MRI findings in a patient with MERRF that can aid in future diagnosis of the disease.

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BRACHIAL AND LUMBOSACRAL PLEXOPATHIES IN A REFERENCE CENTER: A 10-YEAR RETROSPECTIVE STUDY

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INTRODUCTION: Brachial and lumbosacral plexus are complex and affect individuals across all age groups and arising from various etiologies.

OBJECTIVE: To describe the clinical profile and etiology of patients with brachial or lumbosacral plexopathy.

METHODS: We retrospectively reviewed data of patients diagnosed with brachial or lumbosacral plexopathy, utilizing EDX studies, between March 2014 and February 2024. Data was obtained from a reference center in São Paulo, Brazil.

RESULTS: A total of 281 cases of brachial and 43 cases of lumbosacral plexopathy were identified. The age distribution ranged from 0 to 82 years (mean: 32.5), with male predominance (65%). Trauma accounted for 70.3% of plexopathies, among these, 75% attributed to external causes (motor vehicle accidents, penetrating trauma, falls), while 25% were due to obstetric causes. In adults with traumatic plexopathies, the mean age was 34 years, predominantly affecting males (84.7%). Conversely, non-traumatic plexopathies were more prevalent in females (58.3%), with a mean age of 46.6 years. The main non-traumatic etiologies included neoplastic (23.9%), iatrogenic (22.8%), Parsonage-Turner syndrome (17.4%), Thoracic outlet syndrome (15.2%), radiation-induced plexopathy (RIP) (7.6%), hematoma (4.3%), and others. Neural tissue cancer constituted 31.8% of neoplastic plexopathies, followed by bone and soft tissue tumors (27.3%), head and neck tumors (13.6%), and breast tumors (9.1%). Myokymic discharges were observed in 28.6% of patients with RIP on EMG.

SUMMARY/CONCLUSION: Trauma was the predominant cause of plexopathies, notably among young males, while neoplasia emerged as the main etiology in non-traumatic cases. The diagnosis of less common etiologies can be challenging and requires detailed clinical assessment and ancillary studies.

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UTILITY OF QUANTITATIVE GQ1B ANTIBODY TITERS IN MILLER FISHER SYNDROME FOR DIAGNOSIS AND PROGNOSIS - A RETROSPECTIVE STUDY

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INTRODUCTION: Miller Fisher syndrome (MFS) is characterized by acute onset ataxia, ophthalmoplegia, and areflexia, often accompanied by positive GQ1b antibody titers. The quantitative utility of GQ1b titers and characteristics of true/false positive tests are poorly understood.

OBJECTIVE: This study aims to identify patients testing positive for GQ1B antibody and evaluate the utility of quantitative antibody titers in diagnosing and prognosticating MFS.

METHODS: A retrospective, cross-sectional study was conducted at a single center, focusing on patients with positive GQ1b antibody titers (>50 IV). Patients were categorized based on chart review into those diagnosed with MFS and those with alternate diagnoses.

RESULTS: Nineteen patients were included, with 9 diagnosed with MFS (true positives) and 10 with alternate diagnoses (false positives). The average titers for true positives were 307.3 (range: 93-506) and for false positives were 70.7 (range: 52-143), showing a significant correlation with MFS diagnosis ($p < 0.001$). Most false positive titers were <100 IU, while true positives were >100 IU. No statistical correlation was found between antibody titers and hospital stay duration ($p = 0.476$). Amongst the false positive group, the diagnosis included ALS, idiopathic polyneuropathy, and radiculopathy.

SUMMARY/CONCLUSION: Our findings highlight the prevalence of MFS and other diagnoses in patients with positive GQ1b antibody titers. We observed a strong correlation between quantitative titers and MFS diagnosis. Based on the result, we propose considering higher quantitative thresholds (>80 or 100) may reduce false positive rates in GQ1b antibody testing without compromising sensitivity.

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TREATMENT OUTCOMES AMONG PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS IN THE CZECH REPUBLIC: RESULTS FROM MYASTHENIA GRAVIS REGISTRY (MYREG)

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INTRODUCTION: Myasthenia gravis (MG) is a rare, chronic autoimmune disease characterized by antibody-mediated interference with neuromuscular (NM) transmission at the NM junction. There is limited data on the effectiveness of treatment for generalized MG (gMG) in the real-world setting.

OBJECTIVE: To describe treatment outcomes among gMG patients in clinical practice.

METHODS: Between January 2015 and September 2023, 12 Czech clinical centers participated in MyReg. Adult gMG patients with Mythenia Gravis Foundation of America class II-IV who had a MG-Acitivities of Daily Living (MG-ADL) score ≥5 or ≥6, received corticosteroids (CS) and/or immunosuppressant therapy (IST) were included. Clinical improvement was defined as time to first observed reduction of MG-ADL ≥2 points from first (index) visit.

RESULTS: Included were 351 patients with MG-ADL≥ 5 [mean age 63.1±15.1 years, 58.7% female, 72.4% AChR+] and 271 patients with MG-ADL≥6 [mean age 62.7±14.9 years, 60.9% female, 72.3% AChR+]. At index, 11.4% and 12.2% patients used acetylcholinesterase (AChE) inhibitor monotherapy whereas 84.9% and 84.1% used combination therapy consisting of CS/IST in the MG-ADL≥5 and ≥6 cohorts, respectively. Among patients receiving CS/IST combination therapy at index, 24.9% and 47.7% of patients with index MG-ADL≥5 had ≥ 2 points reduction in MG-ADL after 6 months and 12 months, respectively; 25.8% and 50.7% of patients with index MG-ADL≥6 had ≥ 2 points reduction after 6 months and 12 months, respectively.

SUMMARY/CONCLUSION: Only 25% and 50% of gMG patients with MG-ADL≥5 or 6 receiving CS/IST combination therapy achieved clinical improvement after 6 months and 12 months, respectively. These findings underscore the need for more effective treatments to improve patient outcomes.

Disclosures:

Shane Kavanagh - is an employee of Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

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LONG-TERM SAFETY AND EFFICACY OF EFGARTIGIMOD PH20 SC IN GENERALIZED MYASTHENIA GRAVIS: INTERIM ANALYSIS OF ANTI-ACETYLCHOLINE RECEPTOR ANTIBODY SERONEGATIVE PARTICIPANTS IN ADAPT-SC+

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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 (FcRn) blockade. Patients with anti-acetylcholine receptor antibody negative (AChR-Ab-) generalized myasthenia gravis (gMG), comprising 15% to 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 the safety and efficacy of efgartigimod PH20 SC in AChR-Ab- participants with gMG enrolled in ADAPT-SC+.

METHODS: One hundred eighty-four participants rolled over from ADAPT-SC (n=105) and ADAPT+ (n=79). Of the 179 receiving ≥one dose of efgartigimod PH20 SC in ADAPT-SC+ through December 2022, 38 were AChR-Ab-.

RESULTS: Overall, 84.9% of participants had ≥one adverse event (AE), which were mostly mild/moderate. The most commonly reported AEs included injection site erythema, COVID-19, and headache. Injection site reactions were mild/moderate, did not lead to treatment discontinuation, and decreased in incidence with subsequent cycles. AChR-Ab- participants demonstrated improvements in mean [SE] change from study baseline in Myasthenia Gravis Activities of Daily Living (MG-ADL; -3.6 [0.49]) and Myasthenia Gravis Quality of Life 15-item Questionnaire, Revised (MG-QoL15r; -3.5 [0.81]) scores at week 4 of Cycle 1. Consistent improvements in MG-ADL and MG-QoL15r occurred through nine cycles.

SUMMARY/CONCLUSION: Long-term, ongoing treatment with efgartigimod PH20 SC was well tolerated and associated with consistent and repeatable improvements in MG-ADL and MG-QoL15r scores in AChR-Ab- participants in ADAPT-SC+.

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Disclosures:

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Jan Noukens - is a partner in Curare Consulting BV and consultant for argenx.

Benjamin Van Hoorick - is an employee of argenx.

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Andreas Meisel - received speaker honoraria from Alexion Pharmaceuticals, Inc, argenx, Grifols, SA, and Hormosan Pharma GmbH; honoraria from Alexion Pharmaceuticals, Inc, UCB, Janssen, and Merck for consulting services; and financial research support (paid to his institution) from Octapharma, argenx, and Alexion Pharmaceuticals, Inc. He is chairperson of the medical advisory board of the German Myasthenia Gravis Society.

Renato Mantegazza - has received consulting fees/honoraria or support for meeting participation from Alexion Pharmaceuticals, argenx, Ra Pharmaceuticals, Biomarin, Catalyst, UCB, TEVA, Merck, Roche, and Biogen.

James F. Howard Jr - has received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, and UCB Pharma; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc (now Amgen), Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, UCB Pharma, and Zai Labs; and nonfinancial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Pharma, and Zai Labs.

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LONG-TERM CORTICOSTEROID TREATMENT PATTERNS AND STEROID-SPARING EFFECTS OF APPROVED TREATMENTS FOR GENERALIZED MYASTHENIA GRAVIS IN THE UNITED STATES

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INTRODUCTION: Corticosteroids are ubiquitous in the treatment of generalized myasthenia gravis (gMG) despite evidence of adverse effects of long-term corticosteroid use.

OBJECTIVE: To evaluate (1) long-term corticosteroid use patterns in adult patients with gMG and (2) corticosteroid dose changes after initiating approved biologic treatments for gMG.

METHODS: A retrospective cohort study was conducted using the Definitive Healthcare Atlas claims database. Patients with gMG were identified in United States commercial claims data from January 2016 to September 2023. For Objective 1, descriptive statistics and longitudinal figures were used to describe and illustrate corticosteroid utilization over 24 months of follow-up since first gMG claim. For Objective 2, a multivariable regression model was used to estimate changes in corticosteroid dose pre- and post-initiation of C5 inhibitor therapies (C5iTs; eculizumab, ravulizumab) or a neonatal Fc receptor antagonist (FcRn-a; efgartigimod alfa).

RESULTS: Overall, 2237 patients met inclusion criteria comprising three treatment cohorts: no biologic (n=2006); C5iT (n=125); FcRn-a (n=106). Steroid dose journey varied widely, but 454 patients (22.6%) started at doses >10 mg and of those, 194 (42.7%) remained at doses >10 mg at 24 months. In the multivariable analysis, patients had an average reduction in annualized total corticosteroid use of 1562 mg (-36%; p=0.017) following initiation of C5iT and 668 mg (-21%; p=0.08) following initiation of FcRn-a therapy.

SUMMARY/CONCLUSION: Steroid use patterns vary widely in adult patients with gMG, but persistent high-dose corticosteroid use is common, despite adverse effects. This study demonstrated that C5iTs facilitated significant steroid sparing within the first year of their initiation.

Disclosures:

Michael Blackowicz - is an employee of Alexion, AstraZeneca Rare Disease, and owns stock in AstraZeneca.

Emma Weiskopf - is an employee of Alexion and AstraZeneca Rare Disease.

Kathryn Clark - is an employee of Definitive Healthcare.

Jeremy Grant - is an employee of Definitive Healthcare.

Christopher Scheiner - is a Consultant for Alexion, AstraZeneca Rare Disease, and CSL Behring GmbH.

COMBINED ANALYSES OF PARTICIPANTS WITH ANTI-ACETYLCHOLINE RECEPTOR SERONEGATIVE GENERALIZED MYASTHENIA GRAVIS TREATED WITH EFGARTIGIMOD ACROSS CLINICAL STUDIES

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INTRODUCTION: Approximately 15%-20% of patients with generalized myasthenia gravis (gMG) are anti-acetylcholine receptor antibody negative (AChR-Ab-). The lack of approved treatment options for the AChR-Ab- gMG population represents an unmet need.

OBJECTIVE: To describe the efficacy of efgartigimod, a human immunoglobulin G (IgG)1 antibody Fc-fragment that blocks the neonatal Fc receptor (FcRn), in AChR-Ab- participants receiving either efgartigimod IV or subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20).

METHODS: Post hoc analyses were conducted to examine the efficacy and safety of AChR-Ab- participants receiving efgartigimod IV, efgartigimod PH20 SC, or placebo in the ADAPT/ADAPT+ and ADAPT-SC/ADAPT-SC+ trials.

RESULTS: AChR-Ab- participants demonstrated greater mean (95% CI) improvement from baseline to week in Myasthenia Gravis Activities of Daily Living (MG-ADL) total scores with efgartigimod IV (-4.2 (0.82) [n=17]) compared with placebo (−2.7 (0.54) [n=19]) during Cycle 1 of ADAPT. In Cycle 1 of ADAPT+, the mean standard error (SE) MG-ADL total score improvement from baseline to week 3 in AChR-Ab- participants was -5.3 (0.74 [n=34]; no week 4 assessment was performed during ADAPT+). Similar results were observed in participants receiving repeated cycles during ADAPT-SC/SC+ (≤9 cycles). There were no substantial differences in adverse events (AEs) or serious AEs between the AChR-Ab+ and AChR-Ab- populations with either efgartigimod IV or efgartigimod PH20 SC. Additional pooled analyses of AChR-Ab- participants (n=56; >100 participant-years of follow-up) will be presented at the congress.

SUMMARY/CONCLUSION: Both IV efgartigimod and efgartigimod PH20 SC were well tolerated and led to clinically meaningful improvements in symptoms for participants with AChR-Ab- gMG.

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Edward Brauer - is an employee of argenx.

James F. Howard Jr. - has received research support (paid to his institution) from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, Ra Pharmaceuticals/UCB Bioscience, and Takeda Pharmaceuticals; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc, Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, and Zai Labs; and nonfinancial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Bioscience, and Zai Labs

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Renato Mantegazza - has received consulting fees/honoraria or support for meeting participation from Alexion Pharmaceuticals, Inc, argenx, Ra Pharmaceuticals Inc, BioMarin, Catalyst Pharmaceuticals, Inc, UCB, Teva, Merck, Roche, and Biogen Inc

Andreas Meisel - received speaker honoraria from Alexion Pharmaceuticals, Inc, argenx, Grifols, SA, and Hormosan Pharma GmbH; honoraria from Alexion Pharmaceuticals, Inc, UCB, Janssen, and Merck for consulting services; and financial research support (paid to his institution) from Octapharma, argenx, and Alexion Pharmaceuticals, Inc. He is chairperson of the medical advisory board of the German Myasthenia Gravis Society

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GENETIC PATHOGENIC VARIANT LOAD AS POSIBLE CAUSE OF THE CLINICAL HETEROGENEITY IN A PATIENT WITH LIMB GIRDLE MUSCULAR DYSTROPHY (LGMD): CASE REPORT

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INTRODUCTION/BACKGROUND: There is consensus in the literature that exercise testing (ET) can be used instead of high-frequency stimulation (HFS) for presynaptic neuromuscular junction disorders, such as Lambert-Eaton myasthenic syndrome (LEMS). The case presented is an example in which ET was not sufficient for this diagnosis.

CASE REPORT: A 47-year-old female patient presented with symmetric weakness in the lower limbs. After 2 weeks she had hoarseness and eyelid ptosis, with progressive involvement of the upper limbs. Physical examination was consistent with 3/5 lower extremity and 4/5 upper extremity strength bilaterally, areflexia, and preserved sensation. She progressed to respiratory failure and was transferred to the ICU. Theoretically, patients with LEMS have an increase or even normalization of compound muscle action potential after maximum effort. In this clinical case, the EMG showed decrease in the low-frequency repetitive stimulation test (32%) and after maximum effort (10s) there was no significant increase in compound muscle action potential (only raised 25%), leading to the hypothesis of a post-synaptic junction disorder. An increase of 70% was observed with the 30 Hz HFS. Only stimulation at 50Hz (244% increment) led to criteria for presynaptic disorder. Autoimmunity tests showed abnormalities (Anti-Ro and FAN above the reference value). The diagnosis of LEMS was confirmed using voltage gated calcium channel antibodies.

SUMMARY/CONCLUSION: Due to the delay in antibody results, it is essential that the LEMS diagnosis be made by EMG. This case showed that ET with a normal result cannot always be used to rule out presynaptic junction disorders. Given clinical suspicion, high-frequency stimulation is necessary.

NEUROPATHY ASSOCIATED TO AMYLOIDOSIS DUE TO TRANSTHYRETIN VARIANTS AND THE IMPORTANCE OF A MULTIDISCIPLINARY EVALUATION

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INTRODUCTION: Amyloidosis associated to transthyretin variants (ATTRv) is a systemic condition that requires multidisciplinary evaluation.

OBJECTIVE: To determine and characterize the presence of neuropathy as one of the cardinal signs, but on the other hand, to identify different signs that could help in the management of this population.

METHODS: Retrospective study during March 2022 to August 2023 in patients with ATTRv that underwent a multidisciplinary evaluation.

RESULTS: We studied 42 patients with a mean age of 45 years; 29 were female. The most frequent variant was Val50Met, with two patients exhibiting the double variant Val50Met/Val142Ile.Twenty-one patients had distal painful paresthesias. Quantitative sensory testing showed A delta and C fibers compromise in 18 of them, sympathetic skin response (SSR) was absent in 11 and NCS showed sensory axonal damage in 12, 5 of them showed mild signs related to bilateral CTS. The majority of our patients had early onset and distal sensory neuropathy involving small fibers in concordance with the variant Val50Met. Six patients exhibited left cardiac concentric hypertrophy, with five of them displaying abnormalities on EKG. Two patients had high levels of troponins and NT-ProBNP. Cardiac scintigraphy with PDPTc99 was abnormal in three patients. Seventeen patients had mild ophthalmologic changes related to amyloid deposits. Twenty-four-hour urine analysis showed microalbuminuria in four patients and low glomerular filtration rate.

SUMMARY/CONCLUSION: Distal sensory neuropathy involving small fibers was the principal finding in our patients associated in some cases with CTS. However, independent of the characterization of the neuropathy we found other systemic complications that aided in guiding the management and treatments.

EXPANDING THE PHENOTYPE OF DISTAL HEREDITARY MOTOR NEURONOPATHY -7A: A CASE WITH SENSORY INVOLVEMENT

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INTRODUCTION/BACKGROUND: Distal hereditary motor neuronopathies constitute a spectrum of genetically and clinically diverse inherited peripheral neuronopathies. These disorders are delineated by progressive distal lower motor neuron degeneration, sparing the corticospinal tracts, and presenting with minimal sensory dysfunction. Distal hereditary motor neuronopathy -7A (dHMN7A), follows an autosomal dominant inheritance pattern with mutations in the SLC5A7 identified as the causative factor. Thus far, a single SLC5A7 mutation has been reported in a multigenerational family. This case report includes a new finding not previously described in the literature regarding sensory involvement, as evidenced by the study of sensory nerve conduction.

CASE REPORT: A 10-year-old male patient with a 3-year onset of progressive gait instability, walking on tiptoes and muscle cramps in the lower limbs. Subsequently developed paresthesia accompanied by weakness that limits walking for short durations of 5-20 minutes, with subsequent recovery in the gait pattern. He also reports pain that gradually improves with time. The sensory nerve conduction of the sural, superficial peroneal, and ulnar nerves shows absence of potential, as well as the motor nerve conduction with axonal compromise of the peroneal and median nerves. Genetic confirmation with SLC5A7 gen variant: c.319C>T p. (Arg107Cys), heterozygous, with phenotype compatible with dHMN7A of autosomal dominant inheritance.

SUMMARY/CONCLUSION: The identification of sensory involvement in our case challenges the traditional understanding of dHMN7A as primarily a motor neuron disorder. This finding suggests a broader spectrum of clinical manifestations associated with mutations in the SLC5A7 gene, emphasizing the need for comprehensive neurological assessment in patients with suspected dHMN7A.

A REAL-WORLD EXPERIENCE WITH EFGARTIGIMOD IN GENERALIZED MYASTHENIA GRAVIS IN CHINA

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INTRODUCTION/BACKGROUND: For some gMG patients, available therapies do not provide sufficient symptom remission. Efgartigimod, the first FcRn antagonist approved in China, has been shown to improve symptoms rapidly and significantly in clinical studies. Here we report our real-life experience with efgartigimod.

CASE REPORT: Nine gMG patients were admitted between Sep 2023 and March 2024 including (four males and five females, age 32-82, anti-AChR positive). They were previously treated with prednisone, tacrolimus, cyclophosphamide, rituximab, eculizumab, intravenous immunoglobulin (IVIg) or IVMP, in variable combination or order. All patients had previously achieved MMS, but retreatment after relapsing got a poor response. Efgartigimod was then administered. Six of nine patients have completed full treatment cycle. The mean MG-ADL before efgartigimod was 11.3±6.4 and decreased to 8.4±6.4 at Week 1, 6.6±6.0 at Week 2, 6.2±6.7 at Week 4, and 6.1±7.0 at Week 4. QMG was 16.7±7.9 and decreased to 11.6±6.4 at Week 1, 10.6±6.0 at Week 2, 8.8±5.9 at Week 3, and 9.0±7.3 at Week 4. MGC was 14.3±6.8 and decreased to 11.1±6.7 at Week 1，8.9±5.6 at Week 2, 8.9±6.4 at Week 3, and 8.7±6.7 at Week 4. MG-QoL15r was 22.0±11.3 and decreased to 20.7±11.3 at Week 1, 18.7±10.6 at Week 2, 17.8±11 at Week 3, and 17.0±10.8 at Week 4. One patient has achieved MSE (MG-ADL 0 or 1) at Week 4. No adverse events were observed.

SUMMARY/CONCLUSION: The obvious and rapid neurological symptom improvement supports the efficacy of efgartigimod. Our results confirm the efficacy of efgartigimod and strengthens the role as a new effective tool in the management of MG.

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PERIOPERATIVE OUTCOMES OF THEYMECTOMY IN MYASTHENIA GRAVIS WITH EFGARTIGIMOD: A CASE SERIES

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INTRODUCTION/BACKGROUND: Efgartigimod, the first FcRn antagonist approved for the treatment of MG, has been shown to improve symptoms rapidly and significantly in clinical studies. This result provides the possibility as a perioperative management of thymoma. Here we report four cases to investigate the efficacy of efgartigimod.

CASE REPORT: Four gMG patients with thymoma were admitted between Sep 2023 and March 2024 (four males, age 42-62, all anti-AChR positive). The patients were previously treated with prednisone, tacrolimus, and intravenous methylprednisolone, in variable combination or order, with a poor response. Efgartigimod was administered before the operation for achieving optimum control and reducing the possibility of myasthenic crisis (one case before 1 day, and three cases before 7 days). The thymectomy was performed successfully. There were no perioperative complications. Tracheal intubation was removed in three of the four patients after they were awake from anesthesia, and only one patient was extubated for 3 days in ICU. The mean post-operative discharge was 4.5±1.3 days. The mean MG-activities of daily living (ADL) before thymectomy was 6.5±3.8 and decreased to 3.25±4.7 at Month 1, 2.5±3.8 at Month 3, and 1.75±2.9 at Month 6. The mean quantitative myasthenia score was 9.5±4.4 and decreased to 5.0±5.3 at Month 1, 3.5±3.4 at Month 3, 2.5±3.8 at Month 6. Three of the four patients achieved minimum symptom expression (MG-ADL 0 or 1) at Month 6.

SUMMARY/CONCLUSION: The obvious and rapid neurological symptom improvement and possibility of myasthenia crisis minimization support the efficacy of efgartigimod on the management of perioperation. Early administration of efgartigimod is a valuable option for treating thymoma associated MG. It should be further evaluated with well-controlled trials.

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THYMOMA-ASSOCIATED AUTOIMMUNE DISEASE RESPOSIVE TO EFGARTIGIMOD: A CASE REPORT

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INTRODUCTION/BACKGROUND: Thymoma is often associated with autoimmune diseases such as myasthenia gravis (MG), pure red cell aplasia, systemic lupus erythematosus, and myositis. The presence of poly autoimmunity is associated with worse outcomes and thus remains a challenge in clinical practice.

CASE REPORT: The 53-year-old female patient with a thymoma (WHO type B1) developed post-thymectomy proximal limb weakness, respiratory failure, and joint contractures gradually. Early initiation of intravenous immunoglobulin (IVIg) and corticosteroids facilitated the weaning process from mechanical ventilation. However, this patient presented prominent muscle weakness and multiple subcutaneous nodules, with high-titer antibodies targeting acetylcholine receptor (AChR), titin, and cN-1A. There were severe contractures of the interphalangeal joints of the hands and feet, but anti-cyclic citrullinated peptide antibodies and rheumatoid factor were absent. MRI scans revealed bilateral muscle edema. Given the high proportion of peripheral B cell and poly autoantibodies being identified, efgartigimod, a new neonatal Fc receptor (FcRn) blocker which has been approved in treating generalized MG, was initiated (10mg/kg weekly) for 4 weeks. Improvement was observed in MG activity of daily living (ADL) score (from baseline: 10, to 12 weeks post efgartigimod: 2) and muscular edema from MRI of lower limbs. In particular, Jaccoud’s arthropathy was substantially ameliorated.

SUMMARY/CONCLUSION: This case report highlights the therapeutic potential of FcRn antagonists in combination with other immunosuppressants for the polyautoimmunity in thymoma-associated autoimmune disease.

LEVERAGING AI TO CHARACTERIZE MENTAL HEALTH EXPERIENCES THROUGHOUT THE MYASTHENIA GRAVIS DIAGNOSIS JOURNEY

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INTRODUCTION: Individuals living with myasthenia gravis (MG) have higher rates of anxiety and depression compared to the general United States (US) population.

OBJECTIVE: To characterize mental health experiences of anxiety, fear, depression, and hopelessness, as well as potential triggers for individuals throughout management and later stages of the MG diagnosis journey via MG digital conversations using artificial intelligence (AI).

METHODS: Proprietary AI-powered methodology was used to examine US MG-related English-language public-domain online conversations (August 2022–August 2023).

RESULTS: Among 9901 identified discussions capturing the MG diagnosis journey, 21% described pre-diagnosis, 33% diagnosis, 35% management, and 11% ongoing assessment of MG (stages 1–4, respectively). Posts reporting self-described anxiety decreased during management and ongoing-assessment stages from the pre-diagnosis and diagnosis stages (6% and 5% from 48% and 36%, respectively). Self-described fear decreased to 16% in stage-4 conversations from 38%, 43%, and 40%, respectively, from stages 1–3 conversations. Conversely, increasing proportions of posts indicating depressive feelings (14%, 21%, 43%, and 55%, stages 1–4) and hopelessness (0%, 0%, 11%, and 24%) were identified. Triggers for fear and anxiety included symptoms, uncertainty, fatigue, catastrophizing thoughts, and physical, financial, and relationship impacts. Depressive feelings were mainly triggered by impacts on quality-of-life, ineffective treatment, and lack of control.

SUMMARY/CONCLUSION: This digital conversation study identified decreasing rates of self-described anxiety and fear as individuals progressed to maintenance/ongoing-assessment stages, contrasting with increasing proportions of depressive feelings and hopelessness during the same stages. These AI-leveraged insights highlight the importance of establishing effective holistic treatment plans early to support patients with MG.

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DEXAMETHASONE OPHTHALMIC SOLUTION MAY BENEFIT PATIENTS WITH OCULOMOTOR MANIFESTATIONS OF MYASTHENIA GRAVIS

Albert Cook (Johns Creek, GA)

INTRODUCTION: Ocular myasthenia gravis (OMG) is an autoimmune disorder of the neuromuscular junction affecting the extraocular and periocular musculature, producing varying degrees of diplopia and ptosis. To date, pharmacologic treatment consists of administration of pyridostigmine or oral corticosteroids. Improvement is sometimes incomplete, and treatment is often accompanied by short-term and long-term side effects. Dexamethasone ophthalmic solution (DOS) has proven beneficial in a variety of inflammatory ocular disorders (iritis, uveitis) with less systemic adverse effects than produced with oral corticosteroids.

OBJECTIVE: To determine whether DOS (0.1%) can prove beneficial in patients with OMG or those with residual oculomotor symptoms after treatment for generalized myasthenia gravis (gMG).

METHODS: Four patients with OMG or residual oculomotor deficits after treatment of gMG undertook daily administration of DOS 0.1% in both eyes. Length of treatment and observation was between 1 and 15 years. The patients were either anti-acetylcholine receptor antibody-positive (3) or anti-MuSK antibody-positive (1).

RESULTS: Diplopia resolved in all four patients selected and treated with DOS, with no observed or reported treatment-related adverse events. All four patients remained 0rthophoric on repeated exams throughout the course of treatment. Ptosis, when present, did not resolve.

SUMMARY/CONCLUSION: Daily ocular administration of DOS may be of benefit in selected patients with OMG or those with residual oculomotor symptoms after incomplete response to treatment for gMG. Treatment with DOS was safe and well tolerated in the small group of patients.

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Albert Cook - speaker bureau, Argenx.

SPONTANEOUS RESOLUTION OF INFLIXIMAB-ASSOCIATED CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY

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INTRODUCTION/BACKGROUND: Tumor necrosis factor alpha antagonists are frequently used for a range of rheumatologic conditions. There have been few reported cases of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and CIDP-like illnesses associated with use of these drugs, most responding to typical CIDP treatments. Herein, we describe a case of spontaneous improvement of infliximab-associated CIDP after drug discontinuation.

CASE REPORT: A 74-year-old man with a history of rheumatoid arthritis (RA) and baseline mild diabetic neuropathy presented with 4 months of proximodistal sensorimotor deficits. He was started on infliximab for RA, and 6 months into treatment he developed gradual onset difficulty with ambulation and worsening of length-dependent sensory changes. Weakness was noted 1 month into symptom onset. His infliximab was discontinued. Neuromuscular examination showed lower limb-predominant proximal and distal weakness, length-dependent sensory deficits, and areflexia. EMG/NCS showed a diffuse polyradiculoneuropathy with demyelinating and axonal features, meeting current European Academy of NeurologyPeripheral Nerve Society criteria for CIDP. Hemoglobin A1c was 6.7 without major fluctuations. Cerebrospinal fluid protein was 429 with one nucleated cell. Right sural nerve biopsy showed mixed axonal and demyelinating features with small inflammatory collections. He was unable to obtain intravenous immunoglobulin (IVIg) as recommended. Despite this, at his follow up 8 months later, there was near complete resolution of weakness, and sensory deficits significantly improved. Repeat EMG/NCS revealed resolution of demyelinating changes. There was no evidence of relapse at his 14 month follow up.

SUMMARY/CONCLUSION: This case suggests that infliximab-associated CIDP can spontaneously improve in rare cases, though larger and longer studies are needed to clarify characteristics of these patients and to confirm true resolution.

ULTRASONOGRAPHIC EVALUATION OF THE VAGUS NERVE IN PATIENTS CARRYING THE AMYLOIDOSIS GENE

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INTRODUCTION/BACKGROUND: In patients with amyloidosis, polyneuropathy can be found in both myelinated and unmyelinated fibers. Traditionally, the detection of these abnormalities in conventional EDX studies is late, and studies that evaluate unmyelinated or autonomic fibers are not widely available, so their use is not frequent. Increased cross-sectional area of the vagus nerve on neuromuscular ultrasound (NMUS) may show changes that anticipate abnormality in EDX studies.

CASE REPORT: A 77-year-old woman presented with autonomic symptoms (COMPASS 21) and a family history of amyloidosis. Genetic studies showed that she was a carrier of the Val142Ile variant. Neither EDX studies nor small fiber evaluation showed alterations, however, the peripheral nerve NMUS study showed a significant increase in the cross-sectional area of the vagus nerve 8 mm2 , as well as at the arm level in the median and ulnar nerves (21 mm2 and 25 mm2 respectively), fibular at the knee (20 mm2), tibial at the knee (52 mm2) and ankle (31 mm2), obtaining 11 points in the ultrasound pattern sub-score A classification.

SUMMARY/CONCLUSION: NMUS is a painless, accessible, and inexpensive tool that allows, among other things, early detection of vagus nerve involvement in patients with suspected amyloid polyneuropathy, which is known to predict the onset of symptoms and abnormality in EDX tests. Additionally, it can be directly correlated with autonomic symptoms.

EFFECT SIZE ANALYSIS OF CIPAGLUCOSIDASE ALFA PLUS MIGLUSTAT VERSUS ALGLUCOSIDASE ALFA IN ENZYME REPLACEMENT THERAPY-EXPERIENCED ADULTS WITH LATE-ONSET POMPE DISEASE IN PROPEL

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INTRODUCTION: The randomized, double-blind PROPEL study (NCT03729362) compared the efficacy and safety of the two-component therapy cipaglucosidase alfa plus miglustat (cipa+mig) with alglucosidase alfa plus placebo (alg) in adults with late-onset Pompe disease (LOPD); 77% of patients had received enzyme replacement therapy (ERT) with alg before study entry (median 7.4 years).

OBJECTIVE: To analyze effect sizes of cipa+mig and alg for efficacy outcomes in ERT-experienced patients with LOPD.

METHODS: Standardized within-group effect sizes (Cohen's d for correlated measurements, baseline to week 52) were calculated for outcomes including motor and lung function, muscle strength, quality of life and biomarkers in ERT-experienced patients by dividing mean change from baseline by standard deviations of the difference.

RESULTS: Patients remaining on alg (n=30) showed worsening ($d \leq -0.2$) or stability ($-0.2 < d < 0.2$) across most outcomes, while those switching to cipa+mig (n=65) showed improvement ($d \geq 0.2$) or stability. Patients remaining on alg demonstrated statistically significant within-group worsening for sitting and supine forced vital capacity; slow vital capacity; maximal expiratory pressure; creatine kinase (CK) and hexose tetrasaccharide (Hex4) levels, and significant improvement only for Patient-Reported Outcomes Measurement Information System (PROMIS)-Dyspnea score. Patients switched to cipa +mig did not demonstrate significant within-group worsening and showed significant improvements for 6-minute walk distance; manual muscle tests; PROMIS-Fatigue score; Physician and Subject Global Impression of Change (five subdomains); and CK and Hex4.

SUMMARY/CONCLUSION: ERT-experienced patients with LOPD switched to cipa+mig achieved improvements in various outcomes, highlighting the potential of cipa+mig as a treatment option for these patients. Supported by Amicus Therapeutics, Inc.

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Mazen M. Dimachkie - has recently served or serves as a consultant for Abata/Third Rock, Abcuro, Amicus Therapeutics, Inc., argenx, Astellas, Cabaletta Bio, Catalyst, CNSA, Covance/Labcorp, CSL-Behring, Dianthus, Horizon, EMD Serono/Merck, Ig Society, Inc, Janssen, Medlink, Octapharma, Priovant, Sanofi Genzyme, Shire Takeda, TACT/Treat NMD, UCB Biopharma, Valenza Bio and Wolters Kluwer Health/UpToDate. He has received research grants or contracts, or educational grants from Alexion/ AstraZeneca, Alnylam Pharmaceuticals, Amicus Therapeutics, Inc., argenx, Bristol-Myers Squibb, Catalyst, CSL-Behring, FDA/OOPD, GlaxoSmithKline, Genentech, Grifols, Mitsubishi Tanabe Pharma, MDA, NIH, Novartis, Octapharma, Orphazyme, Ra Pharma/UCB, Sanofi Genzyme, Sarepta Therapeutics, Shire Takeda, Spark Therapeutics, The Myositis Association, and UCB Biopharma/RaPharma.

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Fred Holdbrook - is an employee of, and holds stock in, Amicus Therapeutics, Inc.

Sheela Sitaraman Das - is an employee of, and holds stock in, Amicus Therapeutics, Inc.

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Tahseen Mozaffar - has advised for Abbvie, Alexion, Amicus Therapeutics, Inc., Annji, argenx, Arvinas, Audentes, Cabaletta, Maze Therapeutics, Momenta, Ra Pharmaceuticals, Sanofi Genzyme, Sarepta, Spark Therapeutics, and UCB; participates on the speaker's bureau for Sanofi Genzyme and the medical advisory boards for the Myositis Association, Neuromuscular Disease Foundation, Myasthenia Gravis Foundation of California and Myasthenia Gravis Foundation of America; has received research funding from the Myositis Association, the Muscular Dystrophy Association, the NIH and from the following sponsors: Alexion, Amicus Therapeutics, Inc., Annji, argenx, Audentes, Bristol-Myers Squibb, Cabaletta, Cartesian Therapeutics, Grifols, Momenta, Ra Pharmaceuticals, Sanofi Genzyme, Spark Therapeutics, UCB, and Valerion; is on the data safety monitoring board for Acceleron, Applied Therapeutics, Sarepta, and the NIH.

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PITFALLS OF SINGLE FIBER ELECTROMYOGRAPHY (SFEMG) IN THE DIAGNOSIS OF SERONEGATIVE MYASTHENIA GRAVIS

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INTRODUCTION/BACKGROUND: Seronegative myasthenia gravis (MG) often presents a diagnostic challenge and may be misdiagnosed. Repetitive nerve stimulation (RNS) study has high specificity but is limited by its sensitivity, particularly in ocular MG. Single fiber EMG (SFEMG) has high sensitivity but can be limited by its specificity. We report two cases of MG mimics, both have abnormal jitter on SFEMG.

CASE REPORT: A 47-year-old Hispanic woman presented with gradual onset ptosis in her mid-30s. The ptosis improves with rest. She reports infrequent diplopia and fatigue, without dysphagia or dysarthria. She has negative MG antibodies and RNS studies. SFEMG showed increased jitter with blocking. She reports subjective improvement with oral pyridostigmine. Due to symmetrical ptosis and absence of diplopia, alternative etiology was considered. She underwent genetic testing which revealed a pathogenic variant of POLG gene associated with chronic progressive external ophthalmoplegia (CPEO).

A 69-year-old African man presented with gradual onset progressive ptosis for 10 years. Severity of ptosis fluctuates. He reports dyspnea with exertion, difficulty with chewing, swallowing and choking. Positive ice test was noted by his ophthalmologist. Symptoms failed to improve with MG treatments. He has negative MG serologies and RNS. SFEMG showed markedly increased jitter with frequent blocking. Genetic testing revealed 13 GCN repeats on one allele of the PABPN1 gene associated with oculopharyngeal muscular dystrophy (OPMD) and variant of unclear significant in MYH2 gene associated with proximal myopathy and ophthalmoplegia.

SUMMARY/CONCLUSION: Diagnosis of seronegative MG frequently resorts to SFEMG. However, it is worth noting that abnormal jitter can be seen in MG mimics such as CPEO and OPMD.

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RITUXIMAB INDUCED WORSENING OF CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

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INTRODUCTION/BACKGROUND: Although acute neurological worsening after rituximab treatment has been reported in patients with anti-MAG neuropathy, this has not been reported with chronic inflammatory demyelinating polyneuropathy (CIDP). We report a patient with CIDP with acute worsening after rituximab.

CASE REPORT: A 65-year-old woman presented with an 8-month history of progressive weakness and numbness in her legs, which worsened in the setting of a COVID-19 infection. Examination showed severe weakness distally (1 medical research council (MRC) legs, 2 MRC arms) and proximally (4-MRC legs, 3 MRC arms); areflexia and distal sensory loss to small and large fiber modalities. EMG showed severe, length-dependent sensorimotor demyelinating polyneuropathy, partial motor conduction block, and abnormal temporal dispersion in several motor nerves along with absent sensory responses, meeting EFNS criteria for CIDP. Other findings include lumbosacral root enhancement on MRI, albuminocytologic dissociation in spinal fluid, and negative serum tests including immunofixation, nodal, and paranodal antibodies. She was diagnosed with CIDP and had been doing well for over a year on a combination of dexamethasone and intravenous immunoglobulin (IVIg), with 5 MRC in proximal and distal muscles and stable Rasch-built Overall Disability Scale (R-ODS) score (31-36). Rituximab treatment was initiated because of lack of further improvement. Two weeks after receiving rituximab, she declined dramatically with R-ODS score of 8 and weakness with 2 MRC proximally and 0-2 distally. She was treated with high dose steroids and a loading dose of IVIg with improvement back to her prior baseline with a R-ODS score of 32.

SUMMARY/CONCLUSION: Clinicians should be aware of the potential of acute worsening after rituximab in patients with CIDP.

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SERUM NEUROFILAMENT LIGHT CHAIN AS A BIOMARKER IN SENSORY NEURONOPATHY: A CASE SERIES

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INTRODUCTION/BACKGROUND: Sensory neuronopathies demonstrate non-length-dependent sensory axonal loss on electrophysiology. Management of sensory neuronopathies is confounded by description of sensory symptoms versus neuropathy severity and disability. Compared to demyelinating neuropathies where clinical and functional improvements are usually demonstrated within months of immunomodulatory therapy, axonal and neuronal pathologies are less predictable. There is a need for biomarker as a signal of treatment response. We demonstrate in this case series that serum neurofilament light chain (NfL) is a feasible early biomarker to assess treatment response.

CASE REPORT: We present four patients with possible/probable sensory neuronopathy by Camdessanche diagnostic criteria. Serum neurofilament light (NfL) values were obtained, when possible, prior to treatment initiation and at follow up. Treatment responsiveness was measured by functional measures (RODS, timed up-and-go) and examination (neuropathy impairment score (NIS), grip strength, INCAT-SS).

Two patients demonstrate clear treatment-responsiveness by multiple outcome measures with corresponding NfL change from pre and post treatment levels. Patient three showed clear treatment-responsiveness; NfL was not obtained since it was not commercially available at initial presentation. During her convalescence, NfL was normal. Patient four showed no treatment response and NfL was normal at initial presentation.

SUMMARY/CONCLUSION: We demonstrate that 1) significantly abnormal serum NfL corresponds with clinical decline in sensory neuronopathy, 2) decrease in initial abnormal NfL levels corresponds with concomitant exam and functional changes, and 3) the wide spectrum of rate of recovery that can be seen in treatment-responsive disease. NfL may serve as an early biomarker in predicting treatment responsiveness in an axonal or neuronal process.

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ELECTROGRAPHICAL SIGNIFICANCE OF PERIODIC DISCHARGES AND ASSOCIATION WITH ETIOLOGY AND OUTCOMES IN A TERTIARY CARE HOSPITAL IN PAKISTAN, A RETROSPECTIVE COHORT STUDY

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INTRODUCTION/BACKGROUND: Periodic discharges in electroencephalograms (EEGs) represent rhythmic wave patterns and can signal acute or subacute brain damage. While they may predispose patients to seizures, not all are epileptiform. This study focuses on electrographical periodic discharges and aims to elucidate their frequency, etiological associations, and clinical outcomes within a tertiary care hospital setting.

CASE REPORT: This retrospective observational cohort study spanned 2 years, from January 2021 to January 2023. It included patients aged 18 years and above with EEG-confirmed periodic discharges. Data, including demographics, symptoms, EEG findings, neuroimaging results, treatment, and outcomes, were collected. Of the 41 patients analyzed, 51.2% were female, with an average age of approximately 58.5 years. Generalized tonic-clonic seizures were the most common clinical presentation (48.8%), with ischemic stroke being the leading etiological factor (31.7%). Lateralized periodic discharges (LPDs) were the most common EEG finding. Notably, 34% of patients exhibited chronic imaging changes, primarily encephalomalacia and gliosis. The majority (87.8%) were discharged home, with a minority (12.2%) experiencing mortality, often associated with status epilepticus or metabolic encephalopathy. A considerable portion (53.7%) had a modified Rankin Scale (mRS) score of 4 or higher, indicating significant post-discharge functional dependence.

SUMMARY/CONCLUSION: This study highlights the importance of recognizing periodic discharges in EEGs within the context of a tertiary care hospital. The study's findings emphasize the potential gravity of periodic discharges, as indicated by mortality rates and functional outcomes. Improved understanding of these periodic discharges and their associated conditions can guide clinical decision-making and enhance patient care within tertiary care hospital setting.

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EXPOSURE-RESPONSE RELATIONSHIPS: HYALURONIDASE-FACILITATED SUBCUTANEOUS AND INTRAVENOUS IMMUNOGLOBULIN 10% IN CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY

Immanuel Freedman (Cambridge, MA), Stefan Roepcke (Buffalo, NY), Zhaoyang Li (Cambridge, MA)

INTRODUCTION: Exposure-response relationships were simulated for different hyaluronidase-facilitated subcutaneous immunoglobulin (fSCIG) 10% and intravenous immunoglobulin (IVIg) 10% dosing regimens in patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

OBJECTIVE: To characterize population pharmacokinetic-pharmacodynamic (popPK-PD) relationships of fSCIG and IVIg 10% in CIDP.

METHODS: A popPK-PD model was developed using pharmacokinetic data from phase 3 studies in CIDP (NCT02549170, n=132) and multifocal motor neuropathy (NCT00666263, n=44). The final sequential popPK-PD model for binary response data simulated relationships between total serum immunoglobulin G (IgG) concentrations, and probability of increased adjusted Inflammatory Neuropathy Cause and Treatment (INCAT) scores for patients with CIDP over 6 months of continuous IVIG 10% or 9 months of fSCIG 10% maintenance therapy (after 3 months of ramp-up dosing for both therapies). Dosing regimens simulated were: 0.4, 0.8, and 1g/kg every 2 weeks (Q2W); 1 and 2g/kg Q3W; 0.4, 0.8, 1, and 2g/kg Q4W; and 2g/kg split into four daily infusions Q4W.

RESULTS: Across treatments, mean probability of increased INCAT score was <50% for 0.4g/kg Q2W regimens and all regimens ≥0.8g/kg, and ~50% for 0.4g/kg Q4W regimens. Higher doses/more frequent administration meant increased scores were less likely; patients treated less frequently were generally more likely to have increased INCAT scores towards the end of dosing intervals.

SUMMARY/CONCLUSION: The model and simulations successfully described exposure-response relationships for fSCIG and IVIg 10% in CIDP relapse. More frequent dosing may provide more consistent IgG levels and response.

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Disclosures:

Immanuel Freedman - is an employee of Takeda Development Center Americas, Inc. and a Takeda shareholder.

Stefan Roepcke - is an employee of Cognigen, a division of Simulations Plus, which acted as a consultant to Takeda Development Center Americas, Inc. during this study.

Zhaoyang Li - is an employee of Takeda Development Center Americas, Inc. and a Takeda shareholder.

CORTICOSTEROID DOSE TAPERING DURING TREATMENT WITH ZILUCOPLAN IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: 120-WEEK FOLLOW-UP OF RAISE-XT

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INTRODUCTION: The efficacy and safety of zilucoplan in patients with acetylcholine receptor autoantibody-positive generalized myasthenia gravis (gMG) were assessed in two double-blind studies (NCT03315130/NCT04115293). During these studies, and the first 12 weeks of the ongoing, open-label extension study, RAISE-XT (NCT04225871), corticosteroid dose was kept stable. Thereafter, corticosteroid dose could be changed at the investigator's discretion.

OBJECTIVE: Evaluate corticosteroid dose changes in patients with gMG during zilucoplan treatment in RAISE-XT.

METHODS: In RAISE-XT, adults who completed a qualifying double-blind study self-administered once-daily subcutaneous zilucoplan 0.3mg/kg. Primary outcome: incidence of treatment-emergent adverse events (TEAEs). This post hoc interim analysis (November 11, 2023) assessed the proportion of patients who reduced, discontinued, or increased their corticosteroid dose relative to double-blind baseline and change from baseline (CFB) in MG Activities of Daily Living (MG-ADL) score after 120 weeks.

RESULTS: Overall, 200 patients enrolled. Of patients on corticosteroids at double-blind baseline with week 120 data, 61.1% (n=33/54) had reduced or discontinued corticosteroids (mean 15.5mg dose reduction from 23.0 mg at baseline); mean change from baseline (CFB) in MG-ADL score: −6.6 (standard deviation [SD] 3.6). Amongst all patients with week 120 data, 9.3% (n=8/86) increased or started corticosteroids relative to double-blind baseline (mean dose increase: 11.6mg); mean CFB in MG-ADL score: −7.4 (SD 4.6). At week 120, 32% of patients with a ≥7.5mg dose at double-blind baseline had reduced their dose to a dose <7.5mg. TEAEs occurred in 97.0% (n=194/200) of patients.

SUMMARY/CONCLUSION: Treatment with zilucoplan allowed for reduction or discontinuation of corticosteroids in the majority of patients, while demonstrating sustained efficacy.

Disclosures:

Miriam Freimer - has served as a paid Consultant for argenx, UCB Pharma, and Alexion Pharmaceuticals. She receives research support from the NIH, UCB Pharma, Janssen Pharmaceuticals, Alnylam, Avidity, and Fulcrum.

Mark Vanderkelen - is an employee and shareholder of UCB Pharma.

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Kimiaki Utsugisawa - has served as a paid Consultant for UCB Pharma, argenx, Janssen Pharmaceuticals, Viela Bio (now Horizon Therapeutics), Chugai Pharmaceutical, HanAll Biopharma, Merck, and Mitsubishi Tanabe Pharma; he has received speaker honoraria from argenx, Alexion Pharmaceuticals, UCB Pharma, and the Japan Blood Products Organization.

Tuan Vu - is the USF Site Principal Investigator for MG clinical trials sponsored by Alexion Pharmaceuticals, Amgen, argenx, Cartesian Therapeutics, Dianthus, Immunovant, Johnson and Johnson, UCB Pharma, Regeneron Pharmaceuticals, RemeGen and has served as a speaker for Alexion Pharmaceuticals, Allergan/AbbVie, argenx and CSL Behring. He performed consulting work for Alexion Pharmaceuticals, argenx, Dianthus, RemeGen, ImmunAbs and UCB Pharma.

Babak Boroojerdi - is an employee and shareholder of UCB Pharma.

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SELF-ADMINISTRATION OF SUBCUTANEOUS ROZANOLIXIZUMAB IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: CLINICAL STUDY DESIGN

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INTRODUCTION: Generalized myasthenia gravis (gMG) is a chronic autoimmune disease requiring long-term therapy. Rozanolixizumab, indicated for the treatment of adults with acetylcholine receptor or muscle-specific tyrosine kinase receptor autoantibody-positive gMG, is currently administered subcutaneously by healthcare professionals (HCPs) using a programmable syringe driver. The MG0020 study aims to demonstrate whether patients can safely self-administer rozanolixizumab using the syringe driver and manual push methods.

METHODS: MG0020, a Phase 3, open label, randomized, crossover study, will include patients aged ≥18 years with gMG. In total, 75 patients have been screened and 55 will be randomized. Patients will receive once-weekly rozanolixizumab for 18 consecutive weeks consisting of a 6-week self-administration training period followed by two 6-week self-administration periods (at clinic and unsupervised at home). After training, patients will be randomized 1:1 to the syringe driver or manual push self-administration method, subsequently crossing over to the alternative method. A safety follow-up period of up to 7-weeks will follow. The primary endpoint is successful self-administration of rozanolixizumab (choosing the correct infusion site, administering subcutaneously, and delivering intended dose) by syringe driver and manual push, evaluated by an HCP at weeks 12 and 18. Secondary endpoints are occurrence of treatment-emergent adverse events, local site reactions and medication errors resulting in adverse reactions. Additional endpoints include patient preference for subcutaneous infusions performed by an HCP versus self-administration, and preference for manual push versus syringe driver self-administration.

SUMMARY/CONCLUSION: MG0020 will evaluate the safety and success of self-administration of rozanolixizumab using the syringe driver and manual push methods in patients with gMG.

Disclosures:

Rachana K. Gandhi Mehta - has received research support from Akcea (now Ionis Pharmaceuticals, Inc.), Graticule and UCB Pharma. She is a Site Investigator for the Rare Disease Network for Myasthenia Gravis (MGNet) National Institute of Neurological Disorders & Stroke. She has participated in advisory boards for UCB Pharma and has received speaker honoraria from UCB Pharma. She has also served as a NEJM Group Clinical Reasoning Contributing Editor for NEJM Healer.

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M. Isabel Leite - is funded by the NHS (Myasthenia and Related Disorders Service and National Specialised Commissioning Group for Neuromyelitis Optica, UK) and by the University of Oxford, UK. She has been awarded research grants from the UK association for patients with myasthenia (Myaware) and the University of Oxford. She has received speaker honoraria or travel grants from Biogen, Novartis, UCB Pharma and the Guthy-Jackson Charitable Foundation. She serves on scientific or educational advisory boards for UCB Pharma, argenx and Viela Bio (now Horizon Therapeutics).

Vera Bril - is a Consultant for Akcea, Alexion Pharmaceuticals, Alnylam, argenx, CSL, Grifols, Ionis, Immunovant, Janssen Pharmaceuticals, Momenta (now Johnson and Johnson), Novo Nordisk, Octapharma, Pfizer, Powell Mansfield, Roche, Sanofi, Takeda and UCB Pharma. She has received research support from Akcea, Alexion Pharmaceuticals, argenx, CSL, Grifols, Immunovant, Ionis, Momenta (now Johnson and Johnson), Octapharma, Takeda, UCB Pharma and Viela Bio (now Horizon Therapeutics).

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Denis Flemm - is an employee and shareholder of UCB Pharma.

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SAFETY, TOLERABILITY, PHARMACOKINETICS, IMMUNOGENICITY, AND EFFICACY OF ARGX-119 IN PARTICIPANTS WITH DOK7-CONGENITAL MYASTHENIC SYNDROMES: PHASE 1B STUDY IN PROGRESS

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INTRODUCTION: Congenital myasthenic syndromes (CMS) are a rare, heterogeneous group of congenital disorders caused by impaired neuromuscular transmission for which there are currently no approved treatments. CMS are characterized by variable periods of muscle weakness and fatigue and are frequently caused by a mutation in the DOK7 gene (DOK7 CMS). DOK7 is a protein coactivator of MuSK, which is essential for neuromuscular junction development and optimal neurotransmission. ARGX-119, a humanized, agonistic, monoclonal antibody, specifically targets and activates MuSK, which may stabilize, mature, and improve the function of the neuromuscular junction in participants with DOK7-CMS, significantly reducing muscle weakness and fatigability and improving quality of life.

OBJECTIVE: To evaluate the safety, tolerability, pharmacokinetics, immunogenicity, and efficacy of ARGX-119 in participants with DOK7-CMS.

METHODS: This Phase 1b study is planned to enroll approximately 15 participants with DOK7-CMS, blinded randomized 4:1 to either IV ARGX-119 or placebo for six doses with a follow-up period of approximately 7 months. Six infusions will be administered once every other week to each participant.

RESULTS: The primary endpoint is assessment of safety. Secondary endpoints are assessment of pharmacokinetic parameters of ARGX-119, development of antidrug antibodies against ARGX-119, and efficacy measures. Efficacy measurements include change from baseline over time in key components of the Quantitative Myasthenia Gravis score, Myasthenia Gravis Activities of Daily Living score, and Patient-Reported Outcomes Measurement Information System Global Health score.

SUMMARY/CONCLUSION: This Phase 1b study will assess the safety, tolerability, pharmacokinetics, immunogenicity, and efficacy of ARGX-119 in participants with DOK7-CMS.

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Steven J. Burden - research support provided by argenx; consultant for argenx, holds patents licensed by argenx.

Javier Avendano - is an employee of argenx.

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PERSISTENT DYSAUTONOMIC MANIFESTATIONS IN PATIENTS PREVIOUSLY DIAGNOSED WITH GUILLAIN-BARRÉ SYNDROME

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INTRODUCTION: In the acute phase of Guillain-Barré syndrome (GBS), potentially fatal dysautonomic symptoms may occur but remains unclear in the long term.

OBJECTIVE: Evaluate the persistence of dysautonomia in individuals with a GBS history

METHODS: In a study involving 10 GBS patients aged 18 and older, dysautonomic signs and symptoms were assessed using the Mayo Clinic questionnaire, skin wrinkling test, blood pressure (BP), and EKG for evaluating R-R interval and heart rate variability (HRV) through the root mean square of successive differences between normal heartbeats (RMSSD). A healthy control group (HC) was included. The somatic component was evaluated using the Medical Research Council (MRC) sum score, considering muscle strength, sensation, and osteotendinous reflexes (OTR). Daily limitations were measured using the Rasch-built Overall Disability Scale (R-ODS).

RESULTS: In GBS patients, all reported at least one dysautonomic symptom, with postprandial symptoms and blurred vision being the most common. The skin wrinkling test showed a significant difference compared to HC (GBS 2.4 vs HC 1.2, p=0.01). BP measures were similar between GBS and HC. Regarding HRV, GBS patients exhibited decreased RMSSD in both supine (GBS 55.64 vs HC 35.47, p=0.0006) and sitting positions (GBS 49.29 vs HC 33.78, p=0.0017), with no significant difference in the standing position (GBS 37.17 vs HC 36.99). Despite 80% of patients having a normal somatic physical examination, the mean R-ODS scale value was 86.4 ± 14.37.

SUMMARY/CONCLUSION: The data indicates that clinical manifestations are consistent with persistent sympathetic/parasympathetic dysautonomia even after the resolution of the somatic component of GBS.

CASE REPORT: BILATERAL CYCLIST'S PALSY

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INTRODUCTION/BACKGROUND: Cyclist's palsy (CP) is caused by sustained compression of the ulnar nerve (CN) at the bicycle handlebars. It debuts with various motor and sensory symptoms, depending on the location of the lesion. Gross and Gilberman's classification describe 3 zones: Zone 1, before the bifurcation of the CN, results in sensory and motor deficits; Zone 2 affects the deep motor branch, causing weakness in the intrinsic muscles of the hand; Zone 3 involves the superficial branch, presenting sensory deficits in fingers four and five.

CASE REPORT: A 54-year-old man presented with paresthesias in his hands while riding a bicycle. Physical examination revealed hypoesthesia in the fifth finger of the left hand. The EDX showed reduced bilateral CN sensory potential amplitude and prolonged left sensory latency, consistent with a bilateral CN neuropathy in Guyon's canal, with greater left involvement. Ultrasound (US) revealed an increased area cross section of the ulnar nerve at the level of Guyon's canal, 6 mm2 bilateral. The symptoms resolved when he stopping cycling

SUMMARY/CONCLUSION: The ulnar nerve can be injured at the level of Guyon's canal in cyclists; injury is rare and presentation bilateral, as is the exclusive commitment of the sensitive fibers. US and EDX are essential for the diagnosis and localization of the injury.

CASE REPORT: SMALL FIBER NEUROPATHY IN A PATIENT WITH LEPROSY EVALUATED WITH A QUANTITATIVE SENSORY TESTING

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INTRODUCTION/BACKGROUND: The prevalence of leprosy in Colombia is less than 1 case per 100,000 inhabitants and can trigger neuropathic pain in 22% of patients, including painful paresthesias secondary to small fiber neuropathies (SFN) from immune mediated lesions of thinly myelinated (Aδ) and unmyelinated (C) fibers. Some authors propose two of the following abnormal tests for SFN diagnosis: (1) clinical impairment of small fibers, (2) quantitative sensory testing (QST) with abnormal thresholds, (3) reduced density of intraepidermal nerve fibers. There are no reported cases of QST in leprosy patients in the literature.

CASE REPORT: A 57-year-old male diagnosed with multibacillary lepromatous leprosy by skin biopsy (April 2023), EDX described mild axonal and myelinic sensory-motor polyneuropathy of the four extremities with predominance in the lower limbs. He presented on February,13 2024 with persistent paresthesias, screened with the Small Fiber Neuropathy Screening List questionnaire scoring 30/84, indicating probable SFN. QST was performed, revealing increased thresholds for cold thermal perception in all four extremities and increased thresholds for heat nociceptive perception in the lower limbs, demonstrating hyposensitivity to thermal-painful stimuli.The conclusion was severe functional impairment of Aδ and C small-caliber fibers in all four extremities.

SUMMARY/CONCLUSION: Bacillus invasion of Schwann cells and myelinated and unmyelinated nerve fibers, and subsequent replacement by connective tissue, leads to axonal degeneration, triggering various neuropathies, including SFN. As demonstrated in this case, QST is a valuable and non-invasive tool for guiding SFN diagnosis in clinical practice.

THE COST OF ENDURANCE: INVESTINGATING NERVE INJURIES IN ULTRACYCLING ATHLETES

Nathali Carolina González Alvarado (Bogotá, Colombia), Jorge Munoz (Bogotá, Colombia), Liliana Rodriguez (Bogotá, Colombia), Jorge Arturo Diaz Ruiz (Bogotá, Colombia)

INTRODUCTION/BACKGROUND: Ultra cycling, a rapidly growing discipline involving traversing distances exceeding 1000 km across various terrains, has garnered significant attention.

CASE REPORT: A 36-year-old male ultradistance cyclist with no notable medical history, experiencing paresthesia in both hands following intense sporting activities was seen. Symptoms manifested in the first, second, and third fingers of both hands after a 1000-km gravel race, and previously, in the fourth and fifth fingers after a 2800-km race on paved terrain. Despite persisting for 6 months, symptoms resolved. Lower limb examination showed no abnormalities, with normal motor function observed in the extremities.

EDX studies of the upper and lower limbs revealed an absence of sensory response in the left median nerve, decreased sensory amplitudes in the right median and bilateral ulnar nerves, along with prolonged latencies and reduced conduction velocity. Sensory NCS in the right dorsal cutaneous and left superficial radial nerves remained within normal parameters. Motor NCS of the left median nerve exhibited a 62% decrease in amplitude compared to the contralateral side, with normal conduction velocity despite a distal latency limit. Motor NCS in the right median and bilateral ulnar nerves, assessed in the first dorsal interosseous and abductor digiti minimi muscles, was normal. Sensory NCS in the lower limbs was normal.

SUMMARY/CONCLUSION: This case emphasizes the importance of EDXI monitoring in ultradistance cyclists for early detection and management of peripheral nerve injuries. Strategies like bike adjustments, glove use, and optimizing hand positioning to reduce vibration and prevent future injuries are recommended.

USE OF ULTRASONOGRAPHY AND "J-IMAGE" TO APPROACH INFLAMMATORY MYOPATHY SECONDARY TO AUTOIMMUNE DISEASE: CASE REPORT

Juan Esteban Gonzalez Camargo (Bogotá, Colombia), Liliana Rodriguez (Bogotá, Colombia), Jorge Nicolás Muñoz (Bogotá, Colombia), Jorge Arturo Diaz Ruiz (Bogotá, Colombia)

INTRODUCTION: The measurement of muscle echogenicity by ultrasonography (US) together with "J-image" analysis has become a decisive diagnostic tool in the study of muscle pathologies. This method uses grayscale analysis and reference values to quantify echogenicity.

AIM: To present a case of measuring muscle echogenicity in a patient with inflammatory myopathy using US and J-image analysis as novel diagnostic tools.

CASE REPORT: A 76-year-old woman treated for an autoimmune disease characterized by skin symptoms manifested by the appearance of brown macules in the region of the back and arms, associated with myalgia and polyarthralgia. She was being treated with methotrexate and oral prednisolone and wasreferred for EDX study due to proximal muscle weakness in all four extremities, associated with elevated creatine phosphokinase and transaminases.

RESULTS: Quantitative electromyography and interference pattern analysis corroborated muscle fiber involvement, NCSs were normal. During US, hyperechogenicity was determined in the right vastus lateralis muscle, with a value of echogenicity of 62%. These findings were related to an inflammatory myopathy secondary to the autoimmune disease.

SUMMARY/CONCLUSION: This case highlights the importance of US and the use of the "J-image" tool for the assessment and quantitative analysis of muscle echogenicity. These methods may be useful in assessing muscle quality, understanding disease etiologies, selecting muscles for biopsies, and facilitating disease research. It is important to note that these resources are easy to use and free. In this way, these tools can be decisive support in the diagnosis of muscle diseases, including inflammatory myopathies.

IMPACT OF ALS-CBS PERFORMANCE ON ALS-RELATED SYMPTOM MANAGEMENT: A RETROSPECTIVE ANALYSIS

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INTRODUCTION: ALS is a neurodegenerative disorder with potential cognitive/behavioral impairment, which can be detected by the ALS-Cognitive Behavioral Screen (ALS-CBS) and may affect disease management.

OBJECTIVE: To evaluate whether ALS management differs between those with normal and abnormal ALS-CBS scores.

METHODS: Retrospective review of individuals with Gold Coast criteria-confirmed ALS in a single-center multidisciplinary clinic between 2018 and 2022 was performed including presenting features, ALS-CBS scores at initial evaluation, and ALS-related symptom management.

RESULTS: Of 142 patients, 49% were female. Mean age, ALS Functional Rating Scale-Revised (ALSFRS-R), and median disease duration at diagnosis was 62 years (Standard deviation [SD] ±10.1), 37 (SD ±7), and 10 months (range 2-210), respectively. Disease onset was spinal in 76% and bulbar in 24%.

Ninety-nine patients (70%) had abnormal ALS-CBS scores at their initial visit. Disease characteristics were similar between abnormal and normal score groups. Medications for sialorrhea, spasticity, mood, and sleep were less frequently prescribed to patients with abnormal versus normal scores (p=0.01) while disease-modifying therapy had similar use (48 versus 53%, p=0.58). Non-invasive ventilation use (p=0.25), gastrostomy tube placement (p=0.35), pursuit of augmentative/alternative communication evaluation (p=0.17), and survival (p=0.18) were not statistically significant between the two groups.

SUMMARY/CONCLUSION: Patients with abnormal ALS-CBS scores were less likely to use medications for ALS-related symptoms. While cognitive impairment as identified by the ALS-CBS did not impact survival compared to patients with normal scores, it may lead to undertreated symptoms and impact quality of life.

OBTURATOR NEUROPATHY: A RETROSPECTIVE REVIEW OF 36 PATIENTS

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INTRODUCTION: The primary objective of this research study is to gain understanding of electrophysiological findings and value of EMG/NCS for prognostication in patients with obturator neuropathy.

OBJECTIVE: Obturator neuropathy presents as an uncommon cause of lower extremity weakness with other symptoms including medial thigh numbness and lower extremity pain.

METHODS: This single center retrospective study aimed to summarize various clinical features of obturator neuropathy. A total of 36 patients with obturator neuropathies diagnosed over a 20-year period, August 2002 to July 2022 were evaluated. Demographic, clinical, and electrographic data were collected, and descriptive statistics were used to analyze the variables of interest.

RESULTS: Of the 36 patients evaluated, surgery related trauma (n=21; 58%) was the most common etiology, and lower extremity pain (n=30; 86%) was the most common symptom. Based on diagnoses made through EMG, 23 patients (79%) had pure obturator neuropathy. Treatments led to improvement or complete resolution in 18 (50%) patients while 11 (31%) had no relief. No significant difference in time to diagnosis was observed based on sex, race, or insurance type.

SUMMARY/CONCLUSION: Surgical trauma was the most common cause in our patient group, followed by cancer related causes. EDX findings, aid in definitive diagnosis. The lack of statistically significant differences between race, sex, or insurance in our patient group suggests an equitable process of evaluation of patient from their initial presentation with a provider to a definitive diagnosis. The lack of symptomatic improvement in 31% of patients in our group demonstrates the continued need for advancements in nerve repair and regrowth.

A CASE SERIES OF ORAL CORTICOSTEROID TAPERING AFTER TREATMENT WITH EFGARTIGIMOD IV IN FOUR PATIENTS WITH ANTI-ACETYLCHOLINE RECEPTOR AUTOANTIBODY SEROPOSITIVE GENERALIZED MYASTHENIA GRAVIS

Raghav Govindarajan (O'Fallon, IL), Alexis King (Kirskville, MO)

INTRODUCTION: Corticosteroids are a mainstay of treatment in generalized myasthenia gravis (gMG). Reducing corticosteroids use can alleviate the risk of many adverse events related to long-term corticosteroid use. Data are limited on how novel therapies, such as the human IgG1 antibody Fc-fragment efgartigimod, impact long-term corticosteroid use in patients with gMG.

OBJECTIVE: To describe a series of cases in which patients presenting with gMG were able to taper their dose of corticosteroids after efgartigimod treatment.

METHODS: A retrospective chart review of patients with gMG was conducted to examine corticosteroid use after efgartigimod treatment.

RESULTS: Four patients 42 to 82-years-old presented to the clinic with anti-acetylcholine receptor autoantibody seropositive gMG that was diagnosed between 1 and 4 years prior. The patients had a Myasthenia Gravis Activities of Daily Living (MG-ADL) score ranging from 10 to 12 (potential maximum: 24) at presentation. All patients were being treated with prednisone (20-25 mg QD) and pyridostigmine (30-60 mg TID) upon presentation, and one patient was being treated with mycophenolate mofetil (750 mg BID). Two patients had a prior history of treatment with intravenous immunoglobulin (1 g/kg Q4W). Patients were treated with 4 once-weekly injections of efgartigimod IV with 6 weeks between cycles for three cycles. After three cycles, patients saw improvement in their MG-ADL scores of 5 to 8 points, and their daily dose of prednisone was tapered by 25% to 87.5% (5- to 20-mg reduction).

SUMMARY/CONCLUSION: Treatment with efgartigimod in these cases improved patient MG-ADL scores and allowed for the dose of corticosteroids to be tapered.

Disclosures:

Raghav Govindarajan - has served on advisory boards for argenx, UCB, Janssen, and Roche; and speakers bureaus for argenx, Alexion, and UCB.

DRY BERIBERI AND WERNICKE'S ENCEPHALOPATHY DUE TO THIAMINE DEFICIENCY WITH ALBUMINOCYTOLOGICAL DISSOCIATION MIMICKING GUILLAIN-BARRÉ SYNDROME: A DIAGNOSTIC CONUNDRUM

Supreeth Gowda (Lexington, KY), Shreyak Sehgal (Meerut, India), Nakul Katyal (Lexington, KY)

INTRODUCTION/BACKGROUND: Dry beriberi is known to mimic Guillain-Barre syndrome (GBS). Here we report a case of thiamine deficiency with albuminocytological dissociation mimicking GBS.

CASE REPORT: A 51-year-old woman presented to our hospital from outside facility for evaluation of severe weakness. In mid-October, she developed vomiting and diarrhea. Later diagnosed with cholelithiasis and underwent cholecystectomy. She developed sudden onset ascending weakness and numbness 1 week later that progressed within the week requiring hospitalization. Examination notable for proximal > distal and lower >upper extremity weakness with areflexia. Cerebrospinal fluid testing showed albuminocytoalbuminologic dissociation with protein of 112 mg/dl and 2 white blood cells. Thiamine level was drawn on admission. MRI brain showed subtle bilateral medial thalami and peri-aqueductal T2 hyperintensities. Patient received intravenous immunoglobulin (IVIg) 2 gm/Kg over 5 days. However, weakness progressively worsened, and she developed confusion. She developed respiratory distress requiring intubation. Thiamine level resulted after 5 days notably low at 33 nmol/L. Patient was started on IV thiamine 100 mg daily. Repeat MRI brain showed improvement in hyperintensities. EMG study, 3 weeks after showed severe sensory motor polyneuropathy with axonal loss features. Her symptoms in the setting of thiamine deficiency with corroborating imaging evidence were suggestive of thiamine deficiency resulting in dry beriberi and Wernicke's encephalopathy. The patient eventually required tracheostomy and feeding tube placement was discharged to rehab facility.

SUMMARY/CONCLUSION: A high index of suspicion for thiamine deficiency in patients presenting with progressive neuropathy is required. Preemptive administration of high-dose intravenous thiamine, following thiamine lab tests, should be considered, delay in treatment might result in symptom worsening.

THE ROLE OF CUTANEOUS SILENT PERIOD IN SENSORY GANGLIONOPATHIES AVALIATON: A CASE SERIES AND REVIEW

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INTRODUCTION/BACKGROUND: Sensory ganglionopathies consist of conditions characterized by involvement of the dorsal root ganglion, leading to a pure sensory deficit syndrome, not length-dependent, with involvement of the face, trunk, and upper limbs before involvement of the lower limbs, in general. Most ganglionopathies affect primarily the large fibers, leading to symptoms such as sensory ataxia. Less commonly, ganglionopathy can affect only the small sensory fibers, leading to burning pain, tingling, shock pain, and dysautonomia. In general, routine neurophysiological assessment does not evaluate the small sensory fibers, requiring specific tests, such as the cutaneous silent period, to access them.

CASE REPORT: We present a series of cases of sensory ganglionopathy at different stages of evolution, from initial to chronic conditions, followed in a referenced center, in which we perform a cutaneous silent period test protocol. Our objectives were to use this information to differentiate cases of ganglionopathy from cases of asymmetric peripheral polyneuropathy, evaluate the involvement of small sensory fibers and the evolution of this involvement according to the course of the ganglionopathy.

SUMMARY/CONCLUSION: This pilot study allows us to establish a low-cost standardized evaluation protocol to evaluate the involvement of small sensory fibers in cases of ganglionopathy, to assist in the differential diagnosis and in an attempt to establish a prognostic assessment and relationship between the underlying cause and the type of compromised fiber, thus assisting in the etiological investigation.

EFFICACY AND SAFETY OF SUBCUTANEOUS EFGARTIGIMOD PH20 IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY: ADHERE TRIAL SUBGROUP ANALYSIS

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INTRODUCTION: Efgartigimod, a human immunoglobulin G (IgG)1 antibody Fc fragment, blocks the neonatal Fc receptor, reducing IgG levels, including pathogenic autoantibodies. Multistage, double-blind, placebo-controlled ADHERE assessed efficacy/safety of subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20) in chronic inflammatory demyelinating polyneuropathy (CIDP).

OBJECTIVE: To assess the efficacy of weekly efgartigimod PH20 SC 1000 mg by patient subgroups.

METHODS: Efgartigimod PH20 SC efficacy was assessed during stage A (≤12 weeks open-label treatment) and stage B (≤48 weeks randomized-withdrawal, double-blind, placebo-controlled period). Subgroups were based on prior CIDP therapy at screening (corticosteroids, intravenous immunoglobulin (IVIg)/SCIg, and off-treatment [treatment naïve and those who received CIDP treatment ≥6 months before study entry]) and different patient/disease characteristics. Endpoints included participants with confirmed evidence of clinical improvement (ECI), time to ECI (stage A), time to first adjusted Inflammatory Neuropathy Cause and Treatment (aINCAT) deterioration (≥1-point score increase [relapse], stage B), and safety (stages A/B).

RESULTS: Most participants had confirmed ECI with efgartigimod PH20 SC regardless of prior therapy; corticosteroids: 77.8% (95% CI,65.5–87.3); IVIg/SCIg: 58.8% (95% CI,50.9–66.4); off-treatment: 72.3% (95% CI,62.2–81.1). Kaplan-Meier analysis demonstrated the probability of ECI over time was similar across prior therapy subgroups. Analysis of different patient/disease characteristics by subgroups showed mostly similar rates of ECI (stage A) and hazard ratio for reduction in the risk of relapse (stage B). Efgartigimod PH20 SC was well tolerated; most treatment-emergent adverse events were mild/moderate in severity.

SUMMARY/CONCLUSION: Clinical benefit with efgartigimod PH20 SC was demonstrated across a range of patient subgroups.

Disclosures:

Jeffrey A. Allen - consultant fees: Akcea Therapeutics, Alexion, Alnylam, Annexon Biosciences, argenx, CSL Behring, Grifols, Immunovant, Immupharma, Johnson & Johnson, Pfizer, Takeda.

Trevor Mole - is an employee of argenx.

Satoshi Kuwabara - consultant/lecture fees: Alexion, argenx, CSL Behring, Takeda.

Ivana Basta - consultation fees/ speaker honoraria: Actavis, Dinathus, Mylan, Pfizer, Salveo.

Pieter A. Van Doorn - consultant fees: Annexon Biosciences, argenx, Grifols, Hansa Biopharma, Immunic Therapeutics, Octapharma, Prinses Beatrix Spierfonds, Roche, Sanofi, Sanquin.

Richard A. Lewis - consultant fees: Akcea Therapeutics, Alexion, Alnylam, Annexon Biosciences, argenx, Boehringer Ingelheim, CSL Behring, GBS/CIDP Foundation International, Grifols, Johnson & Johnson, Medscape, MGFA, Novartis, Peripheral Nerve Society, Pfizer, Roche, Sanofi, Takeda.

Luis Querol - consultant fees: Alnylam, Annexon Biosciences, argenx, Avilar Therapeutics, Biogen, CIBERER, CSL Behring, Dianthus, Fundació La Marató, GBS/CIDP Foundation International, Grifols, Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), Janssen, LFB, Lundbeck, Merck, Novartis, Octapharma, Roche, Sanofi, UCB.

Kelly Gwathmey - consultant fees: Alexion, argenx, UCB, Xeris Pharmaceuticals.

Niraja Suresh - advisory board member: TakedaSpeaker program member: Alnylam.

Jeffrey T. Guptill - is an employee of argenx.

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EFFICACY AND SAFETY OF SUBCUTANEOUS EFGARTIGIMOD PH20 IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY: ADHERE/ADHERE+ TRIAL

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INTRODUCTION: Efgartigimod, a human immunoglobulin G (IgG)1 antibody Fc fragment, blocks the neonatal Fc receptor, decreasing IgG recycling and reducing pathogenic IgG autoantibody levels. Multi-stage, double-blind, placebo-controlled randomized-withdrawal ADHERE, and ongoing open-label extension ADHERE+, assessed the efficacy and safety of efgartigimod PH20 subcutaneous (SC; coformulated with recombinant human hyaluronidase PH20) in chronic inflammatory demyelinating polyneuropathy (CIDP).

OBJECTIVE: To report primary outcomes from ADHERE and ADHERE+.

METHODS: Enrolled participants included those with CIDP (off-treatment or on standard treatments withdrawn during run-in) who had active disease and received weekly efgartigimod PH20 SC 1000 mg (stage A). Responders were randomized (1:1) to weekly efgartigimod PH20 SC 1000 mg or placebo (stage B). Participants with clinical deterioration in stage B or those who completed ADHERE could enter ADHERE+ (weekly efgartigimod PH20 SC 1000 mg). Primary outcomes were clinical improvement (stage A), efficacy (stage B), and safety (ADHERE+).

RESULTS: In stage A, 214/322 (66.5%) participants demonstrated clinical improvement. In stage B, efgartigimod significantly reduced relapse risk (Hazard ratio [HR]: 0.394 [95% CI, 0.253-0.614]) vs placebo (P=0.00004). Reduced risk of relapse was shown in participants regardless of prior CIDP therapy. Ninety-nine percent of eligible participants entered ADHERE+. The safety profile of efgartigimod-treated participants was consistent over 137.42 total patient-years of follow-up for ADHERE+. Most treatment-emergent adverse events were mild/moderate; their incidence/severity did not increase in ADHERE+.

SUMMARY/CONCLUSION: ADHERE+ demonstrated long-term effectiveness of efgartigimod PH20 SC for reducing the risk of relapse. The safety profile of efgartigimod PH20 SC was similar between ADHERE and ADHERE+ and was consistent with the previously demonstrated safety profile of efgartigimod.

Disclosures:

Satoshi Kuwabara - consultant fees: Alexion, argenx, CSL Behring, Takeda.

Jeffrey T. Guptill - is an employee of argenx.

Christian Eggers - consultant fees: argenx, Biogen, GlaxoSmithKline, UCB.

Frank Leypoldt - consultant fees: Alexion, Bayer, Biogen, Fresenius, Grifols, Merck, Novartis, Roche, Teva Pharmaceuticals.

Jeffrey A. Allen - consultant fees: Akcea Therapeutics, Alexion, Alnylam, Annexon Biosciences, argenx, CSL Behring, Grifols, Immunovant, ImmuPharma, Johnson & Johnson, Pfizer, Takeda.

Niraja Suresh - advisory board member: TakedaSpeaker program member: Alnylam.

Channa Hewamadduma - speaker honoraria or consultant fees: argenx, Biogen, Lupin, Roche, UCB.

Marta Lipowska - consultant fees: argenx, CSL Behring, Kedrion Biopharma, Medison Pharma/Alnylam, Pfizer, Sanofi, Sobi, Takeda.

Giuseppe Lauria - consulting fees: Biogen, Chromocell, CSL Behring, Home Biosciences, Janssen, Lilly, Sangamo Therapeutics, Vertex Pharmaceuticals, Zambon.

PHASE 3 TRIAL INVESTIGATING IMPACT OF INTRAVENOUS EFGARTIGIMOD IN ANTI-ACETYLCHOLINE RECEPTOR ANTIBODY NEGATIVE GENERALIZED MYASTHENIA GRAVIS

Jeffrey Guptill (Ghent, Belgium), Rosa H. Jimenez (Ghent, Belgium), James F. Howard Jr. (Chapel Hill, NC)

INTRODUCTION: Approximately 15-20% of patients with generalized myasthenia gravis (gMG) are anti-acetylcholine receptor antibody negative (AChR-Ab-). The lack of approved treatment options for the AChR-Ab- gMG population represents an unmet need in the gMG treatment landscape. Efgartigimod is a human immunoglobulin G (IgG)1 antibody Fc-fragment that reduces IgG levels (including pathogenic autoantibodies) through blockade of the neonatal Fc receptor. This phase 3 (NCT06298552) trial will investigate the efficacy and safety of efgartigimod in participants with AChR-Ab- gMG.

OBJECTIVE: To determine the efficacy and safety of 10 mg/kg IV efgartigimod compared with placebo in AChR-Ab- participants with gMG.

METHODS: Adult participants with AChR-Ab- gMG who have a Myasthenia Gravis Activities of Daily Living (MG-ADL) total score of ≥5 (with >50% of the score due to nonocular symptoms) and are on a stable dose of ≥1 concomitant gMG treatment will be included. One hundred ten adjudicated participants will be randomized 1:1 to either receive 10 mg/kg IV efgartigimod or placebo. The study has 2 stages: the double-blinded placebo-controlled part A, consisting of 4 once-weekly infusions and 5 weeks of follow-up, and the open-label extension part B, consisting of varying number and frequency of cycles and weekly infusions for ≤2 years.

RESULTS: The primary endpoint is the change in MG-ADL total score from study baseline to day 29 in part A. Additional efficacy outcomes (QMG, MG-QoL15r, EQ-5D-5L), safety/tolerability, and pharmacokinetic/pharmacodynamic effects are also being assessed.

SUMMARY/CONCLUSION: This phase 3 trial will provide important data on the efficacy and safety of efgartigimod IV in the treatment of AChR-Ab- gMG.

Disclosures:

Jeffrey Guptill - is an employee of argenx.

Rosa H. Jimenez - is an employee of argenx.

James F. Howard Jr. - has received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, and UCB Pharma; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc (now Amgen), Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, UCB Pharma, and Zai Labs; and nonfinancial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Pharma, and Zai Labs

THE RAPID ACCESS ALS CLINIC MODEL: CAN WE MOVE THE NEEDLE AND IMPROVE ALS DIAGNOSTIC DELAY?

Kelly Gwathmey (Richmond, VA), Paula Brockenbrough (Richmond, VA), Shanshan Chen (Richmond, VA), Demetrius Carter (Richmond, VA)

INTRODUCTION: ALS diagnostic delay (DD) averages 10-16 months. FDA-approved disease modifying treatments (DMTs) have improved benefit when initiated earlier, stressing the need of prompt diagnosis. Between September 2022 and February 2024, the Virginia Commonwealth University (VCU) Health ALS Clinic piloted a monthly Rapid Access Clinic (RAC) for any patient suspected to have ALS. This clinic was advertised to community and academic health care providers via webinars, email, and print communication.

OBJECTIVE: The objective of this study was to evaluate the DD and baseline disease severity at initial visit for patients with ALS (PALS) referred to the RAC versus external ALS diagnosis and referral to the VCU multidisciplinary clinic (MDC).

METHODS: All patients referred to the VCU MDC and RAC were evaluated for DD, baseline ALS Functional Rating Scale-Revised (ALSFRS-R) score, upright and supine forced vital capacities (FVCs), and compared to historical data from 2017-2023. RAC patients without an ALS diagnosis were captured.

RESULTS: 28 PALS were seen in the RAC. 20 PALS were diagnosed externally. 25 RAC patients did not have ALS. DD was 9.49 months for RAC PALS, 11.9 months for external PALS. Baseline ALSFRS-R was 36.8 and 34.7 for RAC PALS and external PALS, respectively. Upright/supine FVC was 77.2%/63.8% for RAC PALS and 68.5%/64.6% for external PALS. These data compare to historical data of a 10.8-month DD, ALSFRS-R score of 38 and upright FVC of 76.8%.

SUMMARY/CONCLUSION: The RAC model has the potential to improve DD in ALS, resulting in earlier access to DMTs and better clinical outcomes.

Disclosures:

Kelly Gwathmey - unrelated to this topic, I have consulted for argenx, Alexion, and UCB pharmaceuticals.

SAFETY PROFILE OF INTRAVENOUS EFGARTIGIMOD FROM CLINICAL TRIALS IN IMMUNOGLOBULIN G-MEDIATED AUTOIMMUNE DISEASES

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INTRODUCTION: Efgartigimod (EFG), a human immunoglobulin G (IgG)1 Fc fragment, blocks the neonatal Fc receptor, selectively decreasing IgG levels.

OBJECTIVE: To assess the safety profile of IV efgartigimod across different IgG-mediated diseases.

METHODS: Efgartigimod was assessed in different dosing regimens (10–25 mg/kg IV, including cyclical and continuous weekly dosing) in generalized myasthenia gravis (gMG; Phase 2 trial, Phase 3 placebo-controlled ADAPT and open-label extension ADAPT+ trials) and primary immune thrombocytopenia (ITP; Phase 3 placebo-controlled ADVANCE IV and ongoing open-label extension ADVANCE IV+ [data cut-off: 24 November 2023] trials). Pooled data represent participants receiving efgartigimod 10 mg/kg IV in the Phase 2, ADAPT and ADAPT+ trials for gMG and in the ADVANCE IV and ADVANCE IV+ trials for ITP.

RESULTS: Efgartigimod IV was well-tolerated and demonstrated a consistent safety profile across all indications and doses studied, with comparable rates of treatment-emergent adverse events (TEAEs) to placebo and across indications (TEAEs ranged from 77.4–95.6% across studies/pooled analyses). Most TEAEs were mild to moderate in severity, with consistently low TEAE-related discontinuation rates across all indications and pooled analyses (ranged from 0–9.1%). There was no increase in TEAE or infection event rates with repeated or continuous treatment. Efgartigimod treatment did not reduce albumin levels or increase cholesterol levels.

SUMMARY/CONCLUSION: Efgartigimod IV was well-tolerated across all indications and doses. Most TEAEs were mild to moderate in severity and event rates did not increase with repeated treatment.

Disclosures:

Andreas Meisel - Alexion, argenx, Axunio, Grifols, Hormosan, Janssen, Merck, Octapharma, UCB, Vitaccess.

Ming Jiang - is an employee of argenx.

James F. Howard - investigator/consulting Fees: AcademicCME, Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Biologix, Cartesian Therapeutics, Centers for Disease Control and Prevention, CheckRare CME, F. Hoffmann-LaRoche Ltd, Amgen, Medscape CME, Merck EMB Serono, MGFA, Muscular Dystrophy Association, NIH, NMD Pharma, Novartis, PCORI, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, Toleranzia AB, UCB, Zai Lab.

Kristl Claeys - consulting fees: Alexion, Alnylam, Amicus, argenx, Biogen, CSL Behring, Ipsen, Janssen, Roche, UCB.

Kelly Gwathmey - consulting fees: Alexion, argenx, UCB Pharma, Xeris Pharmaceuticals.

Catherine M. Broome - consulting fees: Alexion, Apellis, argenx, Sanofi.

Hiroyuki Murai - consulting fees: Alexion, argenx, Chugai, Japan Blood Products Organization, Roche, UCB.

Adrian Newland - consulting fees: Amgen, Angle, argenx, Dova, Novartis, Ono, Rigel, Shionogi.

Peter Ulrichts - is an employee of argenx.

René Kerstens - is an employee of argenx.

Jeffrey Guptill - is an employee of argenx.

Sofiane Agha - is an employee of argenx.

SAFETY PROFILE OF SUBCUTANEOUS EFGARTIGIMOD PH20 FROM CLINICAL TRIALS IN IMMUNOGLOBULIN G–MEDIATED AUTOIMMUNE DISEASES

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INTRODUCTION: Efgartigimod (EFG), a human immunoglobulin G (IgG)1 Fc fragment, blocks the neonatal Fc receptor, selectively decreasing IgG levels.

OBJECTIVE: To assess the safety profile of subcutaneous (SC) efgartigimod PH20 (co-formulated with recombinant human hyaluronidase PH20) across generalized myasthenia gravis (gMG) and chronic inflammatory demyelinating polyneuropathy (CIDP).

METHODS: Efgartigimod PH20 SC was assessed using cyclical dosing (4 once-weekly injections) in gMG (ADAPT-SC noninferiority study [SC vs intravenous efgartigimod] and ongoing open-label extension ADAPT-SC+ trial [data cut-off: 19 June 2023]) and weekly continuous dosing in CIDP (ADHERE [stage A: open-label; stage B: placebo-controlled] and ongoing open-label extension ADHERE+ trials [data cut-off: 15 June 2023]).

RESULTS: Efgartigimod PH20 SC was well-tolerated and demonstrated a consistent safety profile, with similar rates of treatment-emergent adverse events (TEAEs) to placebo in ADHERE, across indications, and across routes of administration; a higher rate of injection site reactions (ISRs) was observed with efgartigimod PH20 SC versus placebo in ADHERE. Most TEAEs were mild to moderate in severity across studies. Discontinuation rates due to TEAEs were consistently low, ranging from 0–6.8% across studies. There was no increase in TEAE rates, including infections, with repeated treatment. ISRs were mild to moderate in severity, and only one participant (in CIDP studies) discontinued efgartigimod PH20 SC because of an ISR (rash at injection site). Efgartigimod PH20 SC did not reduce albumin or increase cholesterol levels.

SUMMARY/CONCLUSION: Efgartigimod PH20 SC was well-tolerated across indications and dosing regimens. Most TEAEs were mild to moderate in severity and did not increase in frequency with recurrent dosing.

Disclosures:

Pieter Van Doorn - consulting fees: Annexon Biosciences, argenx, Grifols, Hansa Biopharma, Immunic Therapeutics, Prinses Beatrix Spierfonds, Octapharma, Roche, Sanofi, Sanquin.

Jeffrey Guptill - is an employee of argenx.

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Richard Lewis - consulting fees: Akcea Therapeutics, Alexion, Alnylam, Annexon Biosciences, argenx, Boehringer Ingelheim, CSL Behring, GBS/CIDP Foundation International, Grifols, Johnson & Johnson, Medscape, MGFA, Novartis, Peripheral Nerve Society, Pfizer, Roche, Sanofi, Takeda.

Kelly Gwathmey - consulting fees: Alexion, argenx, UCB Pharma, Xeris Pharmaceuticals.

Jan L. De Bleecker - Alexion, Alnylam, argenx, CSL Behring, Janssen, Sanofi Genzyme, UCB.

James Howard - investigator/consulting Fees: AcademicCME, Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Biologix, Cartesian Therapeutics, Centers for Disease Control and Prevention, CheckRare CME, F. Hoffmann-LaRoche Ltd, Amgen, Medscape CME, Merck EMB Serono, MGFA, Muscular Dystrophy Association, NIH, NMD Pharma, Novartis, PCORI, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, Toleranzia AB, UCB, Zai Lab.

Tuan Vu - Alexion, Amgen, argenx, Dianthus, Cartesian Therapeutics, Dianthus, ImmunAbs, Immunovant, Janssen/Momenta, Regeneron, Remegen, Sanofi, UCB.

Jeffrey Allen - consulting fees: Akcea Therapeutics, Alexion, Alnylam, Annexon, argenx SE, CSL Behring, Grifols, Immuovant, ImmuPharma, Johnson & Johnson, Pfizer, Takeda.

Sofiane Agha - is an employee of argenx.

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CYCLIC AND EVERY-OTHER-WEEK DOSING OF INTRAVENOUS EFGARTIGIMOD FOR GENERALIZED MYASTHENIA GRAVIS: PART A OF ADAPT NXT

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INTRODUCTION: Individualized cyclic dosing of efgartigimod, a human immunoglobulin G1 Fc-fragment that blocks the neonatal Fc receptor, was well tolerated and efficacious in the ADAPT/ADAPT+ phase 3 trials in generalized myasthenia gravis (gMG).

OBJECTIVE: The phase 3b ADAPT NXT study (NCT04980495) investigated the efficacy, safety, and tolerability of efgartigimod administered either every other week (Q2W) or in fixed cycle dosing regimens.

METHODS: Adult participants with anti-acetylcholine receptor antibody positive gMG were randomized 3:1 to Q2W or cyclic (four once-weekly infusions, 4 weeks between cycles) dosing of 10 mg/kg efgartigimod for a 21-week period.

RESULTS: Sixty-nine participants were treated (cyclic, n=17; Q2W, n=52). Least squares mean (95% confidence index [CI]) of the change from baseline in MG Activities of Daily Living (MG-ADL) total score from week 1-21 (primary endpoint) was -5.1 (-6.5 to -3.8) in the cyclic arm and -4.6 (-5.4 to -3.8) in the Q2W arm; changes remained similar through week 21. Clinically meaningful improvements in mean standard error (SE) MG-ADL total scores were observed as early as week 1 (-2.0 [0.4], both arms) and were maintained over time. Achievement of minimal symptom expression (MG-ADL score 0-1) was observed in 47.1% (n=8/17) and 44.2% (n=23/52) of participants in the cyclic and Q2W arms, respectively. Efgartigimod was well tolerated; COVID-19, upper respiratory tract infection, and headache were the most common treatment-emergent adverse events.

SUMMARY/CONCLUSION: The results of ADAPT NXT build upon previous studies and provide additional efgartigimod dosing approaches (fixed cycles and Q2W) to maintain clinical efficacy in participants with gMG.

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Daniela Hristova - is an employee of argenx.

Delphine Masschaele - is an employee of argenx.

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DESIGN OF KYSA-6, A PHASE 2, OPEN-LABEL, MULTICENTER STUDY OF KYV-101, A NOVEL FULLY HUMAN ANTI-CD19 CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY IN REFRACTORY GENERALIZED MYASTHENIA GRAVIS

Aiden Haghikia (Magdeburg, Germany), Dominic Borie (Emeryville, CA), James Chung (Emeryville, CA), Ralf Gold (Bochum, Germany)

INTRODUCTION: Myasthenia gravis (MG) is a B-cell-mediated autoimmune disease for which new therapeutic paradigms are needed that can improve disease activity in refractory patients and enable sustained treatment-free remission. KYV-101 is a first-in-class, fully human autologous anti-CD19 CAR T-cell therapy containing a CAR demonstrated to have a favorable clinical safety profile in oncology. In the compassionate use setting, KYV-101 demonstrated rapid, profound improvements in disease severity and was well-tolerated in patients with severe refractory MG. KYV-101 is being investigated in KYSA-6, a multicenter, open-label, phase 2 study in MG (NCT06193889).

OBJECTIVE: Primary objectives are to evaluate the safety and efficacy of KYV-101, assessing adverse events and MG Activities of Daily Living (MG-ADL) at 24 weeks. Secondary objectives include evaluation of further efficacy, disease-related autoantibodies, and patient-reported outcomes.

METHODS: Twenty patients ages 18–75 years old, with generalized MG (class IIB-IV per MG Foundation of America), the presence of disease-related autoantibodies, an MG-ADL score ≥6, who failed prior immunosuppressive/immunomodulatory therapy, are eligible. After lymphodepletion (fludarabine 30 mg/m^2/day, cyclophosphamide 300 mg/m^2/day; 3 days), patients will receive a single infusion of 1×10^8 CAR T cells. Descriptive statistics will be provided.

RESULTS: KYV-101 received FDA fast track designation for MG. KYSA-6 is being initiated in the United States and other regions.

SUMMARY/CONCLUSION: KYV-101 is a novel therapy with the potential to change the treatment paradigm through deep B-cell depletion and immune reset with a single infusion in patients with B-cell driven autoimmune diseases like MG. KYV-101 is also under investigation in additional neurologic and rheumatologic diseases.

Disclosures:

Dominic Borie - is an employee of Kyverna Therapeutics, Inc.

James Chung - is an employee of Kyverna Therapeutics, Inc.

Ralf Gold - serves on scientific advisory boards for Teva Pharmaceutical Industries Ltd., Biogen, Bayer Schering Pharma and Novartis; has received speaker honoraria from Biogen, Teva Pharmaceutical Industries Ltd., Bayer Schering Pharma and Novartis; serves as editor for Therapeutic Advances in Neurological Diseases and on the editorial boards of Experimental Neurology and the Journal of Neuroimmunology; and receives research support from Teva Pharmaceutical Industries Ltd., Biogen Idec, Bayer Schering Pharma, Genzyme, Merck Serono and Novartis.

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AMYOTROPHIC LATERAL SCLEROSIS: FUCTIONAL BRAIN CHANGES

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INTRODUCTION: ALS is a progressive, fatal disorder, with signs of motor neuron degeneration in one or more regions: bulbar, cervical, thoracic, or lumbosacral. It causes muscular atrophy, disability, and death.

OBJECTIVE: Describe functional brain changes in a group of ALS patients through post-processing EEG techniques and correlate it with clinic abnormalities.

METHODS: Thirty adult sporadic ALS patients and 30 healthy subjects matched in age and sex with the patients, were recruited for the study. Resting state was performed and EEG-based features, (power spectrum, source location and functional connectivity) were applied. All measures from patients and healthy subjects were compared by statistical methods.

RESULTS: The ALS patient group showed an increase of grand total EEG (GTE) score (p=0.00), a global reduction in spectral energy of the alpha frequency band, and an increase in theta and delta frequency bands in the centro-temporo-parietal areas. Additionally, there was an increase of font generators of slow frequencies on fronto-centro-temporal areas (delta) and fronto-central areas (theta). We also observed an increase of the connectivity of delta band on the frontal, parietal, and temporal areas.

SUMMARY/CONCLUSION: Post-processing EEG methods showed functional changes in a group of ALS patients. These changes worsened when evolution time was increased and when clinical aspects worsened.

DUAL INNERVATION OF THE EXTENSOR DIGITORUM BREVIS MUSCLE

Jesus Hernandez (Miami, FL), Marc Swerdloff (Boca Raton, FL)

INTRODUCTION: Anomalous innervations in the lower extremities are uncommonly mentioned in EDX medicine literature. The most frequently mentioned anomalies include accessory deep peroneal nerve, complete tibial foot innervation, and deep peroneal to posterior tibial anastomosis. We discovered a new anomalous innervation variation to add to this list. In this case, the tibial and peroneal nerves simultaneously provide motor innervation to the extensor digitorum brevis (EDB) muscle.

OBJECTIVE: To present a case of dual innervation of the EDB muscle by the tibial and peroneal nerves, highlighting its EDX characteristics.

METHODS: NCSs were performed to evaluate motor innervation of the EDB muscle.

RESULTS: Normal compound muscle action potentials were observed when stimulating the peroneal nerve at the anterior ankle, below the fibular head, and above the fibular head during recording over the extensor digitorum brevis. Proximal stimulations above and below the fibular head showed higher amplitudes compared to the anterior ankle stimulation (Figure 2.B, 2.C). Stimulation posterior to the lateral malleolus revealed a small compound muscle action potential, demonstrating an accessory peroneal nerve (Figure 2.D). Additionally, stimulation of the tibial nerve posterior to the medial malleolus elicited a compound muscle action potential (Figure 2.E). Findings suggest a dual innervation supply from the tibial and peroneal motor nerves to the EDB.

CONCLUSION: Further research into the innervation of the EDB muscle is recommended to determine the prevalence of this anomalous pattern. Providers who perform EDX studies must be aware of these anomalous variations during the execution and interpretation of NCSs.

LUMBOSACRAL PLEXOPATHY AS A COMPLICATION OF RETROPERITONEAL HEMORRHAGE SECONDARY TO ENDOVASCULAR INTERVENTION

Wilmer Santiago Herrera Malpica (Bogotá, Colombia), Liliana Rodriguez (Bogotá, Colombia), Jorge Nicolás Muñoz (Bogotá, Colombia), Jorge Arturo Diaz Ruiz (Bogotá, Colombia)

INTRODUCTION/BACKGROUND: Lumbosacral plexus injuries are uncommon. A common structural cause is retroperitoneal hemorrhage with subsequent hematoma formation in the psoas-iliac muscle as a complication of anticoagulation, rupture of an aortic aneurysm, femoral vascular access, and aneurysms or pseudoaneurysms of the common iliac artery.

CASE REPORT: A 64-year-old man presented with a history of endovascular repair of abdominal aortic aneurysm and left common iliac artery in 2022. 2 years later, he presented with occlusion of the left common iliac artery, which was treated with thrombolysis. Following the procedure, he developed weakness of the hip flexors and adductors, neuropathic pain in the left lower limb associated with paresthesias in the anterior and medial aspect of the left thigh. MRI revealed a hematoma over the psoas-iliac muscle, compressing the extraforaminal segment of the left L3, L4, and L5 nerve roots. 3 weeks later, EDX studies showed absence of sensory response of the left superficial peroneal nerve and reduced recruitment in the left vastus medialis, iliopsoas, and abductor longus without signs of denervation, indicating a postganglionic injury of the left lumbosacral plexus consistent with neuropraxia. Finally, hematoma drainage led to symptom improvement.

SUMMARY/CONCLUSION: This case highlights a complication of common iliac artery thrombolysis resulting in a hematoma at the level of the psoas-iliac muscle causing lumbosacral plexus injury. EDX studies differentiate from radicular injury despite the extensive hematoma described on MRI. Prognosis of the injury is defined considering the absence of axonal compromise and clinical improvement.

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LARYNGEAL NEUROPATHY: A RETROSPECTIVE REVIEW OF 52 PATIENTS

Elizabeth Ho (Centennial, CO), Samuel Goorman (Detroit, MI), Iram Zaman (West Bloomfield, MI), Anza Memon (Detroit, MI), Lonni Schultz (Detroit, MI)

INTRODUCTION: Laryngeal neuropathy presents as an infrequently diagnosed cause of vocal dysfunction with symptoms including cough, voice changes, difficulty swallowing, and throat pain.

OBJECTIVE: The primary objective of this research study is to gain understanding of electrophysiological findings and value of repeat EMG/NCS for prognostication in patients with laryngeal neuropathies.

METHODS: This single center retrospective study aimed to summarize various clinical features of laryngeal neuropathy A total of 52 patients with laryngeal and vagal neuropathies diagnosed over a 22-year period, 2000 to 2022 were evaluated. Demographic, clinical and electrodiagnostic data were collected, and descriptive statistics were used to analyze the variables of interest.

RESULTS: Of the 52 patients evaluated, surgery related trauma (n=23; 44%) was the most common etiology, and speech difficulty (n=49; 94%) was the most common symptom. Based on diagnoses made through EMG, 25 patients (48%) had vagal neuropathy, 8 (15%) had recurrent vagal neuropathy, 13 (25%) had other laryngeal conditions. Treatments including surgical repair, speech therapy, medical therapy, and several others led to improvement or complete resolution in 23 (44%) patients. No significant difference in time to diagnosis was observed based on sex or race. Patients with post-surgical etiology had a significantly shorter time to diagnosis (p=.015).

SUMMARY/CONCLUSION: Laryngeal neuropathies are commonly associated with vocal cord dysfunction leading to significant speech impairment. Surgical trauma was the most common cause in our patient group. Electrodiagnostic findings, including EMG studies, aid in definitive diagnosis. The shorter time to diagnosis in patients who develop post-surgical manifestation may be due to in-patient status enabling faster evaluation.

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EFGARTIGIMOD TREATMENT IN IDIOPATHIC INFLAMMATORY MYOPATHY

Ying Hou (Jinan, China), Tingjun Dai (Jinan, China), Wei Li (Jinan, China), Yuying Zhao (Jinan, China)

INTRODUCTION/BACKGROUND: This study aimed to explore the treatment outcome of efgartigimod which is a kind of FcRn inhibitors in idiopathic inflammatory myopathy (IIM) patients with anti-Mi2 antibody.

CASE REPORT: In this case, a 66-year-old woman presented with muscle weakness accompanied by myalgia for 1.5 months. Muscle biopsy showed perifascicular necrosis and MHC-I expression with perifascicular enhancement. Anti-Mi2 antibody was detected by immunodot assay. Unfortunately, after 1 month of prednisone therapy (1mg/kg), her muscle weakness worsened though creatine kinase (CK) level decreased from 7492U/L to 1967 U/L. We added efgartigimod regimen besides prednisone treatment. Indeed, Efgartigimod was prescribed 10mg/kg/qw for 4 weeks. CK level decreased from 1967U/L to 159U/ L and HAQ score decreased from 2.25 to 1.65 after Efgartigimod usage. Moreover, MMT260 score increased from 175 to 226 and anti-Mi2 antibody became negative. No severe adverse events were observed.

SUMMARY/CONCLUSION: This case may suggest that efgartigimod is a promising option for IIM.

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DEMOGRAPHICS AND BASELINE DISEASE CHARACTERISTICS IN THE INEBILIZUMAB, A SELECTIVE CD19+ B CELL DEPLETER, GENERALIZED MYASTHENIA GRAVIS REGISTRATIONAL STUDY (MINT)

James F. Howard Jr. (Chapel Hill, NC), Michael Benatar (Miami, FL), Emma Ciafaloni (Rochester, NY), Maria Isabel Leite (Oxford, United Kingdom), Richard J. Nowak (New Haven, CT), Kimiaki Utsugisawa (Hanamaki, Japan), John Vissing (Copenhagen, Denmark), Yanping Wu (Gaithersburg, MD), Mikhail Rojavin (Upper Holland, PA), Nishi Rampal (Branford, CT)

INTRODUCTION/OBJECTIVE: Myasthenia Gravis Inebilizumab Trial (MINT) is a randomized, double-blind, placebo-controlled trial evaluating the safety and efficacy of inebilizumab in generalized myasthenia gravis (gMG) subjects with acetylcholine receptor (AChR+) or muscle-specific kinase receptor (MuSK+) antibodies (NCT04524273).

METHODS: The MINT study enrolled 238 gMG subjects (190 AChR+ and 48 MuSK+) across 103 sites in 18 countries. Baseline demographics and disease characteristics were collected.

RESULTS: Of the total study population, 61% were females. Geographic distribution was 41.6% patients from Asia, 38.2% from Europe, 14.7% from North America, and 5.5% from Latin America. Ages ranged from 18 to 82-years with median ages comparable between AChR+ and MuSK+ cohorts. The female subjects' share in these two cohorts were 57% and 75%, respectively. Racial distribution differed with Asian study participants constituting 62.5% of MuSK+ cohort vs. 37.4% in the AChR+ cohort.
At baseline, AChR+ and MuSK+ participants had similar gMG duration (mean: 6.7 and 5.2 years, respectively) and comparable baseline MGFA class distribution. MG-ADL and QMG baseline scores were also similar between the two cohorts. At baseline, the majority of study participants were on corticosteroids ranging from 5-40 mg/day (83% AChR+ and 73% MuSK+ subjects, respectively). Compared to AChR+, fewer MuSK+ subjects had a history of thymoma (8.3% vs. 14.8%) and thymectomy (14.6% vs. 28.6%). Additionally, MuSK+ subjects required less gMG rescue therapy prior to study entry (18.8% vs.32.8%).

SUMMARY/CONCLUSION:
AChR+ and MuSK+ cohorts in the MINT study demonstrated overall similar baseline demographics and disease entry characteristics supporting a pooled analysis in the largest registrational gMG study to date.

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James F. Howard Jr. - research funding (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, and UCB Pharma; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics (now Amgen Inc.), Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, UCB Pharma, and Zai Labs; non-financial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Pharma and Zai Labs.

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Michael Benatar - receives research support from Immunovant and Alexion. He has served as a consultant to Alexion, Cartesian, Horizon Therapeutics (now Amgen Inc.), Immunovant, Sanofi, Takeda and UCB.

Emma Ciafaloni - received personal compensation for serving on advisory boards and/or as a consultant for Alexion, Argenx, Biogen, Amicus, Pfizer, Italfarmaco, Sarepta, Janssen, NS Pharma, and Roche.

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Richard J. Nowak - reports research support from the National Institutes of Health, Genentech, Inc., Alexion Pharmaceuticals, Inc., argenx, Annexon Biosciences, Inc., Ra Pharmaceuticals, Inc. (now UCB S.A.), the Myasthenia Gravis Foundation of America, Inc., Momenta Pharmaceuticals, Inc. (now Janssen), Immunovant, Inc., Grifols, S.A., and Viela Bio, Inc. (Horizon Therapeutics, now part of Amgen Inc.). Served as a consultant and advisor for Alexion Pharmaceuticals, Inc., argenx, Cabaletta Bio, Inc., Cour Pharmaceuticals, Ra Pharmaceuticals, Inc. (now UCB S.A.), Immunovant, Inc., Momenta Pharmaceuticals, Inc. (now Janssen), and Viela Bio, Inc. (Horizon Therapeutics, now part of Amgen Inc.).

Kimiaki Utsugisawa - served as a paid consultant for UCB Pharma, Argenx, Janssen Pharma, Viela Bio, Chugai Pharma, Hanall BioPharma, Merck and Mitsubishi Tanabe Pharma, and has received speaker honoraria from Argenx, Alexion Pharmaceuticals, UCB Pharma and the Japan Blood Products Organization.

John Vissing - advisor on advisory boards for Regeneron, UCB Pharma, Argenx, Alexion Pharmaceuticals, Horizon Therapeutics (now Amgen Inc.), Dianthus Therapeutics, Janssen, Roche

Yanping Wu - is an employee and stockholder in Amgen Inc.

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DESIGN OF THE PLACEBO-CONTROLLED PHASE 3 STUDY OF INEBILIZUMAB, A SELECTIVE CD19+ B CELL DEPLETER, IN GENERALIZED MYASTHENIA GRAVIS: THE MINT STUDY

Nishi Rampal (Branford, CT), Michael Benatar (Miami, FL), Emma Ciafaloni (Rochester, NY), James F. Howard Jr. (Chapel Hill, NC), Maria Isabel Leite (Oxford, United Kingdom), Kimiaki Utsugisawa (Hanamaki, Japan), John Vissing (Copenhagen, Denmark), Mikhail Rojavin (Upper Holland, PA), Richard J. Nowak (New Haven, CT)

INTRODUCTION/OBJECTIVE: Myasthenia Gravis Inebilizumab Trial (MINT is a phase 3 study of inebilizumab in generalized myasthenia gravis (gMG) patients (NCT04524273).

METHODS: MINT is a randomized, double-blind, placebo-controlled Phase 3 study evaluating the efficacy and safety of inebilizumab in adults with gMG. The randomized controlled period (RCP) is 12 months for AChR+ subjects and 6 months for MuSK+ subjects, followed by a 3-year open-label period. The primary study objective assesses the efficacy of inebilizumab in gMG. The primary endpoint is change from baseline in Myasthenia Gravis Activities of Daily Living (MG-ADL) score at Week 26 in the overall study population. Secondary objectives include inebilizumab's impact on gMG exacerbations, MG-related quality of life, minimal symptom expression, the pharmacokineticprofile and immunogenicity, corticosteroid usage, and safety and tolerability.
Key eligibility criteria include AChR+ or MuSK+ antibody status, MGFA class II-IV, MG-ADL score 6-10 with >50% attributed to non-ocular items or MG-ADL score ≥11, Quantitative Myasthenia Gravis score ≥11, current corticosteroids (≤40 mg/day), alone or in combination with azathioprine, mycophenolate mofetil, or mycophenolic acid. Of note, corticosteroids are tapered per protocol to 5 mg/day.

RESULTS: 190 AChR+ and 48 MuSK+ patients were randomized 1:1 into active or placebo treatment. Enrollment is complete.

SUMMARY/CONCLUSION: The MINT trial has successfully enrolled the largest gMG population, with the largest MuSK+ cohort, in any registrational study to date. Additionally, AChR+ patients will provide controlled data for 12 months, aiming to demonstrate durability of treatment effect. The protocol-specified corticosteroid taper uniquely addresses chronic corticosteroid burden and should be considered when assessing future study results.

Disclosures:

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Michael Benatar - receives research support from Immunovant and Alexion. He has served as a consultant to Alexion, Cartesian, Horizon Therapeutics (now Amgen Inc.), Immunovant, Sanofi, Takeda and UCB.

Emma Ciafaloni - received personal compensation for serving on advisory boards and/or as a consultant for Alexion, Argenx, Biogen, Amicus, Pfizer, Italfarmaco, Sarepta, Janssen, NS Pharma, and Roche.

James F. Howard Jr. - research funding (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, and UCB Pharma; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics (now Amgen Inc.), Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, UCB Pharma, and Zai Labs; non-financial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Pharma and Zai Labs.

Maria Isabel Leite - funded by the NHS (Myasthenia and Related Disorders Service and National Specialised Commissioning Group for Neuromyelitis Optica, UK) and by the University of Oxford, UK. She has been awarded research grants from the UK association for patients with myasthenia (Myaware), Muscular Dystrophy UK and the University of Oxford. She has received speaker honoraria or travel grants from Biogen, Novartis, UCB Pharma, and the Guthy-Jackson Charitable Foundation. She serves on scientific or educational advisory boards for UCB Pharma, argenx, and Horizon Therapeutics (now Amgen Inc.).

Kimiaki Utsugisawa - served as a paid consultant for UCB Pharma, Argenx, Janssen Pharma, Viela Bio, Chugai Pharma, Hanall BioPharma, Merck and Mitsubishi Tanabe Pharma, and has received speaker honoraria from Argenx, Alexion Pharmaceuticals, UCB Pharma and the Japan Blood Products Organization.

John Vissing - advisor on advisory boards for Regeneron, UCB Pharma, Argenx, Alexion Pharmaceuticals, Horizon Therapeutics (now Amgen Inc.), Dianthus Therapeutics, Janssen, Roche

Mikhail Rojavin - is an employee and stockholder in Amgen Inc.

Richard J. Nowak - reports research support from the National Institutes of Health, Genentech, Inc., Alexion Pharmaceuticals, Inc., argenx, Annexon Biosciences, Inc., Ra Pharmaceuticals, Inc. (now UCB S.A.), the Myasthenia Gravis Foundation of America, Inc., Momenta Pharmaceuticals, Inc. (now Janssen), Immunovant, Inc., Grifols, S.A., and Viela Bio, Inc. (Horizon Therapeutics, now part of Amgen Inc.). Served as a consultant and advisor for Alexion Pharmaceuticals, Inc., argenx, Cabaletta Bio, Inc., Cour Pharmaceuticals, Ra Pharmaceuticals, Inc. (now UCB S.A.), Immunovant, Inc., Momenta Pharmaceuticals, Inc. (now Janssen), and Viela Bio, Inc. (Horizon Therapeutics, now part of Amgen Inc.).

EFFICACY OF ZILUCOPLAN IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS WITHOUT PRIOR IMMUNOGLOBULIN OR PLASMA EXCHANGE TREATMENT IN THE RAISE STUDY

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INTRODUCTION: RAISE (NCT04115293) was a randomized, double-blind, placebo-controlled, Phase 3 study of zilucoplan, a macrocyclic peptide complements component 5 inhibitor with a dual mechanism of action, in patients with acetylcholine receptor autoantibody-positive (AChR+) generalized myasthenia gravis (gMG). RAISE showed clinically meaningful improvements in myasthenia gravis (MG)-specific outcomes in patients with gMG.

OBJECTIVE: To assess the efficacy of zilucoplan in patients with no previous treatment with immunoglobulin (Ig; either intravenous or subcutaneous [SC]) or plasma exchange (PLEX) treatment, both of which are typically used for severe exacerbations.

METHODS: Adults with AChR+ gMG were randomized 1:1 to daily, self-administered SC zilucoplan 0.3 mg/kg or placebo injections for 12 weeks. The primary efficacy endpoint was change from baseline (CFB) to week 12 in Myasthenia Gravis Activities of Daily Living (MG-ADL) score. A secondary endpoint was CFB to week 12 in quantitative MG (QMG) score. We conducted a prespecified, descriptive efficacy analysis of a patient subgroup without prior Ig or PLEX treatment.

RESULTS: Fifty patients without prior Ig or PLEX were randomized to zilucoplan (n=27) or placebo (n=23). Mean CFB in MG-ADL score was −4.22 (standard deviation [SD] 3.68) with zilucoplan 0.3 mg/kg compared to −2.61 (2.41) with placebo. Mean (SD) CFB in QMG score was −6.48 (4.56) with zilucoplan 0.3 mg/kg compared to −3.04 (4.52) with placebo.

SUMMARY/CONCLUSION: In line with the overall study population, patients with gMG without prior Ig or PLEX treatment also showed relevant improvements in MG-specific outcomes. This supports the earlier use of zilucoplan.

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Kimiaki Utsugisawa - has served as a paid Consultant for UCB Pharma, argenx, Janssen Pharmaceuticals, Viela Bio (now Horizon Therapeutics), Chugai Pharmaceutical, HanAll Biopharma, Merck and Mitsubishi Tanabe Pharma; he has received speaker honoraria from argenx, Alexion Pharmaceuticals, UCB Pharma, and the Japan Blood Products Organization.

LONG-TERM SAFETY AND EFFICACY OF ZILUCOPLAN IN GENERALIZED MYASTHENIA GRAVIS: 120-WEEK INTERIM ANALYSIS OF RAISE-XT

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INTRODUCTION: RAISE-XT (NCT04225871), an ongoing, Phase 3, open-label extension study, will further enhance understanding of the safety and efficacy of zilucoplan, a macrocyclic peptide complement component 5 inhibitor, in patients with acetylcholine receptor autoantibody-positive generalized myasthenia gravis (gMG).

OBJECTIVE: Evaluate the long-term safety, and efficacy up to 120 weeks, of zilucoplan treatment in patients with gMG in an interim analysis of RAISE-XT.

METHODS: RAISE-XT enrolled adults with gMG who completed a qualifying double-blind study (NCT03315130/NCT04115293). Patients self-administered daily subcutaneous injections of zilucoplan 0.3mg/kg. Primary outcome was incidence of treatment-emergent adverse events (TEAEs). Change from double-blind baseline to week 120 in Myasthenia Gravis Activities of Daily Living (MG-ADL) score was analyzed for pooled data from participants who received zilucoplan 0.3mg/kg or placebo in the qualifying studies.

RESULTS: Overall, 200 patients enrolled in RAISE-XT. At data cutoff (November 11, 2023), median (range) exposure to zilucoplan was 2.2 (0.11–5.6) years. TEAEs occurred in 194 (97.0%) patients; 81 (40.5%) experienced a serious TEAE. The most common TEAEs were COVID-19 and myasthenia gravis worsening, occurring in 71 (35.5%) and 59 (29.5%) patients, respectively. Of 183 patients who received zilucoplan 0.3mg/kg or placebo in the qualifying study, 93 continued zilucoplan 0.3mg/kg and 90 switched from placebo to zilucoplan 0.3mg/kg. At week 120, mean reduction from double-blind baseline in MG-ADL score in pooled zilucoplan 0.3mg/kg patients was 7.14 (standard error 0.44).

SUMMARY/CONCLUSION: In this RAISE-XT interim analysis, zilucoplan demonstrated a favorable long-term safety profile with sustained efficacy up to 120 weeks of treatment.

Disclosures:

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PERIPHERAL CD4+ T PROFILE IN REFRACTORY MYASTHENIA GRAVIS

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INTRODUCTION: Treatment-refractory myasthenia gravis (MG) represents a subgroup of generalized MG (GMG) characterized by a poor response to standard immunotherapies, leading to continued disabling symptoms. Peripheral immune signatures were rarely explored in refractory MG.

OBJECTIVE: To measure CD4+ T lymphocyte and serum cytokine profiles in refractory GMG.

METHODS: This study assessed CD4+ T cells and subtypes including naïve, central memory, effector memory, CD45RA-positive effector memory T cells (TEMRA), Th1, Th2, Th9, Th17, Th17/1, follicular T cells in refractory and non-refractory GMG patients using flow cytometry. Activation markers (CD38, HLA-DR) and cytokines (IL-1β, IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-12p70, IL-13, IL-17A, IL-18, IL-21, IL-22, IL-23, IL-27, IFN-γ, TNF-α, GM-CSF) were measured, correlating their levels with MG clinical scores. (MGFA-QMG, MG-MMT, MG-ADL, MG-QOL-15).

RESULTS: The study enrolled 67 refractory and 67 non-refractory GMG patients. Refractory GMG patients had significant higher proportions of CD4+T cells in lymphocytes (36.91%±13.19% vs 31.74%±11.54%, p=0.0029) with higher levels of CD38(26.38%±17.29% vs 17.34%±11.74%, p=0.00035) and HLA-DR (15%±11.6% vs 10.86%±5.69%, p=0.048). Notably, TEMRA (5.75%±5.75% vs 2.91%±2.20%, p=0.0038) and Th1 cell (12.70%±4.62% vs 10.57%±2.68%, p=0.014) populations were upregulated in the refractory group, accompanied by heightened serum cytokine levels. TEMRA cells correlated closely with clinical scores.

SUMMARY/CONCLUSION: Refractory GMG is marked by elevated activation of CD4+ T cells and features a significant upregulation of Th1 and TEMRA subsets, accompanied by an increase in serum cytokine concentrations. These findings highlight the distinctive immune profile in refractory GMG and the critical role of both specific T cell subsets and broad cytokine responses in the pathophysiology of refractory GMG.

IMPACT OF NEUROPATHIC PAIN ON LIFE SATISFACTION AND MENTAL HEALTH AMONG SPINAL CORD INJURY PATIENTS IN EGYPT

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INTRODUCTION: Neuropathic pain (NP) is one of the most frequent complications of spinal cord injury (SCI). In addition to undermining rehabilitation outcomes, pain affects satisfaction with life (SWL). Addressing pain in this population is important since SCI patients report lower SWL than the general population.

OBJECTIVE: To assess the characteristics of NP among Egyptian SCI patients and determine its effects on patients' mental health and SWL.

METHODS: This study included 105 SCI patients, recruited from the Al-Hassan Foundation in Egypt. In addition to sociodemographic characteristics, we asked participants to complete the SWL scale, the Neuropathic Pain Questionnaire - Short Form, and the Hospital Anxiety and Depression Scale. We used Spearman's rank correlation to test associations between NP, depression, anxiety, and SWL. Finally, a binary logistic regression model was performed to identify predictors of low SWL.

RESULTS: The prevalence of NP among the study participants was 73.3%. The highest mean score was that of tingling intensity, followed by numbness intensity, and then increase in pain due to touch (59.2±30.0, 50.3±33.4, and 38.4±37.3, respectively). A higher percentage of participants (81.7%) with low SWL suffered from NP compared to those with average/high SWL (62.2%). Moreover, NP correlated negatively with satisfaction with life, and positively with anxiety and depression. Predictors of SWL included NP (p=0.04, Odd's Ratio (OR)=2.73), Age (p=0.01, OR=1.11) and depression (p=0.03, OR=1.19).

SUMMARY/CONCLUSION: The majority of patients with SCI suffer from NP, which negatively affects patients' mental health and predicts low SWL. Addressing NP should be a central component of treatment strategies for SCI patients.

FACTORS INFLUENCING EXACERBATIONS AND CRISES IN GENERALIZED MYASTHENIA GRAVIS: FINDINGS FROM A CLAIMS DATABASE STUDY

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INTRODUCTION: Generalized myasthenia gravis (gMG) is a rare, chronic autoantibody disease characterized by muscle weakness and fatigue; worsening symptoms can manifest as exacerbations and/or life-threatening crisis.

OBJECTIVE: Explore the relationship between select patient characteristics and exacerbations/crises among gMG patients.

METHODS: Newly diagnosed (incident) and prevalent gMG patients were identified within Optum's de-identified Clinformatics® Data Mart Database (01/2017-3/2023) for this retrospective cohort study. Associations between baseline characteristics and exacerbations/crises were assessed using case-control methods nested in the gMG cohort: patients who developed event(s) during follow up were classified as cases, and patients without events were controls, with relevant patient characteristics collected over the 12 months preceding the event (cases), or the 12 months preceding the follow-up end date (controls).

RESULTS: We identified 12,813 prevalent and 3,748 incident gMG patients. Rates of exacerbations and crises were 19.2 and 3.5 per 100 patient-years for prevalent patients and 33.9 and 7.5 per 100 patient-years for incident patients, respectively. Among prevalent gMG patients, prior exacerbation was significantly associated with future exacerbation (odds ratio [OR] 7.05, 95% confidence interval [CI]: 4.24-11.71); prior crisis was significantly associated with future crises (OR 3.29, 95% CI: 2.05-5.28). Among incident patients, late-onset MG (onset after age 50) was significantly associated with exacerbation events (OR 2.89, 95% CI: 1.40-5.95).

SUMMARY/CONCLUSION: Exacerbations/crises occur at a notable rate among patients with gMG, particularly patients with late-onset myasthenia gravis (MG), and prior history of an exacerbation/crisis is a strong predictor of future occurrences. These findings suggest that an outstanding need remains for gMG treatments that provide stable disease control and avoidance of exacerbations/crises.

Disclosures:

Louis Jackson - is an employee of Janssen Scientific Affairs, LLC.

Zhiwen Liu - is an employee of Janssen Scientific Affairs, LLC.

Jacqueline Pesa - is an employee of Janssen Global Services, LLC.

Alicia Campbell - is an employee of Janssen Scientific Affairs, LLC.

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DELAYED DIAGNOSIS OF HEREDITARY NEURALGIC AMYOTROPHY DUE TO NOVEL SEPT9 VARIANT C988G>A

Min Kang (San Francisco, CA)

BACKGROUND: Hereditary neuralgic amyotrophy (HNA) is an autosomal dominant disease characterized by recurring neuropathic pain followed by paresis, with sensory deficit occurring rarely. It primarily affects the brachial plexus but can involve other areas. This rare disorder is associated with SETP9 on chromosome 17q25.3.

CASE REPORT: A 52-year-old man presented with slowly progressive, fluctuating pain predominantly affecting his upper extremities over the past decade. Following a car accident, he developed paresthesia in his right arm, followed by hand weakness and numbness. Recurring symptoms over subsequent years led to a clinical diagnosis of bilateral thoracic outlet syndrome and bilateral meralgia paresthetica. MR neurography revealed abnormality in the bilateral brachial plexi and the right proximal median nerve. No obvious evidence of compressibility was observed on ultrasound (US) study. In the lower limbs, neuromuscular US revealed impingement of the bilateral anterior and lateral cutaneous femoral nerves at the inguinal ligaments, and prominent echogenicity of the right sural nerve at the distal ankle and hindfoot. Subsequent genetic evaluation disclosed a SETT9 variant, which is likely pathological.

SUMMARY/CONCLUSION: This case illustrates a progressive, recurrent, and painful multifocal compressive plexopathy and neuropathy, affecting both compressive and non-compressive sites, initially attributed to a common compressive plexoneuropathy. The SEPT9 variant is likely pathological, given the classical fluctuating course observed. The function of Septin-9, encoded by SEPT9, in HNA remains unclear; however, the relapsing and remitting course suggests an inflammatory etiology. Furthermore, this case suggests an additional mechanism of susceptibility to compression, particularly evident due to the predominant changes in proximity to compressive sites.

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DISEASE SEVERITY AND HEALTHCARE RESOURCE UTILIZATION FOR CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY AND MULTIFOCAL MOTOR NEUROPATHY: RESULTS FROM AN INTEGRATED DATABASE

Deborah Kuk (Arlington, VA), Ade Ajibade (Lexington, MA), Chafic Karam (Philadelphia, PA), Michelle Kirby (Lexington, MA), Megan Gower (Lexington, MA), Chris Blair (Lexington, MA), Faisal Riaz (Lexington, MA), Josh Feldman (Arlington, VA), Brian Chen (Arlington, VA), Jeffrey Allen (Minneapolis, MN)

INTRODUCTION: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and multifocal motor neuropathy (MMN) are rare neurological diseases characterized by muscle weakness and/or sensory loss.

OBJECTIVE: To analyze healthcare resource utilization (HCRU) and all-cause paid amount by disease severity for patients with CIDP or MMN, using patient-reported outcome measures.

METHODS: A mixed-method study enrolled United States adults diagnosed with CIDP or MMN. Inflammatory Neuropathy Cause and Treatment (INCAT) scores were collected via a survey of patients with open medical/pharmacy claims and ICD-10 codes of G61.81 or G61.82. Included patients had claims data available ≥1 year before and after the index diagnosis date.

RESULTS: Overall, 56 patients with CIDP and 13 patients with MMN were included; median follow-up times from index diagnosis were 43 months (CIDP) and 54 months (MMN). Per INCATv1 score, 58% of patients with CIDP and 62% of patients with MMN had moderate/severe impairment. All-cause paid amount 1 year after CIDP diagnosis was available for 46 CIDP patients, of which 14 had intravenous immunoglobulin (IVIg) paid amount available. IVIg paid amount accounted for 96% of the all-cause paid amount. One year after CIDP diagnosis, patients with severe impairment had more hospitalizations (4.5 vs 1.5) and higher median IVIg paid amount than those with mild impairment ($125,538 vs $80,248). IVIg paid amount 1 year after MMN diagnosis was available for only one patient ($64,982).

SUMMARY/CONCLUSION: More severe impairment among patients with CIDP is associated with higher HCRU and costs. MMN results were inconclusive due to limited sample size. Takeda Pharmaceuticals USA, Inc. funded the study and writing support.

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EMPASIPRUBART (ARGX-117) IN MULTIFOCAL MOTOR NEUROPATHY: INITIAL SAFETY AND EFFICACY DATA OF THE PHASE 2 ARDA STUDY

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INTRODUCTION: Multifocal motor neuropathy (MMN) is a rare, peripheral, immune-mediated, chronic neuropathy resulting from motor nerve conduction block and complement activation, leading to axonal degeneration and progressive, disabling asymmetric limb weakness with absence of sensory loss. Currently, intravenous immunoglobulin (IVIg) is the only proven efficacious therapy. Empasiprubart is a first-in-class monoclonal antibody that binds C2 thereby blocking activation of classical, and lectin complement pathways.

OBJECTIVE: To assess the safety, efficacy, and tolerability of empasiprubart in adults with MMN in ARDA (NCT05225675), a Phase 2, multicenter, randomized, placebo-controlled, double-blinded, parallel-group study.

METHODS: ARDA enrolled 52 participants with probable or definite MMN (2010 European Federation of Neurological Societies/Peripheral Nerve Society guidelines) and proven IVIg dependency as confirmed by committee. All were on a stable IVIg regimen leading to randomization. Enrolled participants were assigned to one of two dosing cohorts; each randomized 2:1 to empasiprubart or placebo. Key efficacy endpoints include IVIg retreatment, change in muscle strength, and disability scores.

RESULTS: Cohort 1 randomized 27 participants. During the double-blind treatment period, empasiprubart demonstrated a 91% reduction (Hazard ratio: 0.09 [95% confidence interval, 0.02–0.44]) in the risk for IVIg retreatment compared with placebo. Since starting therapy, 94% of empasiprubart-treated participants reported their condition as improved, with 55% being much/very much improved (Patient Global Impression of Change scale) and 89% of placebo-treated participants reporting no change/worsened condition. Empasiprubart was well tolerated overall; most adverse events were mild or moderate.

SUMMARY/CONCLUSION: Early efficacy and safety signals in cohort 1 from the ongoing ARDA study support proof of concept of empasiprubart in MMN.

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A CASE OF SOD1 AMYOTROPHIC LATERAL SCLEROSIS TREATED WITH TOFERSEN: SLOWED PROGRESSION AND RENEWED HOPE

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INTRODUCTION: Mutations in the gene encoding superoxide dismutase 1 (SOD1) have been associated with about 2% of sporadic cases of ALS and 20% of familial cases. Tofersen is an antisense oligonucleotide which reduces toxic SOD1 protein synthesis and prevents neuronal degeneration caused by gain of function of the mutant protein. In the phase 3 trial of tofersen for SOD1 ALS, although it resulted in reductions of SOD1 protein and neurofilament light chains in plasma, it was not associated with a significant improvement in the primary clinical endpoint quantified by the ALSFRS-R score.

OBJECTIVE: In this case report, we describe a 71-year-old male with a history of familial ALS, who presented to the neuromuscular clinic for 1 year of progressive right leg weakness and received tofersen for SOD1 ALS.

CASE REPORT: Exam findings of right lower extremity weakness and atrophy with cramping and fasciculations were indicative of lower motor neuron disease, while diffuse hyperreflexia and the release of primitive reflexes were indicative of upper motor neuron findings. Genetic testing for ALS revealed the missense SOD1 variant c.256G>C (p. Gly86Arg). We report a positive response to intrathecal tofersen, with stability of the ALSFRS-R score, at 41/48, as well as a sustained decrease in cerebrospinal fluid levels of neurofilament light chain.

SUMMARY/CONCLUSION: One consideration for our patient's response is the early initiation of tofersen (ALSFRS-R 40/48 at time of initiation). Though further study is needed, our case suggests that early genetic evaluation for ALS patients and early enrollment for treatment with tofersen may be clinically beneficial.

A RARE PRESENTATION OF MYASTHENIA GRAVIS WITH NEUROMYELITIS OPTICA

Esha Kataria (Greer, SC), Eduardo Cortez-Garcia (Taylors, SC)

INTRODUCTION/BACKGROUND: Myasthenia gravis (MG) is an autoimmune disease caused by impaired neuromuscular transmission at the postsynaptic membrane of the neuromuscular junction. Studies have shown that about 65.4% of patients with MG have another disease and 15.0% of patients have associated another autoimmune disease. Most commonly associated is thyroid disease, with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and other autoimmune diseases being rare.

CASE REPORT: We present a case of 70-year-old male whose initial symptoms were difficulty focusing, proximal muscle weakness and blurred vision. He was diagnosed with Ach receptor positive MG. On primary encounter, he presented to establish care and management of the disease. MRI Brain and orbits obtained during initial presentation did not show any intracranial findings suggestive of demyelinating disease. He then continued mestinon and prednisone with a plan to transition to steroid a sparing agent. Two weeks after clinic visit, he was diagnosed with pneumonia and admitted for possible MG exacerbation. He was evaluated by neurology at that time, and it was felt that he was not having an MG exacerbation. He notes that shortly after this he began having blurred vision in his left eye. Due to persistent blurred vision, he was further evaluated by ophthalmologist and subsequent testing showed blurred disc and edema on the left eye concerning for viral induced optic neuritis. Further studies showed positive serum neuromyelitis iptica (NMO) AQP4 Auto Ab confirming diagnosis of neuromyelitis optica.

SUMMARY/CONCLUSION: Myasthenia gravis has increased incidence of presenting with other autoimmune diseases and this case illustrates NMO with MG; A rare presentation.

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DNTH103 SHOWS SUSTAINABLE INHIBITION OF COMPLEMENT AND PREVENTS NERVE CONDUCTION VELOCITY IMPAIRMENT IN A PRECLINICAL MODEL OF CIDP

Hans Katzberg (Toronto, CA), Caitlin Briggs (Raleigh, NC), Rokhand Arvin (New York, NY), Jeffrey Stavenhagen (New York, NY), Sankalp Gokhale (New York, NY)

INTRODUCTION: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an autoimmune disease with complement pathway involvement. DNTH103 is a fully human, potent, monoclonal antibody with a long half-life that selectively blocks the classical complement pathway. DNTH103 is in phase 2 for gMG (2024 phase 2 planned for multifocal motor neuropathy and chronic inflammatory demyelinating polyneuropathy).

OBJECTIVE: Three studies aimed to demonstrate the selectivity, potency, and efficacy of DNTH103 in a CIDP model and sustained pharmacokinetic/pharmacodynamic activity in nonhuman primates (NHPs).

METHODS: 1: Real-time binding of DNTH103 to C1s and proC1s by surface plasmon resonance (Biacore). 2: Characterization of DNTH103 pharmacokinetic/pharmacodynamic by ligand-binding assay and CH50 hemolysis (HaemoScan) in NHPs. 3: DNTH103 functional activity characterized with Human-on-a-Chip Motoneuron Axon Model using healthy iPSC-derived motoneurons, Schwann cells, and sera from three healthy and three CIDP patients (2 anti-NF155+). Conduction velocity was assessed with and without DNTH103.

RESULTS: DNTH103 bound selectively to active C1s with high affinity (KD: 7.1pM) with minimal binding to proC1s (KD: ~500nM). After single subcutaneous administration of 20mg/kg DNTH103 in NHPs, drug levels reached a Cmax of 191µg/mL between 60–72hrs; the circulating level of drug resulted in a sustainable >90% reduction in CH50 levels for the duration of the study. DNTH103 prevented nerve conduction velocity slowing in antibody-positive CIDP patient sera.

CONCLUSION: DNTH103 selectively binds to active C1s and effectively blocks complement-mediated inhibition of conduction detected in sera from CIDP patients. DNTH103 is an attractive development candidate for CIDP due to potent activity, selectivity for active C1s, and extended circulating half-life.

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Caitlin Briggs - employee of Dianthus Therapeutics.

Rokhand Arvin - employee of Dianthus Therapeutics.

Jeffrey Stavenhagen - is an employee of Dianthus Therapeutics.

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RARE CASE OF POSTERIOR INTEROSSEOUS NEUROPATHY SECONDARY TO SCHWANNOMA

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INTRODUCTION/BACKGROUND: In the realm of upper extremity neuropathies, posterior interosseous neuropathy stands as a rare entity marked by weakness and discomfort within the posterior extensor compartment of the forearm. While schwannomas are commonly encountered in the peripheral nervous system, their impact on the posterior interosseous nerve remains infrequent. Here, we present an unusual case of posterior interosseous neuropathy stemming from a schwannoma.

CASE REPORT: A 51-year-old male, with a history of remote traumatic brain injury, presented with a 13-year history of gradually progressive weakness in the left upper extremity. Examination revealed weakness in wrist, finger, and thumb extension, along with thumb abduction. Sensory deficits or weakness affecting the forearm flexor muscles, proximal muscles above the elbow, or signs of myelopathy were absent. Diagnostic imaging, including MRI of the elbow and forearm, disclosed a well-defined 6 mm mass consistent with a peripheral nerve sheath tumor compressing the posterior interosseous nerve. Additionally, significant fatty atrophy of specific muscles, indicative of posterior interosseous denervation changes was observed involving the extensor carpi ulnaris, extensor digitorum, extensor digiti minimi, abductor pollicis longus and extensor pollicis longus. EMG confirmed severe isolated posterior interosseous neuropathy. The patient was subsequently referred for neurosurgical assessment and is currently awaiting schwannoma resection along with targeted physical therapy.

SUMMARY/CONCLUSION: This case underscores the importance of considering schwannoma in the differential diagnosis of patients presenting with posterior interosseous neuropathy, despite its rarity in this anatomical location. Timely recognition and appropriate management are imperative for optimizing outcomes in such cases.

REDUNDANT NERVE ROOTS ON MAGNETIC RESONANCE IMAGING CAN PREDICT ONGOING DENERVATION IN PATIENTS WITH LUMBAR SPINAL STENOSIS

Seoyeong Park (Seoul, Korea, South), Keewon Kim (Seoul, Korea, South)

INTRODUCTION: Redundant nerve roots (RNRs) are abnormally elongated and tortuous nerve roots that develop secondary to degenerative spinal stenosis. RNRs have been associated with worse clinical outcomes after decompression surgery; however, studies on their clinical characteristics are limited.

OBJECTIVE: This study aimed to investigate the association between RNRs and denervation potentials, specifically abnormal spontaneous activity (ASA), on electromyography.

METHODS: We retrospectively reviewed data of patients who underwent an electrodiagnostic study of the lower extremities between January 2020 and March 2023. Among them, patients with lumbar spinal stenosis on magnetic resonance imaging were included. We analyzed patients' clinical and imaging data, including presence of ASA, and compared them according to the presence of RNRs. Multivariable logistic regression analysis was employed to identify factors associated with development of ASA.

RESULTS: Among 2,003 patients screened, 193 were included in the study. RNRs were associated with advanced age ($p<0.001$), longer symptom duration ($p=0.009$), smaller cross-sectional area ($p<0.001$), and higher frequency of ASA ($p<0.001$). Higher probability of ASA was correlated with greater RNR severity ($p<0.001$). In the multivariable logistic regression analysis, ASA occurrence was associated with smaller cross-sectional area, multiple stenotic sites, and severe-grade RNRs.

SUMMARY/CONCLUSION: Presence of RNRs, particularly severe-grade RNRs, was identified as a significant risk factor for development of ASA on electromyography. This finding may aid physicians to predict the prognosis of patients with spinal stenosis.

SYMTOMATIC MANIFESTATION OF SPINAL AND BULBAR MUSCULAR ATROPHY (SBMA) IN HETEROZYGOUS FEMALE: A CASE REPORT

Seoyeong Park (Seoul, Korea, South), Keewon Kim (Seoul, Korea, South)

INTRODUCTION: X-linked recessive spinal and bulbar muscular atrophy (SBMA) is a low motor neuron disease characterized by slowly progressive limb weakness and bulbar symptoms. As the causative gene is localized on X-chromosome, a SBMA female carrier is usually asymptomatic or shows only mild clinical manifestations. However, in this case report, we describe a case of a female carrier of SBMA who presented obvious bulbar symptoms.

CASE REPORT: A 60-year-old Asian woman visited the clinic complaining of dysarthria and dysphagia without limb weakness. On examination, tongue atrophy and fasciculation were observed. At the initial clinical diagnosis, progressive bulbar palsy or bulbar-onset ALS were considered. Her older brother and sisters showed similar symptoms, with her brother displaying the most severe symptoms. Familial ALS gene panel was tested, and no relevant mutation was reported. The EDX study showed a marginal decrease in sensory nerve action potential (SNAP) amplitudes in bilateral median, ulnar nerve, superficial peroneal nerves. Active denervation potentials and reinnervation potentials were observed mainly in bulbar muscles, and partially in cervical myotomes. Given her family history and the electrodiagnostic findings, there was a possibility of slow-progressing familial ALS, SBMA, or some other hereditary motor neuron disease. We decided to conduct a genetic test for SBMA, which revealed an abnormal expansion of CAG repeats in one allele (27/45).

CONCLUSION: This case presented a symptomatic SBMA heterozygous female, which could have been easily misdiagnosed. It highlights the importance of detailed investigation into family history and shows that even marginal decreases in SNAP amplitudes can provide valuable clues.

CHARACTERISTICS OF INFLAMMATORY MYOPATHY PATIENTS IN A REGIONAL MYOSITIS CENTRE: DATABASE DEVELOPMENT AND EXPLORATORY ANALYSIS

Priscilla Moon Young Kim (Toronto, CA), Charles Kassardjian (Toronto, CA), Ophir Vinik (Toronto, CA)

INTRODUCTION: Myopathies represent a significant burden of disease affecting adolescents to the elderly, causing impairment to mobility, swallowing, and breathing, often with multi-systemic involvement. As myopathies are rare, the overall management needs and patient outcomes are not well-established.

OBJECTIVE: To characterize the demographic and clinical characteristics of patients with inflammatory myopathy (IIM) at a tertiary centre, St. Michael's Hospital (SMH), in Toronto, Canada.

METHODS: The database is currently being developed through an exploratory retrospective chart review of an estimated 300 patients with a diagnosis of myopathy seen at SMH from 2010 to 2023. Medical history, investigations, and treatments were among the standardized metrics collected and populated into a REDCap database. Retrospective review of the database and descriptive statistics were used to conduct an initial analysis of the first 50 IIM patients out of the expected 300.

RESULTS: Diagnoses captured include dermatomyositis (28.0%), inclusion body myositis (16.0%), anti-synthetase syndrome (10.0%), necrotizing autoimmune myopathy (8.0%), and overlap syndromes (8.0%). Average age of diagnosis was 40 years. A history of malignancy was present in 6.0% of patients. In this initial random sample, 42.0% of patients had an identified myositis antibody, and anti-Jo-1 and anti-HMGCR were the most common. The most common steroid-sparing agent in this sample was methotrexate. Twenty-six percent of patients received combination therapy with intravenous immunoglobulin (IVIg). Further results regarding investigations and treatment will be presented at the time of the conference.

SUMMARY/CONCLUSION: Characterization of these rare diseases through this myopathy database will help better understand the disease and its variability and identify gaps in care and areas for further research.

FOCAL MYOSITIS OF THE DISTAL LOWER EXTREMITIES WITH SUBSEQUENT PERONEAL NEUROPATHIES IN A PATIENT WITH COVID-19 INFECTION

Travis Kooima (Madison, WI), Nassima Baba-Ahmed Fertikh (Madison, WI)

INTRODUCTION/BACKGROUND: COVID-19 is associated with muscle disorders, possibly related to direct viral invasion, or virally triggered autoimmunity. We present an unusual case of COVID-19 focal myositis in a patient who subsequently developed bilateral common peroneal neuropathy.

CASE REPORT: A 52-year-old male presented with leg aching and malaise. On admission, he tested positive for COVID-19. His leg pain worsened, and he developed tight swelling in both distal lower extremities. Lab work showed rhabdomyolysis and kidney injury. His creatine kinase peaked at 61,475 units/Liter. Several days later, he developed persistent inability to dorsiflex at the ankle. Work up for systemic autoimmune conditions was unrevealing. He was treated with intravenous fluids. Leg swelling and pain slowly resolved, but at discharge he continued to exhibit foot drop. MRI of the lower legs revealed edema and heterogenous T2 signal changes in the anterior and lateral compartment of both lower legs. One year later, his exam showed 1-2/5 strength in bilateral dorsiflexion, 3/5 strength in bilateral foot eversion, and diminished sensation to crude touch and pinprick in the lateral legs and dorsum of the feet. He could not stand on his heels and had bilateral steppage gait. EMG/NCS revealed severe bilateral peroneal neuropathy.

SUMMARY/CONCLUSION: Muscular manifestations of COVID-19 include rhabdomyolysis, myalgia, and dermatomyositis. More rarely, cases of focal myositis (including myofascial compartment syndromes) have been described. We hypothesize that the acute swelling in our patient's legs caused secondary compressive peroneal nerve damage. In patients with focal myositis, COVID-19 viral myositis should be considered.

ROLE OF PRAZOSIN IN PATIENTS WITH GUILLAIN BARRE SYNDROME WITH DYSAUTONOMIA WITH SYMPATHETIC OVER-ACTIVITY: A PROSPECTIVE COHORT STUDY

Mritunjai Kumar (Rishikesh, India)

OBJECTIVE: In Guillain barré syndrome (GBS) patients with dysautonomia, the sympatho-vagal balance is shifted towards sympathetic overactivity (SO). This study assessed the role of prazosin (α1-blocker) in the management of dysautonomia associated with SO.

METHODS: This prospective cohort study was conducted during January 2022 and September 2023 (study period). Thirty-two GBS patients with dysautonomia received prazosin (2.5–10 mg 3 times a day) (prazosin arm). For comparison, we also included 33 age and disability matched GBS patients with dysautonomia (control group), who did not receive prazosin, from a prospectively maintained GBS registry, admitted during February 2018 through December 2021. The primary endpoint was days to resolution of SO. Secondary endpoints were daily fluctuations in the systolic (SBP) and diastolic blood pressure (DBP), duration of hospital stay, in-hospital mortality and 3 months disability.

RESULTS: The median age was 36 (IQR 25–49) years and 43 (66.2%) were males. The demographic and clinical parameters were comparable. Prazosin resulted in significantly earlier normalization of SO compared to the control (median 15vs20 days; p=0.01). The mean fluctuations in the SBP (30 vs 44 mmHg, p=0.002) and DBP (21 vs28 mmHg, p=0.02) at 15 days were significantly lower in the prazosin group. However, duration of hospital stay (30 vs 27 days; p=0.54) and good recovery at 3 months (71.9%vs63.6%; p=0.48) were comparable. Three (9.3%) patients developed hypotension, while two patients died (ventilator associated pneumonia) in the prazosin group.

SUMMARY/CONCLUSION: Prazosin resulted in earlier normalization of SO but did not affect three months outcome and duration of hospital stay This study provides new evidence supporting the role of prazosin in SO and needs further randomized trials to confirm our findings.

IMPACT OF VUTRISIRAN ON ACTIVITIES OF DAILY LIVING AND FUNCTIONAL STATUS IN PATIENTS WITH HATTR AMYLOIDOSIS

Varun Kumar (Cambridge, MA), Matthew Doenges (Cambridge, MA), Daniel Rodriguez Duque (Montreal, CA), Shaun Bender (Cambridge, MA), Kelley Capocelli (Cambridge, MA)

INTRODUCTION: The Rasch-built Overall Disability Scale (R-ODS) is a patient-reported 24-item linearly weighted scale that captures activity and social participation limitations. It describes the rate of decline in activity and social limitations in patients with hereditary transthyretin amyloidosis with polyneuropathy (hATTR-PN), who received vutrisiran or placebo.

OBJECTIVE: Investigate vutrisiran's impact on functional activity and social participation in patients with hATTR-PN.

METHODS: R-ODS raw scores were measured at baseline (M0) and month 18 (M18) for vutrisiran-treated patients from HELIOS-A (NCT03759379), vutrisiran’s pivotal phase 3 trial in hATTR-PN patients, and for placebo-administered patients from APOLLO (NCT01960348), patisiran’s pivotal phase 3 trial in hATTR-PN patients. HELIOS-A was designed to evaluate efficacy and safety of vutrisiran against that of external placebo arm from APOLLO. Each patient’s raw score was converted into Rasch person-location values and mapped to a logit scale. Median logit values were computed by treatment group and visit and plotted alongside R-ODS item locations, representing item difficulty.

RESULTS: Median R-ODS raw scores were recorded in n=122 (vutrisiran) and n=76 (placebo) patients at M0 and n=113 (vutrisiran) and n=54 (placebo) patients at M18. The raw R-ODS and converted logits remained stable in the vutrisiran arm (R-ODS: M0=35, M18=36; Logit: M0=2.04, M18=2.28), indicating preservation of activity as reflected by patients’ ability to walk outdoors for <1 km, and deteriorated in the placebo arm (R-ODS: M0=30.5, M18=19.5; Logit: M0=1.05, M18=-1.06), indicating worsening of activity as such as losing even the ability to take a shower.

SUMMARY/CONCLUSION: Vutrisiran treatment preserved functional activity and social participation in patients with hATTR-PN in HELIOS-A.

Disclosures:

Varun Kumar - is an employee of study sponsor.

Matthew Doenges - fellowship funded by study sponsor.

Daniel Rodriguez Duque - is a paid consultant.

Shaun Bender - is an employee of study sponsor.

Kelley Capocelli - is an employee of study sponsor.

A PATIENT WITH PARAMYOTONIA CONGENITA DUE TO A NOVEL SCN4A GENE MUTATION

Carlos Lara (Chicago, IL), Zachary Osborn (Chicago, IL), Shubadra Priyadarshini (Chicago, IL), Betty Soliven (Chicago, IL), Kourosh Rezania (Chicago, IL)

INTRODUCTION/BACKGROUND: SCN4A-gene mutations encode an abnormal α-subunit of the voltage-gated sodium channel 1.4(NaV1.4) can be associated with paroxysmal abnormal skeletal muscle excitability leading to stiffness, delayed muscle relaxation and transient paralysis. Paramyotonia congenita (PMC) is a rare, highly penetrant autosomal dominant disease resulting from the gain of function of the SCN4A gene. PMC's presentation is characterized by paradoxical delayed relaxation (paramyotonia) of the facial, tongue, and hand muscles after repeated contraction and cold exposure, with electrical myotonia on EMG. More than 70 skeletal-muscle-associated-disease mutations of SCN4A have been identified. Functional expression studies could result in a better understanding of the genotype-phenotype association of the allelic disorders of the muscle sodium channelopathies.

CASE REPORT: 24-year-old Caucasian male with episodic muscle stiffness, difficult hand-relaxation, and eye-opening since his teens. Symptoms exacerbate with stress, caffeine, exercise, and in the winter months. His father reports similar symptoms. Physical examination showed normal muscle tone without weakness, myotonia, or paramyotonia at baseline but decreased hand relaxation after 2-minute cooling. Thyroid function and ionized calcium were normal, with elevated CK 499U/L. NCS was normal. EMG showed generalized myotonic discharges, less prominent after hand cooling and consistent with PMC. Genetic sequencing showed a heterozygous mutation of the SCN4Agene, exon 24, c.5024A>G with 95% protein-disruption likelihood. Exon 24 of the SCN4 is highly conserved and is a hotspot for pathogenic mutations. This variant has not been reported and is not present in population database.

SUMMARY/CONCLUSION: This case showed hallmark clinical and electrophysiological features of PMC with a mild phenotype, not-previously-reported genetic mutation of the SCN4A gene, exon 24, c.5024A>G.

PHASE 2 EFFICACY AND SAFETY OF RILIPRUBART, A C1S-COMPLEMENT INHIBITOR, IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

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INTRODUCTION: Riliprubart is a first-in-class humanized IgG4-monoclonal antibody, which selectively inhibits activated-C1s within the classical-complement pathway.

OBJECTIVE: To report efficacy and safety of riliprubart in chronic inflammatory demyelinating polyneuropathy (CIDP).

METHODS: Global, multicenter, Phase-2, open-label trial (NCT04658472) evaluating riliprubart across three CIDP patient subgroups: Standard-of-care (SOC)-Treated, SOC-Refractory, and SOC-Naïve. Participants undergo 24-week treatment (Part-A), followed by optional treatment-extension (Part-B: 52-weeks, Part-C: until end-of-study). The primary endpoint of Part-A is %-participants with relapse (SOC-Treated) or response (SOC-Refractory/Naïve), defined as ≥1-point change in adjusted Inflammatory Neuropathy Cause and Treatment (INCAT) disability score from baseline up to 24-weeks. Part-B evaluates safety and efficacy durability based on % relapse-free participants (SOC-Treated) or those with sustained-response (SOC-Refractory/Naïve), defined as no-increase in adjusted INCAT score ≥2-points relative to 24-weeks. Exploratory endpoints include additional efficacy measures (INCAT, I-RODS, MRC-SS, grip-strength), change in total complement, and plasma neurofilament-light chain (NfL).

RESULTS: As of May, 2023, Part-A results from pre-specified interim-analysis show 88% (N=22/25) SOC-Treated participants improved/remained stable (44%; N=11/25 improved), and 12% relapsed (N=3/25). 50% (N=9/18) of SOC-Refractory participants responded to riliprubart. Clinically meaningful improvements were observed across secondary efficacy measures. Sustained inhibition of complement activity and reduction in NfL-levels were also observed in these subgroups. Treatment-emergent adverse events occurred in 65.1% (N=28/43) participants. Two deaths were reported in participants with significant medical comorbidities aside from CIDP. Available Part-A and Part-B data for the three subgroups will be presented at the meeting.

SUMMARY/CONCLUSION: These preliminary results support proof-of-concept for riliprubart in CIDP, with a favorable benefit-risk profile, supporting further investigation in Phase-3.

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Richard A. C. Hughes - is a consultant with Hansa Biopharma, and Sanofi.

Richard A. Lewis - is a consultant with CSL Behring, Grifols, Pfizer, Sanofi (Steering Committee), argenx, Pharnext, Roche, Johnson & Johnson, Takeda, Boehringer Ingelheim (DSMB), and Momenta. He is also part of scientific advisory boards Alnylam and Akcea and medical advisory board: The GBS| CIDP Foundation International.

Hans-Peter Hartung - is a consultant with Sanofi and Octapharma. He has received fees for serving on Steering and Data Monitoring Committees from Biogen, BMS Celgene, GeNeuro, Merck, Novartis, Octapharma, Roche, and TG Therapeutics.

Pieter A. van Doorn - is a consultant with Annexon, argenx, Hansa Biopharma, Immunic, Octapharma, Roche, Sanofi (institutional research fund received all honoraria), and received grants from the Prinses Beatrix Spierfonds, Sanquin, and Grifols.

Erik Wallstroem - is an employee of Sanofi and may hold shares and/or stock options in the company.

Kristen Auwarter - is an employee of Sanofi and may hold shares and/or stock options in the company.

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Miguel Alonso-Alonso - is an employee of Sanofi and may hold shares and/or stock options in the company.

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LONG-TERM SAFETY, TOLERABILITY, AND EFFICACY OF SUBCUTANEOUS EFGARTIGIMOD PH20 IN PARTICIPANTS WITH GENERALIZED MYASTHENIA GRAVIS: INTERIM RESULTS OF THE ADAPT-SC+ STUDY

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INTRODUCTION: Efgartigimod is a human IgG1 antibody Fc-fragment that reduces IgG levels (including pathogenic autoantibodies) through neonatal Fc receptor blockade. 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 in participants with generalized myasthenia gravis (gMG). Participants completing ADAPT-SC or enrolled in ADAPT+ (efgartigimod IV open-label extension [OLE]) were eligible for the ADAPT-SC+ OLE.

OBJECTIVE: Evaluate long-term safety, tolerability, and efficacy of efgartigimod PH20 SC in participants with gMG enrolled in the ADAPT-SC+ OLE.

METHODS: Efgartigimod PH20 SC 1000 mg was administered in cycles of four once-weekly injections. Subsequent cycles were initiated based on clinical evaluation. Myasthenia Gravis Activities of Daily Living (MG-ADL) score assessed clinical efficacy.

RESULTS: Through December 2022, 179 participants received ≥one dose of efgartigimod PH20 SC, with a mean (SD) study duration of 413 (105) days. Adverse events were predominantly mild/moderate. Injection site reactions were mild/moderate, did not lead to treatment discontinuation, and decreased in incidence with subsequent cycles. Improvement from cycle baseline (mean [SE]) in MG-ADL total score was observed in week 4 of Cycle 1 (-4.1 [0.27]) in anti-acetylcholine receptor antibody positive participants, with consistent/repeatable improvements seen through Cycle 9. Similar results were seen on quality-of-life measures. The proportion of participants achieving minimal symptom expression (MG-ADL 0-1) at any time through nine cycles was 54.6%. Clinical improvements were similar to those seen with efgartigimod IV during ADAPT/ADAPT+.

SUMMARY/CONCLUSION: Treatment with multiple cycles of efgartigimod PH20 SC was well tolerated and efficacious.

The authors acknowledge the contributions of the ADAPT-SC+ Study Group.

Disclosures:

Yuebing Li - has served as a consultant for argenx, UCB Pharma, Alexion, Catalyst, and Immunovant.

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Jan L. De Bleecker - has served as a consultant for argenx, Alexion Pharmaceuticals, Inc, CSL, UCB Pharma, Alnylam Pharmaceuticals Inc, Janssen, and Sanofi Genzyme.

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James F. Howard Jr - has received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, and UCB Pharma; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc (now Amgen), Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, UCB Pharma, and Zai Labs; and nonfinancial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Pharma, and Zai Labs.

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Sophie Steeland - is an employee of argenx.

Benjamin Van Hoorick - is an employee of argenx.

Jana Podhorna - is an employee of argenx.

Moana Hodari - is an employee of argenx.

Kimiaki Utsugisawa - has served as a paid Consultant for UCB Pharma, Janssen Pharma, Horizon Therpeutics (Viela Bio), Chugai Pharma, Hanall BioPharma, Merck, and Mitsubishi Tanabe Pharma and has received speaker honoraria from argenx, Alexion Pharmaceuticals, UCB Pharma, and the Japan Blood Products Organization.

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CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY MISDIAGNOSIS: A META-ANALYSIS

Ziqiang Lin (Minneapolis, MN), Jeffrey Allen (Minneapolis, MN)

INTRODUCTION: Chronic inflammatory demyelinating polyneuropathy (CIDP) misdiagnosis presents a significant challenge in clinical practice, leading to inappropriate treatments and potentially worsening patient outcomes. Major factors contributing to misdiagnoses include understanding of CIDP variants, interpretation of NCSs and cerebrospinal fluid protein levels, and perceived responses to immunotherapy.

OBJECTIVE: To identify specific diagnoses commonly mistaken for CIDP to further categorize and characterize these misdiagnoses.

METHODS: We conducted a meta-analysis by searching PubMed and MEDLINE databases for relevant studies published since 2010 and pooled data from a total of eight studies, encompassing 315 cases initially diagnosed as CIDP but later reclassified as alternative conditions.

RESULTS: We identified the specific diagnoses commonly mistaken for CIDP including acquired axonal neuropathy (20%), autoimmune neuropathy (16%), idiopathic polyneuropathy (14%), motor neuron disease (12%), hereditary neuropathy (10%), and small fiber neuropathy (8%). We further categorize these misdiagnosed conditions into four classes including length dependent axonal polyneuropathy (53.97%), conditions leading to progressive weakness (62.22%), conditions leading to prominent pain (53.97%), and other immunological conditions (23.81%).

SUMMARY/CONCLUSION: These classes represent the mimics of distal CIDP, motor CIDP, sensory CIDP, and conditions responsive to immunotherapy, respectively. By further characterizing these classes we provided insights into characteristics to distinguish CIDP from its mimics, with a goal of improving diagnostic accuracy and optimizing patient care in neuropathic disorder management.

PAINLESS NEURALGIC AMYOTROPHY IN A PEDIATRIC PATIENT

Tiffany Lin (Los Angeles, CA), Dana O'Rourke (Los Angeles, CA)

INTRODUCTION: Neuralgic amyotrophy is a rare, poorly understood, brachial plexopathy. The exact etiology is not known, but it is thought to be an immune mediated process. Typical presentations are characterized by intense pain at onset followed by weakness and possible sensory changes of the upper extremity.

OBJECTIVE: We describe a pediatric patient who presented with atypical features for neuralgic amyotrophy.

CASE REPORT: Patient is a 7-year-old male with subacute weakness in the left upper extremity in the context of a recent viral upper respiratory tract infection. There was no pain at the onset of symptoms. Examination was notable for weakness, decreased sensation, and areflexia of the left upper extremity. Workup showed normal basic serum studies, C reactive protein, and creatinine kinase level. MRI of the brain and cervical/thoracic spine were normal. Cerebral spinal fluid labs were bland. EMG and NCSs showed an axonal sensorimotor polyneuropathy and acute denervation changes of left upper extremity consistent with a left brachial plexopathy. Brachial plexus MRI demonstrated T2 hyperintensities in the left brachial plexus and C6-C8 nerve roots. Patient received a course of steroids with mild improvement of symptoms and strength at follow up.

SUMMARY/CONCLUSION: We present a case of a painless neuralgic amyotrophy in a pediatric patient. Case reports suggest a distinct pediatric phenotype compared to the adult population including the absence of pain. This case adds to the growing literature of pediatric presentations of neuralgic amyotrophy that may be underrecognized and present differently from adults.

A NOVEL TREATMENT APPROACH FOR IDIOPATHIC POSTERIOR INTEROSSEOUS NERVE ENTRAPMENT

Daniella Lipnick (New York, NY), Bryan Le (New York, NY), Derek Ho (New York, NY), Marjorie Morales (New York, NY)

INTRODUCTION: Idiopathic radial nerve entrapment is uncommon, especially the deep branch segment known as the posterior interosseous nerve (PIN).

OBJECTIVE: The goal is to highlight a case of a patient with idiopathic PIN entrapment and review the nonsurgical treatment modalities.

RESULTS: The motor NCS was notable for absent right radial nerve at the extensor indicis proprius (EIP) compound motor action potentials. Needle EMG showed abnormal insertional spontaneous activity on the right EIP and extensor digitorum communis (EDC), with sparing of the brachioradialis. A diagnosis of right PIN entrapment was made. The patient was referred to sports medicine, found to have radial nerve swelling between the deep and superficial heads of the supinator on bedside ultrasound examination. The patient received hydro-dissection of the radial nerve, which provided relief of his symptoms.

CASE REPORT: The patient is a 64-year-old male with a past medical history of diabetes and HIV who presented with 3 weeks of atraumatic right wrist drop. He was referred for an EMG test to assess radial neuropathy. The patient reported pain in the right proximal forearm and dorsal wrist. The exam was notable for isolated right wrist and finger extension weakness.

SUMMARY/CONCLUSION: New research suggests that hydro-dissection under ultrasound guidance can help relieve symptoms of nerve entrapments. Given limited efficacy for medications and therapies for PIN, exploration of minimally invasive injection techniques like hydro-dissection highlights a potential conservative treatment modality.

POZELIMAB AND CEMDISIRAN COMBINATION THERAPY IN PATIENTS WITH MYASTHENIA GRAVIS: PHASE 3 NIMBLE TRIAL DESIGN

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INTRODUCTION: Generalized myasthenia gravis (gMG) is a rare autoimmune disease of the neuromuscular junction predominantly due to autoantibodies that bind to the acetylcholine receptor (AChR). In most gMG patients, IgG1 AChR (and less commonly anti-lipoprotein receptor-related protein 4, LRP4) antibodies are responsible for neuromuscular transmission failure via terminal complement activation. Pozelimab and cemdisiran are investigational agents for gMG that both inhibit complement pathway. Cemdisiran is an N-acetylgalactosamine-conjugated small interfering RNA that suppresses liver production of complement component C5 (C5), while pozelimab is a monoclonal antibody inhibitor to C5.

OBJECTIVE: We describe the design of the ongoing phase 3 NIMBLE trial (NCT05070858), which aims to evaluate the efficacy and safety of pozelimab plus cemdisiran in patients with symptomatic gMG.

METHODS: This is a multinational, randomized, double-blind, placebo-controlled trial in patients with clinically confirmed gMG (seropositive for anti-AChR or anti-LRP4 antibodies). The study includes a 5-week screening period, a 24-week double-blind placebo-controlled treatment period, a 28-week double-blind extension treatment period, a 68-week open-label long-term treatment period, and a 52-week post-treatment follow-up period. On Day one, patients will be randomized to one of the four treatment arms. This study will enroll approximately 235 patients. The primary endpoint is the change in Myasthenia Gravis-Activities of Daily Living (MG-ADL) score from baseline to Week 24.

RESULTS: The first patient was enrolled on December 14, 2021.

SUMMARY/CONCLUSION: This ongoing study (open for recruitment) is designed to evaluate the effect of pozelimab plus cemdisiran on daily functioning and other MG efficacy measures, as well as safety in patients with symptomatic gMG.

Disclosures:

Saiju Jacob - has served as an international advisory board member for Alexion, Alnylam, argenx, Immunovant, Regeneron, and UCB; is currently an expert panel member of the Myasthenia Gravis Consortium for argenx; and has received speaker fees from Eisai Pharmaceuticals and Terumo BCT.

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James F. Howard Jr - has received research funding (paid to institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, Ra Pharmaceuticals/UCB Bioscience, and Takeda Pharmaceuticals; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc (now Amgen), Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Ra Pharmaceuticals/UCB Bioscience, Regeneron Pharmaceuticals, Sanofi US, and Zai Labs; non-financial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Bioscience and Zai Labs.

EFGARTIGIMOD IN GENERALIZED MYASTHENIA GRAVIS: A MULTICENTER REAL-WORLD COHORT STUDY IN CHINA

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INTRODUCTION: Efgartigimod is a neonatal Fc receptor antagonist that facilitates antibody degradation including pathogenic IgGs. The ADAPT study demonstrated the tolerability and efficacy of efgartigimod in generalized myasthenia gravis (gMG). However, there is limited evidence from the Chinese population, and it remains inconclusive about which kind of patients with gMG are selected to preferentially receive efgartigimod.

OBJECTIVE: To explore the indications of efgartigimod in a real-world study.

METHODS: This multicenter study included gMG from 14 centres in China. The Myasthenia Gravis Activities of Daily Living (MG-ADL) score and treatment-emergent adverse events (TEAEs) were prospectively collected. Clinically meaningful improvement (CMI) was defined as the change in MG-ADL of ≥2. Minimal symptom expression (MSE) was defined as MG-ADL of 0-1.

RESULTS: Of 1640 gMG patients admitted between September to December 2023, 61 (3.7%) received efgartigimod for at least one treatment cycle. Among them, 56 patients (92%) were anti-AChR antibody positive, 4 were anti-MuSK antibody positive and 1 was seronegative. Thymoma-associated Myasthenia gravis accounts for the majority (44%, 27/61). The principal causes for efgartigimod initiation were MG acute exacerbation (MGAE) (48%, 29/61) and myasthenic crisis (MC) (15%, 9/61). CMI was rapidly achieved in 97% (58/61) of patients with 1.3±0.7 weeks. By Week 12, MG-ADL score was reduced to 3.8±4.1 from 10.5±5.2 at baseline while 39% (23/59) achieved MSE. Patients with MGAE and MC had a minimum MG-ADL score of 4.0 from 11.1 and 3.8 from 15.6 at baseline. 11.55% (7/61) reported ≥1 TEAEs.

SUMMARY/CONCLUSION: This multicenter cohort study demonstrated the efficacy of efgartigimod in rapid disease control for gMG.

CLINICAL OUTCOME IN IMPENDING MYASTHENIC CRISIS WITH RESCUE THERAPIES: A PROSPECTIVE COHORT STUDY

Yuan Wang (Shanghai, China), Xiao Huan (Shanghai, China), Jie Song (Shanghai, China), Xinfang Zhu (Shanghai, China), Chong Yan (Shanghai, China), Yafang Xu (Shanghai, China), Jianying Xi (Shanghai, China), Chongbo Zhao (Shanghai, China), Rong Xia (Shanghai, China), Liewen Pang (Shanghai, China), Xianglin Chu Chu (Shanghai, China), Sushan Luo (Shanghai, China)

INTRODUCTION: Impending myasthenic crisis (MC) was defined as a rapid worsening in myasthenia gravis (MG) which can progress to respiratory failure in days to weeks. Fast-acting rescue therapies are recommended to treat patients with MC. However, the effectiveness of preventing the transition from impending to manifest MC remained unknown and there is a lack of evidence from prospective cohort studies.

OBJECTIVE: To explore the efficacy of timely rescue therapies in transformation from impending crisis to manifest crisis.

METHODS: This multicenter cohort enrolled impending MC from six University hospitals who were given timely rescue therapies with either intravenous immunoglobulin (IVIg) or therapeutic plasma exchange (TPE) within 48 hours of admission. The primary outcome was defined as the transformation to manifest MC.

RESULTS: Among gMG patients with the chief complaint of dyspnea admitted from April 2021 to February 2024, 21.8% (37/170) with hypoxemia and/or hypercapnia in blood gas analysis but still satisfied by oxygen inhalation were included as the impending crisis cohort. With rescue therapies, the transformation rate from impending to manifest MC was 24.32% (9/37), including eight with non-invasive ventilation and one with mechanical ventilation (MV). As compared with those who developed MC, a significantly shorter hospital stay was observed in those who did not (P=0.004). A shorter disease duration from onset to this admission was observed in impending crisis who did not transform (P=0.003) and a lower QoL-15 score at baseline (P= 0.006).

SUMMARY/CONCLUSION: With the timely intervention of fast-acting therapies, patients at impending MC state can effectively be prevented from transforming into MC.

SUBACUTE PROGRESSION ANTI-HU SENSORY GANGLIONOPATHY IN ASSOCIATION WITH MYXOID CHONDROSARCOMA IN REMISSION

Lindsay Malatesta (Nashville, TN), Laiken Griffith (Nashville, TN), Leon Cai (Nashville, TN), Camille Wang (Nashville, TN), Hunter Hewitt (Nashville, TN)

INTRODUCTION/BACKGROUND: Sensory ganglionopathy (SG), or disease of the sensory neurons of the dorsal root ganglia, typically manifests with sensory deficits. Concomitant motor symptoms should prompt consideration of a paraneoplastic etiology, including anti-Hu, or ANNA-1, autoantibodies, which are classically associated with lung cancer. We describe a rare case of paraneoplastic anti-Hu SG in the setting of myxoid chondrosarcoma (MC).

CASE REPORT: 72-year-old man with history of MC in reported remission after below knee amputation, nivolumab infusion, and radiation therapy presented as an inpatient consult due to 1 month of progressive lethargy, dyspnea, bilateral arm and leg numbness, weakness, and involuntary movements of his bilateral hands. On exam, he demonstrated dense bilateral pan-modality sensory loss distal to the mid-forearms and knees, distal greater than proximal upper extremity weakness, areflexia, and pseudo-athetoid movements in the right more than left upper extremity. Lumbar puncture revealed 0 cells and 105 proteins. MRI brain and spine, CT chest, abdomen, and pelvis, and PET did not reveal an underlying cancer. EMG showed a diffuse sensorimotor polyneuropathy with reduced amplitudes. Antibody studies were positive for anti-Hu. Diagnosis was consistent with anti-Hu paraneoplastic SG in association with MC despite chemotherapy and amputation five months prior. Plasmapheresis nor steroids produced significant improvement. Intravenous cyclophosphamide was initiated inpatient and transitioned to oral therapy at discharge.

SUMMARY/CONCLUSION: Typically preceding or coinciding with a cancer diagnosis, most commonly small cell lung cancer, SG should also be considered with a MC diagnosis even if in considered in remission. Unfortunately, response to treatment including immunosuppressants is typically poor.

NEUROSYPHILIS: AN UNSUSPECTING MIMIC TO SERONEGATIVE MYASTHENIA GRAVIS

Lindsay Malatesta (Nashville, TN), Laiken Griffith (Nashville, TN)

INTRODUCTION/BACKGROUND: There has been a fivefold increase in the incidence of primary and secondary syphilis from the year 2000-2018, and from 2020-2021, infection rates increased an additional 32%. Neurosyphilis, an infection of the central nervous system from Treponema pallidum (TP), can occur at any stage, and most frequently noted in secondary syphilis. Onset of symptoms can occur within a few weeks to a year (up to decades). A combination of history, serology, and CSF testing are needed to identify the disease.

CASE REPORT: 61-year-old woman referred for a diagnosis of seronegative Myasthenia Gravis (MG) due to double vision and weakness. Antibodies including serum acetylcholine receptor, muscle specific kinase, P/Q voltage gated potassium channel were negative. Repetitive nerve stimulation of the ulnar and spinal accessory nerves were normal. Single fiber testing on frontalis with mean jitter 40 microseconds and 30% blocking. At the initial visit, she endorsed dizziness, hearing loss, and new daily headaches which did not correlate with MG. Additional workup was perused including MRI brain with meningeal enhancement. TP IgG was positive although she had no identifiable exposure and no sexual relationship in over 1 year. CSF: lymphocytic pleocytosis, 47 protein, and VDRL negative. Infection Disease consulted who agreed with neurosyphilis and initiated IV penicillin for 14 days

SUMMARY/CONCLUSION: Neurosyphilis, the “great imitator”, includes a panoply of symptoms including cranial neuropathies, headache, memory loss, reduced visual acuity, hearing loss, stroke, paresis, and sensory ataxia. With the rise in infection rates, neurologists should include screening for TP for unexplained symptoms, even without clear exposure risks.

UTILITY OF GENETIC PANELS FOR NEUROMUSCULAR DISORDERS IN A TERTIARY REFERRAL CENTER NEUROLOGY CLINIC IN CENTRAL PENNSYLVANIA

Sarah Mauney (Hershey, PA), Mansoureh Mamarabadi (Hummelstown, PA), Eleni Fafoutis (Hershey, PA)

INTRODUCTION: Recent AANEM guidelines state genetic testing is essential to diagnosis of a neuromuscular disease, however, previous studies show a wide range in utility of these tests.

OBJECTIVE: To determine our clinic's genetic panel testing yield, uncover specific patient presentation patterns for target genetic testing and further diagnostic studies.

METHODS: Data will be collected from a tertiary referral center in central Pennsylvania. Gene panel results from Invitae (San Francisco, California) and GeneDx (Gaithersburg, Maryland) for approximately 700 patients will be evaluated in correlation with patient's demographic data, phenotype, family history, and EDX studies.

RESULTS: To date, 317 patients with Invitae genetic panel testing results were reviewed. Mean age at symptom onset and time of genetic testing were 47 and 55 years, retrospectively. Fifty-one percent were female,83% were white, 2.8% African American, 2.2% Asian, 0.3% Hispanic, and 11.7% others or unavailable. Patients' presentation included motor neuron disease (36%), neuropathy (22%), myopathy (18%), neuromuscular junction (1%), and other (28%). EDX patterns revealed: polyneuropathy (12%), myopathic (6%), motor neuron disease (31%), or nonspecific (53%). Genetic panels results demonstrated: positive 14%, negative 42%, uncertain 38%, and carrier 7%. Among those with positive results, 74% had a significant family history, and 51% had diagnostic EDX studies.

SUMMARY/CONCLUSION: Our preliminary results show that those with a positive gene panel result have higher percentage of significant family history and diagnostic EDX. We aim to develop an algorithm for genetic panel testing in our clinic considering family history, EDX, and biopsy results to increase diagnostic yield.

ENZYME REPLACEMENT THERAPY AND IMMUNOTHERAPY YIELD SIGNIFICANT FUNCTIONAL IMPROVEMENT IN TWO CHILDREN WITH POMPE DISEASE: CASE REPORTS IN COLOMBIA

Sandra Milena Castellar Leones (Bogotá, Colombia), Fernando Ortiz-Corredor (Bogotá, Colombia), Daniel Manrique Hernandez (Bogotá, Colombia), Edicson Ruiz Ospina (Bogotá, Colombia)

INTRODUCTION/BACKGROUND: Pompe disease is a multisystemic disorder that can affect individuals at any age, with various signs and symptoms. Enzyme replacement therapy (ERT) is the only approved treatment for Pompe disease and has been available. ERT is administered through bi-weekly infusions of recombinant human GAA and has been shown to reduce complications and maintain motor, ventilatory, and cardiac abilities in patients with Pompe disease, especially when initiated early.

CASE REPORT: A 12-month-old female with early onset Pompe disease (EOPD) was initiated on enzyme replacement therapy (ERT) with recombinant human alpha-glucosidase (rhGAA;alglucosidase alfa) at 20 mg/kg every 2 weeks. The quantification of anti-rhGAA IgG antibody titres was performed, with a result of 1:1800 (reference range: 0-100). Consequently, the patient was commenced on methotrexate (MTX) 15 mg/m2 dose every 2 weeks. The patient's functional evaluation demonstrated substantial improvement in motor skills. The second case involves a 7-year-old female with EOPD diagnosed at 12 months of age. The patient was started on ERT with recombinant human alpha-glucosidase at 20 mg/kg every two weeks at 12 months of age. The quantification of anti-rhGAA IgG antibody titres was performed, which resulted in a positive value of 6400. As a result, management with MTX was started at 15 mg/m2 dose every 2 weeks, leading to improved falls

SUMMARY/CONCLUSION: Overall, ERT has demonstrated significant clinical benefits for individuals with Pompe disease, including improved motor, ventilatory, and cardiac function. This case highlights the importance of early diagnosis and timely initiation of ERT in children with Pompe disease to achieve optimal motor outcomes.

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NEW GENERATION SEQUENCING IN HYPER-CKEMIA EVALUATION

Lucas Marenga de Arruda Buarque (São Paulo, Brazil), Cristiane de Araújo Martins Moreno (São Paulo, Brazil), Carlos Heise (Sao Paulo, Brazil), Antonio Filho (São Paulo - SP, Brazil), Ian Felipe Barbosa Souza (São Paulo, Brazil), Nicolas Ruan dos Santos Cavalcante (São Paulo, Brazil), Jose Pedro Soares Baima (São Paulo, Brazil), Rodrigo de Holanda Mendonça (São Paulo, Brazil), Andre Macedo Serafim da Silva (São Paulo, Brazil), Clara Gontijo Camelo (São Paulo, Brazil), Alulin Tácio Quadros Santos Monteiro Fonseca (São Paulo, Brazil), Stefano Machado (São Paulo, Brazil), Fernando Cavalcante de Sá e Benevides Falcão (São Paulo, Brazil), Felipe Fiorelli Vanlenzuela (São Paulo, Brazil), Edmar Zanoteli (São Paulo, Brazil)

INTRODUCTION: Hyper-CKemia is a common complaint in neuromuscular clinics. Which is the best propaedeutic for its evaluation is still a matter of discussion.

OBJECTIVE: We describe the results of using new generation sequencing in patients with hyper-CKemia.

METHODS: All genetic tests made in the neuromuscular disorders division of HCFMUSP were revisited and only those with a history of rhabdomyolysis and hyperCKemia pauci- or asymptomatic were included. We considered hyper-CKemia as a creatine phosphokinase (CPK) level above 1.5 times above reference value.

RESULTS: Twenty-three patients were selected, 21 were submitted to a gene panel for neuromuscular diseases and 2 to exome: 3 with rhabdomyolysis, 6 with asymptomatic hyper-CKemia, and 14 with paucisymptomatic hyper-CKemia. Six (26%) were diagnosed by genetic test: 03 ANO5, 01 GPMPPB, 01 PYMG (all of which have paucisymptomatic hiper-CKemia) and 01 RYR1 (rhabdomyolysis). Of those 17 who did not reach a diagnosis, one had only one pathogenic variant in ANO5 gene (a recessive condition) and four had one or more VUS in genetic tests. The mean maximum creatine phosphokinase (CPK) levels in the group that reached a diagnosis was 6.977U/L and in the group without genetic diagnosis was 5.851 U/L.

SUMMARY/CONCLUSION: The new generation sequencing has started a new era in neuromuscular disorders diagnostics. We report an efficacy of 26% of its use in hyper-CKemia evaluation and ANO5 gene was the most prevalent.

LOW FREQUENCY REPETITIVE STIMULATION AS A TOOL TO DIFFERENTIATE EATON-LAMBERT MYASTHENIC SYNDROME FROM MYASTHENIA GRAVIS

Lucas Marenga de Arruda Buarque (São Paulo, Brazil), Stefano Machado (São Paulo, Brazil), Fernando Cavalcante de Sá e Benevides Falcão (São Paulo, Brazil), Felipe Fiorelli Vanlenzuela (São Paulo, Brazil), Jose Pedro Soares Baima (São Paulo, Brazil), Nicolas Ruan dos Santos Cavalcante (São Paulo, Brazil), Antonio Filho (São Paulo - SP, Brazil), Lucas Immich (São Paulo, Brazil), Andre Macedo Serafim da Silva (São Paulo, Brazil), Rodrigo de Holanda Mendonça (São Paulo, Brazil), Ian Felipe Barbosa Souza (São Paulo, Brazil), Eduardo Estephan (São Paulo, Brazil), Edmar Zanoteli (São Paulo, Brazil), Carlos Heise (São Paulo, Brazil)

INTRODUCTION: It has long been stated that high frequency repetitive stimulation (HFRS) is a valuable tool to differentiate myasthenia gravis (MG) from Lambert-Eaton myasthenic syndrome (LEMS), nevertheless it is not performed routinely in neuromuscular junction studies.

OBJECTIVE: We describe the use of low frequency repetitive stimulation (LFRS) with a train of six stimuli in order to differentiate between LEMS and MG with antibodies to acetylcholine receptor (AChR).

METHODS: The ratio of the 4th and the 6th amplitude potential were compared between four patients diagnosed with LEMS (group 1) and 11 MG AChR patients (group 2).

RESULTS: The amplitude ratio was 1,21 in group 1 and 0,92 in group 2. Of 11 patients in group 2, only one had a decremental index above 1; and, in group 1, only one patient had a decremental index under 1, with whom was diagnosed myasthenia gravis Lambert-Eaton overlap syndrome.

SUMMARY/CONCLUSION: We suggest LFRS (train of 6 stimuli) in patients with neuromuscular junction syndrome for screening LEMS. A relation above 1,0 of the 4th and the 6th amplitude potentials is suggestive of LEMS.

PREDICTING SURGICAL OUTCOMES FOR CUBITAL TUNNEL SYNDROME WITH THE CONWAY SCALE: A PILOT STUDY

Chrissa McClellan (Columbia, MO), Mark Drymalski (Columbia, MO), Hannah Farmer (Columbia, MO), Carmen Cirstea (Columbia, MO), Ben Gill (Salt Lake City, UT)

INTRODUCTION: Current EDX severity scales have a low sensitivity to predict surgical outcomes in cubital tunnel syndrome (CuTS).

OBJECTIVE: To test the predictive value of a new EDX severity scale, the Conway CuTS severity scale, with surgical outcomes.

METHODS: The Conway scale was developed as follows: mild impairment is defined by an ulnar motor nerve conduction velocity (UMNCV) across the elbow <50m/s with 3 cm inching technique; moderate: UMNCV<50 m/s with standard 10 cm technique; and severe: UMNCV<50 m/s with standard 10 cm technique with decreased amplitudes and/or EMG changes. Preoperative EDX data, acquired with the Zeidman and the Conway scales, and pre-and postoperative Patient Reported Outcome Measure Information System (PROMIS) scores were collected retrospectively from 52 patients who underwent surgery.

RESULTS: The PROMIS scores significantly improved with surgery, from 35.3+ or –8.2 (mean+ or –standard deviation) to 39.6+ or –10.9 (Delta=4.3+ or –10.7, p=0.006). Preoperatively, the sensitivity of the Conway scale is higher for those less affected compared to the Zeidman scale: mild impairment was detected with this scale in those considered as normal with the Zeidman scale (n=9). Although the correlations between baseline evaluations of both scales and DeltaPROMIS didn't reach statistical significance, the predictive value of the Conway scale is likely higher than that of the Zeidman scale (p=0.3 vs. 0.6).

SUMMARY/CONCLUSION: Our preliminary data suggest that the Conway scale has a higher sensitivity in the detection of those with mild impairment compared to currently used scales. However, for the new scale predictive value of surgery outcomes, further work with larger sample sizes is warranted.

ACCURACY OF NEEDLE PLACEMENT IN TERES MINOR USING SURFACE LANDMARKS VERSUS ULTRASONOGRAPHY

Anna McCrate (Atlanta, GA), Di Cui (Atlanta, GA), Anand Joshi (Flowery Branch, GA), Joel Talsma (Biddeford, ME), Milly Seeley (Biddeford, ME), Nicholas LaMothe (Biddeford, ME)

INTRODUCTION: To assist in planning of shoulder surgery, EDX physicians assess the innervation of the various muscles that make up the rotator cuff. Because one of those muscles, the teres minor, is both thin and in close proximity to the infraspinatus, a precise location of the EMG needle is imperative to provide the necessary diagnostics.

OBJECTIVE: We conducted a cadaver study to evaluate whether there is a difference between surface landmark and ultrasound (US) guided needle placement in locating the teres minor.

METHODS: To determine needle accuracy, we injected 44 cadavers with dye using both surface landmarks and US-guided approaches. For landmark based injections, the cadaver was prone, and the needle was inserted at the point one-third of the distance between the posterior aspect of the acromion and the inferior angle of the scapula. For US-guided injections, the probe was used to visualize the posterior acromion, infraspinatus tendon, then teres minor tendon. The probe was then centered in the muscle belly, and the needle inserted in plane. Accuracy was determined visually during anatomy dissection.

RESULTS: Using surface landmarks, dye was successfully placed in 6 of 44 teres minor muscle bellies (13.6%, 95% CI 3.5%-23.7%). Using US, dye was successfully placed in 25 of 44 teres minor muscle bellies (56.8%, 95% confidence index [CI] 42.2%-71.4%). US was statistically superior in correctly identifying the teres minor.

SUMMARY/CONCLUSION: US guidance provides superior control of needle placement in locating the teres minor, which in turn could help EDX physicians better analyze muscle and nerve function.

A CHILDREN'S HOSPITAL'S APPROACH TO OBTAINING OPTIMUM DATA FROM NERVE CONDUCTION STUDIES AND ELECTROMYOGRAPHY MINIMIZES NEED FOR SEDATION

Bridget McGowan (Chicago, IL), Abigail Schwaede (Chicago, IL), Vamshi Rao (Chicago, IL), Kelly Li (Chicago, IL), Margo Gadsden (Chicago, IL), Samantha Sawalski (Chicago, IL), Nancy Kuntz (Chicago, IL)

INTRODUCTION: EDX studies are useful in the diagnosis and monitoring of neuromuscular disorders in infants and children. However, dynamic tension exists between the temperament of young children and the degree of cooperation required for technically excellent studies. Historically, NCS/EMG procedures have been characterized as unpleasant with potential for technical artifacts, post-traumatic stress, and/or having the test aborted before acquiring adequate data. In response, some pediatric EMG/NCS procedures are completed under general anesthesia which introduces additional risks.

OBJECTIVE: Optimizing quality of neurophysiologic data from infants and children.

METHODS: A comprehensive approach has been developed by our pediatric neuromuscular disorders program including control over all aspects of the referral and performance of NCS/EMG in our children's hospital. Developing precise referral questions, preparation of child/family for the study, control of the test environment including language used are all addressed. An experienced team including pediatric neuromuscular specialists, pediatric neurophysiology technologists, and a certified child life specialist has been developed. Acknowledging a child's preferences, common sense measures such as spacing stimuli, and use of topical analgesia to decrease perception of skin needle puncture are measures which increase tolerance and a child's sense of control.

RESULTS: Referral sources and number of studies have increased significantly over the past decade while decreasing reliance on general anesthesia (numbers to be provided). Qualitative patient and family feedback will be provided.

SUMMARY/CONCLUSION: Child and family focused approaches to NCS/EMG can optimize data obtained while minimizing the use of general anesthesia in infants and children.

Disclosures:

Abigail Schwaede - Sarepta and Biogen- paid consultation.

Vamshi Rao - is an advisor for Biogen, Avexis, NSPharma, Sarepta, Genentech, ScholarRock, PTC, Regenxbio; Speakers Bureau-Biogen, Genentech; Speaker- France Foundation; Data Safety monitoring board- Capricor, Syneos.

Nancy Kuntz - is on the Scientific Advisory Board for Argenx, Audentes, Biogen, Genentech, Novartis, Sarepta; Speaker Honoraria- Sarepta; Commercial research support- Argenx, Audentes, Biogen, Fibrogen, Genentech, Novartis, Sarepta.

ULNAR NEUROPATHY AS AN UNCOMMON PRESENTATION OF NEUROSARCOIDOSIS: A CASE SERIES

Jiping Zhou (Detroit, MI), Joseph Craig (Detroit, MI), Anza Memon (Detroit, MI)

INTRODUCTION/BACKGROUND: Sarcoidosis, an idiopathic granulomatous disease affecting multiple systems, rarely presents with neurological symptoms, including involvement of extracranial peripheral nerves, seen in about 1% of cases. While sarcoidosis-associated peripheral neuropathy can manifest as polyradiculopathy or mononeuritis multiplex, literature on sarcoidosis-related ulnar neuropathy is scarce.

CASE REPORT: In this case series we summarize the clinical features of three cases with an established diagnosis of sarcoidosis who experienced ulnar neuropathy during the disease course. All three patients, who were diagnosed with sarcoidosis by tissue biopsy, developed chronic onset of unilateral sensorimotor symptoms of in the ulnar nerve distribution. Diagnosis of ulnar neuropathy confirmed by EMG showed features of mixed demyelinating and axonal loss. Ultrasound (US) of the nerve consistently demonstrated enlargement and a hypoechoic pattern of the ulnar nerve but not consistent with the diagnosis of the cubital tunnel. Exhaustive investigations were done for all three patients and no other etiologies were identified. One patient received immunosuppression therapy with infliximab for refractory neurosarcoidosis affecting the central nervous system that helped with symptom stabilization The other two patient's treatment responses were unclear as they were lost to follow-up.

SUMMARY/CONCLUSION: Ulnar neuropathy secondary to sarcoidosis is uncommon in individuals with systemic sarcoidosis. A thorough diagnostic evaluation including serologic studies, EDX studies, neuroimaging, and biopsy, is essential for accurate diagnosis. In patients with sarcoidosis and ulnar neuropathy, US examination should be considered to exclude cubital tunnel syndrome and other compressive causes, thus preventing unnecessary surgical interventions. Timely and appropriate immunosuppressive therapy may lead to favorable treatment responses.

SAFETY AND EFFICACY OF DELANDISTROGENE MOXEPARVOVEC VERSUS PLACEBO IN DUCHENNE MUSCULAR DYSTROPHY: PHASE 3 EMBARK PRIMARY RESULTS

Jerry Mendell (Cambridge, MA), Francesco Muntoni (London, United Kingdom), Craig McDonald (Sacramento, CA), Eugenio Mercuri (Rome, Italy), Emma Ciafaloni (Rochester, NY), Hirofumi Komaki (Tokyo, Japan), Carmen Leon-Astudillo (MD, FL), Andrés Nascimento Osorio (Barcelona, Spain), Crystal Proud (Norfolk, VA), Ulrike Schara-Schmidt (Essen, Germany), Aravindhan Veerapandiyan (Little Rock, AR), Craig Zaidman (St. Louis, MO), Alex Murphy (Basel, Switzerland), Jacob Elkins (Cambridge, MA), Louise Rodino-Klapac (Cambridge, MA)

INTRODUCTION: Delandistrogene moxeparvovec, an rAAVrh74-based gene transfer therapy designed to address absent functional dystrophin by delivering a transgene encoding engineered micro-dystrophin, is approved in the USA, UAE, Qatar, and Kuwait for treatment of ambulatory pediatric patients ages 4 through 5 years of age with Duchenne muscular dystrophy (DMD) with a confirmed DMD mutation (as of February 2024).

OBJECTIVE: To report findings from Part 1 (Week 52) of the 2-part EMBARK trial (NCT05096221).

METHODS: Key inclusion criteria: Ambulatory males aged ≥4—<8 years with a confirmed DMD mutation within exons 18–79 (inclusive); North Star Ambulatory Assessment (NSAA) score >16 and <29 at screening; rAAVrh74 antibody titers <1:400; stable daily oral corticosteroid dose for ≥12 weeks pre-screening. Patients received single dose delandistrogene moxeparvovec (1.33×1014 vg/kg) or placebo. Primary endpoint was change from baseline to week 52 in NSAA total score.

RESULTS: At week 52 (N=125), the primary endpoint was not statistically significant least-squares mean between-group difference for delandistrogene moxeparvovec (n=63) vs. placebo (n=61) was 0.65 points (P=0.2441). Between-group differences for time to rise, 10-meter walk/run, stride velocity 95th centile, and time to ascend 4 steps favored the treatment group (P<0.05, nominal). Treatment-related treatment-emergent adverse events (AEs) included vomiting (54.0%), nausea (31.7%), and decreased appetite (27.0%), with no study discontinuations, deaths, or complement-mediated AEs. A prespecified global statistical test on a composite of functional endpoints supported treatment benefit (P=0.0044).

SUMMARY/CONCLUSION: Although the primary endpoint was not met, the totality of functional assessments suggested beneficial modification of disease trajectory. The safety profile was manageable and consistent with prior experience.

Disclosures:

Jerry Mendell - received study funding from Sarepta Therapeutics, Inc. while at Nationwide Children's Hospital at the time of the study and is currently an employee of Sarepta Therapeutics. Jerry R Mendell is a co-inventor of AAVrh74.MHCK7.micro-dys technology.

Ulrike Schara-Schmidt - has received honoraria for counseling and participating in invited talks from Sarepta Therapeutics and F. Hoffmann-La Roche Ltd.

Aravindhan Veerapandiyan - has a consultancy/advisory role with AMO Pharma, AveXis, Biogen, Edgewise Therapeutics, FibroGen, Novartis, Pfizer, PTC Therapeutics, Sarepta Therapeutics, Inc., UCB Pharma, Catalyst, and Scholar Rock; has received research funding from AMO Pharma, Capricor Therapeutics, Edgewise Therapeutics, FibroGen, Muscular Dystrophy Association, Novartis, Parent Project Muscular Dystrophy, Pfizer, RegenxBio and Sarepta Therapeutics, Inc.; and has other relationship(s) with MedLink Neurology for editorial services.

Craig Zaidman - has received research support from Biogen and Novartis and has served on an advisory board for Sarepta Therapeutics.

Alex Murphy - is an employee of Roche Products Ltd and may have stock options in F. Hoffmann-La Roche Ltd.

Jacob Elkins - is an employee of Sarepta Therapeutics and may have stock options.

Louise Rodino-Klapac - is an employee of Sarepta Therapeutics and may have stock options. In addition, she is a co-inventor of AAVrh74.MHCK7.micro-dys technology.

Francesco Muntoni - has received honoraria and grants from Sarepta Therapeutics for participating at symposia and advisory boards and is involved as an investigator in Sarepta Therapeutics clinical trials. He reports participation in advisory boards for Novartis, F. Hoffmann-La Roche Ltd, Edgewise, Dyne Therapeutics, Pfizer, PTC Therapeutics, and Italfarmaco.

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Crystal Proud - participates on an advisory board and is a consultant for Biogen, Sarepta Therapeutics, AveXis/Novartis Gene Therapies, Genentech/Roche, and Scholar Rock; serves as a speaker for Biogen; and is a PI of studies sponsored by AveXis/Novartis Gene Therapies, AMO, Astellas, Biogen, CSL Behring, Fibrogen, PTC Therapeutics, Pfizer, Sarepta Therapeutics, and Scholar Rock.

MOTOR UNIT NUMBER INDEX AND REVISED UPPER LIMB MODULE IN SPINAL MUSCULAR ATROPHY

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INTRODUCTION: Late-stage spinal muscular atrophy (SMA) requires sensitive functional and EDX measures to look for treatment response. Motor unit number index (MUNIX) and revised upper limb module (RULM) are two such biomarkers.

OBJECTIVE: To study MUNIX and RULM in non-ambulatory SMA.

METHODS: Retrospective review of genetically confirmed (3SMN2) SMA children (January 2017 to December 2023). Hammersmith functional motor scale-expanded (HFMSE), RULM, Children's Hospital of Philadelphia infant test of neuromuscular disorders (CHOP-INTEND), right abductor pollicis brevis (APB) and abductor digiti minimi (ADM), Compound motor action potencial (CMAP), MUNIX, and motor unit size index (MUSIX) were performed on disease-modifying therapies (intrathecal nusinersen, oral risdiplam) at baseline and follow-up, assessments compared using Wilcoxon rank sum test. Spearman's Rank Correlation Coefficients tested associations between post-therapy functional and EDX measures.

RESULTS: Nine patients, median age 8 years (two girls, seven boys) with median duration of treatment 17 months (n=6 risdiplam, n=1 nusinersen, n=2 switched nusinersen to risdiplam). Baseline and follow-up median values HMFSE (pre 9, post 4, max 66), CHOP-INTEND (pre 44, post 39, max 64), CMAPs right APB (pre 5.91, post 5.29 mV), right ADM (pre 1.64, post 1.33 mV), MUNIX right APB (pre 53, post 66), right ADM (pre 13, post 14) and MUSIX right APB (pre 90, post 127), right ADM (pre 122, post 149) showed no statistical difference. Post-therapy, RULM (15, max 37) correlated moderately with MUNIX APB (Spearman r = 0.77, p = 0.016).

SUMMARY/CONCLUSION: MUNIX APB and RULM are promising measures for disease progression assessment. Study limitations include small samples and short follow-up.

ANOMALOUS INNERVATION OF THE FOOT- TIBIAL FOOT

Igal Mirman (Knoxville, TN)

CASE REPORT: A 68-year-old male was referred for EMG evaluation of peripheral neuropathy with gait disturbance from general neurology due to progressive difficulty walking for 1 year associated with multiple falls, without motor sensory changes. There was a past medical history for squamous cell carcinoma status post resection, L5-S1 fusion with spinal cord stimulator for pain. Physical examination found normal strength and reflexes (including dorsiflexion, toe extensors), and on sensory evaluation, mild vibratory loss at the toes. Other findings included normal gait, toe, and heel walk, Romberg sign, and mild difficulty with tandem walk.

NCSs demonstrated normal sural response (7cm[8.5 µA], 14cm[6.8 µA], and 21cm[4.4 µA]), tibial-abductor hallucis, fibular-tibialis anterior (TA), median-abductor pollicis brevis, and median antidromic (digit-2) responses. During fibular-extensor digitorum brevis (EDB) stimulation no response was elicited at the anterior ankle, lateral to the TA tendon, below the fibular head, or in lateral popliteal fossa above the fibular neck-however a “fibular twitch” was observed at all sites. Lateral malleolus was stimulated without any response. The tibial nerve was attempted to be stimulated in the medial malleolus (with “tibial twitch”) and normal response obtained as it was in middle of the popliteal fossa. (figure, video 1). Tibial foot has been reported priorly. The author had no knowledge of these reports when preforming this study, however normal strength examination and mild sensory abnormality in-setting of absent EDB response isn’t typical, which triggered examining for anomalous innervation including fibular accessory nerve, but also the tibial nerve (with concerns of “ulnar hand” equivalent). Most of the prior reports of all tibial foot had responses of skepticism. However, goal of this case report is to increase awareness.

EVALUATION OF THE DURABILITY OF LONG-TERM IVIG IN MULTIFOCAL MOTOR NEUROPATHY

Jennifer Morganroth (Philadelphia, PA), Madeline Singer (Philadelphia, PA)

INTRODUCTION: Multifocal motor neuropathy (MMN) is a chronic progressive immune mediated motor neuropathy. Intravenous immunoglobulin (IVIg) has shown benefit in several randomized control trials and is currently the first line treatment for MMN. Although the majority of patients show initial improvement with IVIg, a select number of patients in clinical practice develop disease progression overtime despite maintenance IVIg. Some of these patients respond to increased IVIg dosing; however, others continue to progress. With the development of new therapies for MMN, it is important to understand how patients respond to IVIg overtime and which patient would be potential candidates for alternative patients.

OBJECTIVE: To evaluate degree and durability of response to IVIg in patients with MMN.

METHODS: This is a retrospective cohort study based on chart review of patients at The University of Pennsylvania diagnosed with MMN over the last 10 years and who are placed on IVIg therapy. We plan to use descriptive statistics to evaluate time to decline on IVIg therapy as defined by any point reduction in MRC-sum scores. We also assess for any disease progression requiring treatment change.

RESULTS: We have submitted for internal review board approval but expect to begin chart reviewing to obtain these results in the next month. Estimated number of patients is 20-30.

SUMMARY/CONCLUSION: We expect to see a proportion of patients with MMN develop clinical worsening while on IVIg as demonstrated by a decline in MRC-sum score or a change in treatment regimen. This study will potentially highlight the importance of studying new emerging therapies for treatment of MMN.

APPLICATION OF ELECTROPHYSIOLOGICAL TECHNIQUES AND ULTRASONOGRAPHY IN ULNAR NERVE INJURIES: A CASE STUDY IN AN ADULT WORKER

Jorge Nicolas Munoz - Rodriguez (Bogotá, Colombia), Liliana Rodriguez (Bogotá, Colombia), Jorge Diaz-Ruiz (Bogotá, Colombia)

INTRODUCTION: A 46-year-old male patient experienced a work-related accident 3.5 months ago, resulting in sharp pain in the fifth finger and right forearm while pulling a scythe rope. Referred for electro-physiological evaluation of the upper limbs due to decreased sensitivity in the fifth finger of the right hand, associated with a cutting trauma in the right forearm 20 years ago, without subsequently diagnosed nerve injury.

OBJECTIVE: Physical examination revealed hypoesthesia in the middle and distal phalanx of the right fifth finger, with reduced trophism of the right hypothenar eminence. The EDX studies revealed the absence of sensory response in the right ulnar nerve, as well as a motor conduction block below the elbow and a diminished motor conduction velocity along the ulnar nerve. Additionally, EMG demonstrated diminished recruitment, along with signs indicative of acute denervation and chronic reinnervation in the abductor digiti minimi muscle.

METHODS: Neuromuscular ultrasonography demonstrated an increase in the cross-sectional area of the right ulnar nerve at the proximal third of the forearm, with changes in echotexture, coinciding with the old traumatic scar. At the elbow, the cross-sectional area of the nerve was normal.

RESULTS: It was concluded as a partial axonal injury of the right ulnar nerve in chronic phase, related to the previous trauma, which could have been exacerbated by recent traction.

SUMMARY/CONCLUSION: This case highlights the utility of neuromuscular ultrasonography in topographic evaluation and elucidation of injury mechanisms in workers.

SAFETY AND EFFECTIVENESS OF RAVULIZUMAB IN GENERALIZED MYASTHENIA GRAVIS: EVIDENCE FROM A GLOBAL REGISTRY

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INTRODUCTION: Complement C5 inhibitor therapies (C5ITs) eculizumab and ravulizumab are approved in the US and EU for anti-acetylcholine-receptor-antibody-positive (AChR+) generalized myasthenia gravis (gMG).

OBJECTIVE: The ongoing, global MG-SPOTLIGHT Registry is assessing ravulizumab safety and effectiveness in patients with gMG in routine clinical practice using the MG Activities of Daily Living (MG-ADL; includes minimum symptom expression [MSE] outcome) and MG Foundation of America clinical class (MGFA-CC) assessments.

METHODS: This interim analysis includes ravulizumab-treated patients with MG-ADL total scores or MGFA-CC data for ≥2 time points (before and after initiating C5IT). Descriptive statistics were performed and presented as mean (SD). Safety was assessed by frequency of serious adverse events (SAEs).

RESULTS: Of 70/204 enrolled patients (63% male; aged 60.4 [19.0] years at MG diagnosis), 17 received ravulizumab only and 53 transitioned to ravulizumab from eculizumab; ravulizumab treatment averaged three to four months. In ravulizumab-only patients, MG-ADL score decreased from 5.8 (3.4) to 3.4 (3.3) after ravulizumab initiation; in ravulizumab-switch patients, MG-ADL scores remained stable from 3.7 (4.2) to 3.4 (3.2) following ravulizumab initiation. In ravulizumab-only patients, the 66.7% with MGFA-CC 0-II increased to 88.9% after ravulizumab initiation; in ravulizumab-switch patients, the 92.0% with MGFA-CC 0-II remained stable at 96.0% following ravulizumab initiation. Similar patterns were observed in patients achieving MG-ADL MSE. SAEs were similar to previous findings. Limitations included no adjustment for confounders and small sample sizes.

SUMMARY/CONCLUSION: In clinical practice, ravulizumab was well tolerated and effective, with improved activities of daily living and MGFA-CC after initiating ravulizumab and sustained improvements when transitioning from eculizumab.

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James F. Howard Jr. - has received research support (paid to institution) from Alexion, AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention (Atlanta, GA, USA), the Muscular Dystrophy Association, the Myasthenia Gravis Foundation of America, the National Institutes of Health (including the National Institute of Neurological Disorders and Stroke and the National Institute of Arthritis and Musculoskeletal and Skin Diseases), PCORI, Ra Pharmaceuticals (now UCB Pharma), and Takeda Pharmaceuticals; honoraria from AcademicCME, Alexion, AstraZeneca Rare Disease, argenx, Biologix Pharma, F. Hoffmann-La Roche Ltd, Horizon Therapeutics, Immunovant, Medscape CME, Merck EMB Serono, Novartis Pharmaceuticals, PeerView CME, Ra Pharmaceuticals (now UCB), Regeneron Pharmaceuticals, Sanofi US, and Zai Laboratories; and nonfinancial support from Alexion, AstraZeneca Rare Disease, argenx, Ra Pharmaceuticals (now UCB), and Toleranzia AB.

Samir Macwan - has consulted for AbbVie, Alexion, AstraZeneca Rare Disease, argenx, Catalyst, Grifols, KabaFusion, Supernus, and UCB.

James M. Winkley - has consulting agreements with Alexion, AstraZeneca Rare Disease, Biogen, Bristol Myers Squibb, and Teva.

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Michael Pulley - has received compensation for medical advisory board membership or regional advisory board participation from Alexion, AstraZeneca Rare Disease, argenx, Catalyst, CSL Behring, Immunovant, and UCB.

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STEROID USE, TOXICITY, AND MONITORING IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: A SURVEY OF NEUROLOGISTS IN THE UNITED STATES

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INTRODUCTION: The 2020 international consensus guidance recommends corticosteroids (CSs) as standard immunosuppressive therapy for generalized myasthenia gravis (gMG); however, patients treated with CSs should be monitored for CS toxicity/adverse effects.

OBJECTIVE: We surveyed board-certified United States-based neurologists to assess awareness and monitoring of CS toxicity.

METHODS: Cross-sectional online survey was completed by neurologists (n=101) managing ≥10 patients with gMG/year (≥10 mg CS for ≥1 month).

RESULTS: Neurologists reported that ~60% of their patients have been treated with CSs and ~40% with nonsteroidal immunosuppressants. Regarding CS dose and duration, ~50% of neurologists said they consider CS dose ≤10 mg/day (prednisone equivalent) well tolerated in long-term use (≥6 months) but that ~50% of their patients are unable to taper to <10 mg/day. The survey showed that 77% of neurologists were very/extremely familiar with CS toxicity; they identified increased appetite/weight gain (58%), insulin resistance (50%), decreased bone density (48%), and immunosuppression (45%) as the most-common adverse effects of long-term CS use. The neurologists said they typically monitor CS toxicity alone (84%) or in conjunction with primary care providers (41%). To balance effectiveness and toxicity, 48% rely on clinical experience/training alone, and 53% use recommendations from guideline(s). Most neurologists (88%) said a tool for systematically monitoring CS toxicity would be valuable.

SUMMARY/CONCLUSION: Responses show that although more than three-fourths of neurologists monitor and manage CS toxicity in patients with gMG, approximately half use guidelines to do so. This suggests that clearer guidance on how to administer CSs and manage toxicities would be welcomed by neurologists, with potential for benefit to patient care.

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Gil Wolfe - is a consultant/advisor for Alexion, argenx, BPL, Cartesian, Grifols, Janssen, Takeda, and UCB and receives or has received research support from Alexion, argenx, Immunovant, Roche, UCB, and the Myasthenia Gravis Foundation of America.

Deborah Gelinas - is an employee of argenx.

Tom Hughes - is an employee of argenx.

Vijayaraghava Rao - is an employee of argenx.

Paul Nisbet - is an employee of One Research, LLC, which was paid by argenx to conduct the survey and analyze the data.

John Stone - has served as a consultant to argenx on glucocorticoid toxicity and is the chair of the Scientific Advisory Board at Steritas.

Pushpa Narayanaswami - is a consultant/advisor for argenx, Alexion, UCB, Janssen, Dianthus, GSK, and Novartis; has served on a data safety monitoring board for Sanofi; and receives or has received research support from PCORI, Alexion, Janssen, Dianthus, and UCB, and receives royalties from Springer Nature.

CONCOMITANT CORTICOSTEROID USE WITH RAVULIZUMAB IN ADULTS WITH ANTI-ACETYLCHOLINE RECEPTOR ANTIBODY-POSITIVE GENERALIZED MYASTHENIA GRAVIS: PHASE 3 CHAMPION-MG OPEN-LABEL EXTENSION FINAL RESULTS

Michael Nicolle (London, Canada), Djillali Annane (Garches, France), Andreas Meisel (Berlin, Germany), Tuan Vu (Tampa, FL), Renato Mantegazza (Milan, Italy), Masahisa Katsuno (Nagoya, Japan), Vera Bril (Toronto, Canada), Rasha Aguzzi (Boston, MA), Glen Frick (Boston, MA), James F. Howard Jr. (Chapel Hill, NC)

INTRODUCTION: Treatment guidelines recommend steroid-sparing strategies in generalized myasthenia gravis (gMG) to reduce steroid dosages to ≤5 or ≤10 mg/day and minimize risk of steroid-associated adverse effects. Corticosteroid (CS) adjustments were not permitted during the 26-week, double-blind, randomized, placebo-controlled period (RCP) of the CHAMPION-MG study of ravulizumab in adults with anti-acetylcholine receptor antibody-positive (AChR+) gMG, but RCP completers could receive ravulizumab in the open-label extension (OLE), which permitted CS adjustments (at physicians' discretion).

OBJECTIVE: Evaluate changes in CS use in ravulizumab-treated adults with AChR+ gMG.

METHODS: In the OLE (NCT03920293), patients could receive intravenous ravulizumab (blind induction or bridging dose at week 26 [OLE start] for those previously receiving placebo or ravulizumab, respectively, then 3000 mg-3600 mg according to body weight at week 28 and every 8 weeks thereafter) for up to four years. CS use was assessed at each study visit.

RESULTS: Data were available for 161 patients who entered the OLE and received ravulizumab for up to 164 weeks. Overall, 113 received oral/enteral CS during the OLE (112 were receiving CS at OLE start); treated with >10 mg/day CS decreased from 58% (n=66) at first OLE dose to 37% (n=42) (with 35 patients [31%] receiving ≤5 mg/day and 71 [63%] receiving ≤10 mg/day) at last reported dose. Fourteen patients (12%) discontinued CS by the last visit. The mean (SD) CS dosage/patient decreased from 17.5 (11.9) mg/day (first OLE dose) to 11.7 (10.9) mg/day (last assessment).

SUMMARY/CONCLUSION: Decreased CS use was observed in ravulizumab-treated patients with AChR+ gMG, suggesting a steroid-sparing role for ravulizumab.

The authors acknowledge the contributions of the CHAMPION-MG Study Group.

Disclosures:

Michael Nicolle - has received speaker honoraria from Alexion, AstraZeneca Rare Disease, argenx, and UCB; is a member of advisory board and/or consulted for Alexion, AstraZeneca Rare Disease, argenx, Dianthus, Janssen, Kye Pharmaceuticals, and UCB; has worked on clinical trials that received funding from pharmaceutical companies (currently Alexion, AstraZeneca Rare Disease, and Regeneron).

James F. Howard Jr. - has received research support (paid to institution) from Alexion, AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention (Atlanta, GA, USA), the Muscular Dystrophy Association, the Myasthenia Gravis Foundation of America, the National Institutes of Health (including the National Institute of Neurological Disorders and Stroke and the National Institute of Arthritis and Musculoskeletal and Skin Diseases), PCORI, Ra Pharmaceuticals (now UCB Pharma), and Takeda Pharmaceuticals; honoraria from AcademicCME, Alexion, AstraZeneca Rare Disease, argenx, Biologix Pharma, F. Hoffmann-La Roche Ltd, Horizon Therapeutics, Immunovant, Medscape CME, Merck EMB Serono, Novartis Pharmaceuticals, PeerView CME, Ra Pharmaceuticals (now UCB), Regeneron Pharmaceuticals, Sanofi US, and Zai Laboratories; and nonfinancial support from Alexion, AstraZeneca Rare Disease, argenx, Ra Pharmaceuticals (now UCB), and Toleranzia AB.

Djillali Annane - has received study funding (paid to institution) from Alexion, AstraZeneca Rare Disease, and serves on the CHAMPION-MG study steering committee.

Andreas Meisel - has received speaker honoraria from Alexion, AstraZeneca Rare Disease, argenx, Grifols, and Hormosan; honoraria for consulting services from Alexion, AstraZeneca Rare Disease, argenx, Janssen, and UCB; and financial research support from Alexion, AstraZeneca Rare Disease, and Octapharma. He is chairman of the medical advisory board of the German Myasthenia Gravis Society.

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Rasha Aguzzi - is an employee of Alexion, AstraZeneca Rare Disease, and holds stock options in AstraZeneca.

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SAFETY, TOLERABILITY, EFFICACY, PHARMACOKINETICS, AND IMMUNOGENICITY OF ARGX-119 IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS: A PHASE 2A STUDY IN PROGRESS

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INTRODUCTION: ALS is a fatal neurodegenerative disorder of the neuromuscular system, characterized by progressive loss of motor neurons, resulting in muscle weakness and atrophy. Neuromuscular junction disassembly and muscle denervation are key features of ALS. ARGX-119, a humanized, agonistic, monoclonal antibody, specifically targets and activates MuSK, which has a critical role in the establishment, maintenance, and function of the neuromuscular junction. ARGX-119 has the potential to slow muscle denervation and maintain muscle function in patients with ALS.

OBJECTIVE: To assess the safety, tolerability, preliminary efficacy, pharmacokinetics, and immunogenicity of ARGX-119 in participants with ALS.

METHODS: This Phase 2a multicenter, double-blinded study is planned to enroll approximately 60 participants, randomized 1:1:1:1 to one of three dose levels of ARGX-119 or placebo IV once every other week for the first 4 weeks, then every 4 weeks, for the 24-week double-blinded treatment period. Participants will then enter the 48-week active treatment extension period, and all will receive ARGX-119, but remain blinded for the initial allocation (delayed-start design). After the extension period, participants will enter a 32-week safety follow-up period.

RESULTS: The primary endpoint is safety. Key secondary endpoints are rate of change of MScan-derived motor unit number from baseline to week 24, assessment of pharmacokinetic parameters of ARGX-119, and development of antidrug antibodies against ARGX-119. Multiple exploratory endpoints are included to assess additional neurophysiology endpoints, clinical outcome measures, and mobility at home.

SUMMARY/CONCLUSION: This Phase 2a study will assess the safety, tolerability, preliminary efficacy on motor unit number, pharmacokinetics, and immunogenicity of ARGX-119 in ALS.

Disclosures:

Ruben P. A. van Eijk - research funding (paid to Institute): argenx.

Roeland Vanhauwaert - is an employee of argenx.

Rebecca Shilling - is an employee of argenx.

Leonard van den Berg - is a consulting honoraria for argenx, Biogen, Novartis, Roche, Takeda.

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PRIMARY SPEECH APRAXIA FOR NEARLY 10 YEARS THAT DEVELOPS INTO MOTOR NEURON DISEASE: AMYOTROPHIC LATERAL SCLEROSIS VARIANT

Emma Orozco (Albuquerque, NM), Jonathan Cauchi (Albuquerque, NM), John Adair (Albuquerque, NM), Amanda Deligtisch (Albuquerque, NM)

INTRODUCTION/BACKGROUND: ALS patients typically have a lifespan of 3 to 5 years from symptom onset, with shorter survival in bulbar presentations. Despite known clinical variability, apraxia is rarely found as feature of the disease. This case describes a patient with apraxia developing over a decade before the onset of limb weakness and lower motor neuron (LMN) signs.

CASE REPORT: A 57-year-old woman presented after 4 years of progressive dysarthria. Exam showed no neurogenic atrophy or pyramidal signs. Initial diagnostic work-up was inconclusive, including EMG/NCS evaluation. Brain MRI showed bilateral frontoparietal atrophy.

By 7 years, she was aphemic but communicated effectively through text-to-speech, demonstrating intact cognitive functions. Clinical assessment revealed buccolingual and limb apraxia, inability to fixate on objects, and lip closure weakness. ALS genetic testing, including C9ORF72 was negative.

Dysphagia progressed, requiring gastrostomy tube placement. Subsequently, severe sialorrhea manifested. Nearly 10 years later, she exhibited muscle atrophy, upper extremities weakness, and increased tone in left arm. Ambulation remains minimally affected and she has not exhibited personality or mood symptoms.

SUMMARY/CONCLUSION: This case exemplifies a rare presentation of progressive apraxia, extending the clinical spectrum of motor neuron diseases. The decade-long presence of apraxia preceding weakness suggests discrete degeneration of prefrontal rather than primary motor cortex. Clinical features of ALS with frontotemporal dementia (FTD) spectrum (including corticobasal syndrome and progressive nonfluent aphasia), reflect premotor dysfunction. Our patient’s disorder falls beyond clinical boundaries ascribed to ALS with FTD due to protracted survival with delayed motor neuron findings, emphasizing ALS and similar conditions' complexity and variability.

THE USE OF MUSCLE ULTRASONOGRAPHY IN DIAGNOSING AMYOTROPHIC LATERAL SCLEROSIS.

Jerne Kaz Niels Paber (Zamboanga, Philippines)

INTRODUCTION: Ultrasonography has been extensively studied in various neuromuscular disorders, including demyelinating polyneuropathy, leprosy, traumatic neuropathy, and motor neuron disease. This case will specifically focus on the use of neuromuscular ultrasound (US) in amyotrophic lateral sclerosis (ALS).

The patient was positioned supine during the US examinations. Consistent with previous studies, the US was conducted in the transverse plane using standard transducer placements over the muscle bellies. Muscle observations were conducted for 60 s to identify the presence or absence of fasciculations. Fasciculations were defined as involuntary twitching of small portions of the muscle, with a minimum of two required for classification as present. Due to the patient's greater weakness on the right side, unilateral testing of the upper and lower limbs on the right side was performed. Eleven muscles were selected, and muscle US revealed fasciculations in 10 out of the 11 muscles.

SUMMARY/CONCLUSION: Muscle US can detect fasciculations, which are early signs of ALS. Further evaluation by a neurologist or an expert in neuromuscular disorders can lead to early diagnosis and disease management which are essential in ALS to provide appropriate care and to optimize quality of life.

INCIDENCE AND OUTCOME OF MENINGOCOCCAL INFECTION WITH ECULIZUMAB OR RAVULIZUMAB IN PATIENTS WITH GMG OR NMOSD: AN ANALYSIS OF US CLINICAL PRACTICE

Shirali Pandya (Boston, MA), Lokesh Jha (Boston, MA), Imad Al-Dakkak (Boston, MA), Feifei Yang (Boston, MA), Vidya Chitikireddi (Boston, MA), Hua Zhang (Boston, MA), Arshad Mujeebuddin (Boston, MA)

INTRODUCTION: Eculizumab and ravulizumab are effective treatments for generalized myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD). Safety mitigations, including vaccinations, are used to reduce the risk of Neisseria meningitidis (Nm) infection associated with these treatments.

OBJECTIVE: To evaluate US exposure-adjusted Nm infection and mortality in eculizumab- or ravulizumab-treated patients with gMG and NMOSD using postmarketing pharmacovigilance data (Nm case counts) and commercial data (exposure).

METHODS: The United States (US) Alexion safety database was searched for eculizumab and ravulizumab (data cutoff: December 2022) across approved indications (gMG, NMOSD, paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome) using the MedDRA High Level Term “Neisseria infection.” Only Nm-associated cases were included. Reporting rates were calculated cumulatively per 100 patient-years (PY).

RESULTS: US Nm infection and mortality annual reporting rates in eculizumab-treated patients remained stable over 15 years across approved indications (2022: 0.13 and 0.01, respectively; exposure: 29,758.4 PY). In 2022, US postmarketing Nm infection reporting rates in eculizumab-treated patients with gMG and NMOSD were 0.02 (exposure: 8,042.0 PY) and 0.07 (exposure: 1,470.1 PY), respectively. At data cutoff, there were no Nm infections among ravulizumab-treated patients with gMG. No Nm fatalities were noted for eculizumab- or ravulizumab-treated patients with gMG and NMOSD.

SUMMARY/CONCLUSION: Nm infection and mortality reporting rates for patients with gMG and NMOSD remained stable despite increasing eculizumab and ravulizumab exposure over time. These results suggest US Nm-related risk mitigation strategies are effective in patients receiving eculizumab or ravulizumab.

Disclosures:

Shirali Pandya - is an employee of, and holds stock in, Alexion, AstraZeneca Rare Disease.

Lokesh Jha - is an employee of, and holds stock in, Alexion, AstraZeneca Rare Disease.

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EVOLVING GLOBAL EPIDEMIOLOGY OF MYASTHENIA GRAVIS: RESULTS FROM A SYSTEMATIC LITERATURE REVIEW

Jenny Y. Park (Thousand Oaks, CA), Moon Seok Kim (Thousand Oaks, CA), Conor McCloskey (London, United Kingdom), Kristina R. Patterson (Thousand Oaks, CA), Andrea Meyers (Thousand Oaks, CA)

INTRODUCTION: Myasthenia gravis (MG) is a rare, chronic, autoimmune disease which can cause significant disability and reduce quality of life. Recent publications characterize the increasing prevalence and evolving global epidemiology of MG.

OBJECTIVE: To describe global MG epidemiology trends with a focus on incidence, prevalence, comorbidities, and mortality.

METHODS: A comprehensive search was conducted across Embase, Medline, Cochrane Database, and congress submissions from 2006 to 2023. MG studies reporting epidemiology outcomes were identified with prespecified PICOS criteria.

RESULTS: Eighty-eight publications were identified, predominantly from Europe (65%) and 18% from the US. MG incidence rates varied widely by region, ranging from 9.4 (Denmark) to 38.8 (Argentina) per million person-years. Prevalence also varied, ranging from 12.9/100,000 (Italy) to 39.2/100,000 (Germany). Despite geographic differences, studies consistently demonstrated an increase in MG incidence and prevalence over time. MG prevalence increased 7-fold from 1934 to 2021, more than doubling in the last 20 years. The substantial increase may partially be attributed to prolonged MG survival: in-hospital MG mortality considerably decreased from 15.4% in 1992 to 12.6% in 2002 and further to 1.8% in 2019. Respiratory failure and age were the most important predictors of death. Comorbidities among patients with MG were common and frequently included depression and other autoimmune conditions such as thyroid disease.

SUMMARY/CONCLUSION: Epidemiology of MG varies by region, age, sex, and antibody status. Overall, the increasing number of patients with MG are aging and presenting with more comorbidities. These findings underscore the need for effective and tailored therapies to reduce treatment burden and improve patient outcomes.

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Jenny Y. Park - is an employee and stockholder of Amgen Inc.

Moon Seok Kim - is a contract worker for Amgen Inc.

Conor McCloskey - is an employee of Clarivate, which was commissioned to perform this systematic literature review by Amgen Inc.

Kristina R. Patterson - is an employee and stockholder of Amgen Inc.

Andrea Meyers - is an employee and stockholder of Amgen Inc.

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THE BURDEN OF GLUCOCORTICOID USE AMONG PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS IN THE UNITED STATES

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INTRODUCTION: While glucocorticoids (GCs) are commonly used to manage generalized myasthenia gravis (gMG), GC-associated toxicities may result in adverse patient outcomes.

OBJECTIVE: To characterize real-world GC burden, toxicities, and health outcomes among patients with gMG.

METHODS: Adults with gMG were identified in the IQVIA PharMetrics+ database (10/01/2015–12/31/2022). Patients were stratified by mean daily prednisone equivalent dose (PED) over the most recent 12 months of health plan enrollment: No-GC, GC (PED>0mg), 5-GC (PED≥5mg), and 10-GC (PED≥10mg) cohorts. Clinical characteristics, incident GC toxicities, healthcare resource utilization (HRU), and costs were described.

RESULTS: The cohort included 8,833 gMG patients: No-GC (n=5,076), GC (n=3,757), 5-GC (n=1,537), and 10-GC (n=860). Higher GC use was associated with considerably higher rates of incident toxicities. Patients in the 5-GC and 10-GC cohorts were more likely to have ≥3 toxicities than the No-GC cohort. Both acute and chronic toxicities were more commonly observed in the 5-GC (acute: 30.1%, chronic: 53.4%) and 10-GC (acute: 36.0%, chronic: 57.1%) cohorts than the No-GC cohort (acute: 19.1%, chronic: 43.8%). Notable GC toxicities included sepsis (No-GC: 1.7%, 5-GC: 5.5%, 10-GC: 7.4%), fungal infections (No-GC: 3.8%, 5-GC: 6.4%, 10-GC: 8.7%), hypertension (No-GC: 7.2%, 5-GC: 9.0%, 10-GC: 9.5%), osteoporosis (No-GC: 1.6%, 5-GC: 4.5%, 10-GC: 5.1%). HRU and costs were higher among patients treated with steroids and further increased with increasing GC use.

SUMMARY/CONCLUSION: Patients with gMG were characterized by substantial GC burden associated with increased toxicities and suboptimal health outcomes. This study highlights the need for effective disease-modifying treatments to mitigate GC exposure for improved gMG management and patient outcomes.

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Nicholas Silvestri - is a consultant/advisor for Argenx, Alexion, Immunovant, Janssen, and UCB; speaker for Argenx, Alexion, and UCB.

Jenny Y. Park - is an employee and stockholder of Amgen Inc.

Elizabeth Serra - is an employee of Analysis Group Inc, providing paid consulting services for Amgen Inc.

Annie Guerin - is an employee of Analysis Group Inc, providing paid consulting services for Amgen Inc.

Kristina Patterson - is an employee and stockholder of Amgen Inc.

Andrea Meyers - is an employee and stockholder of Amgen Inc.

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INFLAMMATORY MYOPATHY, A RARE ENTITY IN PEDIATRICS

Dary Parra Parraga (Bogotá, Colombia)

INTRODUCTION/BACKGROUND: Juvenile idiopathic or childhood-onset inflammatory myopathies (JIIMs) are a group of rare but serious conditions in children and young adults that predominantly affect the muscles and skin, but may also affect other organs, including the lungs, intestine, joints, heart and central nervous system.

CASE REPORT: The case of a 14-year-old patient is described, presenting with predominantly proximal muscle weakness in upper and lower limbs for 2 months, recurrent falls, and denying recent flu symptoms. The patient has a history of surgical correction of bilateral clubfoot. The patient was referred to the electrodiagnostic laboratory due to hypotonia, muscle weakness, and gait alterations, without sensory alterations. In the study, sensory nerve action potental and compound muscle action potential of all four limbs were present. However, EMG documented electrical silence at rest, myopathic motor unit potentials in bilateral biceps and left gastrocnemius muscles, rapid recruitment in biceps, vastus medialis, gastrocnemius and left deltoid muscles. The rest of the muscles examined were normal, concluding intrinsic disease of the muscle fiber predominantly muscular. An MRI of the bilateral thigh was suggestive of inflammatory myopathy with a heterogeneous fatty infiltration pattern. Report of CPK in 12394, with therapeutic response to corticosteroids, decrease in creatine phosphokinase (CPK)to 3166. Infectious, metabolic, and inflammatory cause is ruled out.

SUMMARY/CONCLUSION: Inflammatory myopathy is a rare entity in the pediatric population that may be associated with immunological etiology. Its clinical course may be similar to dystrophinopathy, however the findings in EMG, CPK, and muscle magnetic resonance are initial studies that can guide the diagnosis.

WEST NILE ENCEPHALITIS ADVANCING TO ACUTE FLACCID MYELITIS

Krima Patel (Brick, NJ), Sameer Ali (West Haven, CT), Divisha Raheja (Center Valley, PA)

INTRODUCTION/BACKGROUND: Patient is a 75-year-old male presented for altered mental status, fever, and general malaise for 5 days. Prior to presentation, the patient had an active lifestyle with fulfilling his own activities of daily living (ADL)s. With testing, he was diagnosed with acute flaccid myelitis (AFM) secondary to West Nile encephalitis (WNE).

CASE REPORT: During the hospital course, the patient had waxing and waning mental status. MRI Brain was unremarkable. Lumbar puncture (LP) showed 35 white blood cells and 118 proteins. Lyme IgG positive and Neg IgM, and IgM positive West Nile. Then, the patient was noted to have mild weakness in the lower extremities, L>R. Patient was treated with doxycycline for 14 days for possible Lyme and supportive care for WNE. Of note, patient developed urinary retention and constipation. Spine imaging was recommended but not performed given family's wishes. Patient was discharged to rehab.

One week later, patient was noted to have increased weakness, areflexia, urinary retention, and constipation and was re-hospitalized. A repeat LP was performed which showed pleocytosis of 249 and confirmed West Nile. EDX testing was consistent with acute neuropathy affecting predominantly motor fibers with axonal changes, no demyelinating features. These findings with confirmed West Nile correlate with an anterior horn cell disorder such as AFM.

Due to the clinical decline and the higher cerebral spinal fluid protein level, patient was treated with intravenous immunoglobulin (IVIg), symptoms stabilized, and was discharged to rehab.

SUMMARY/CONCLUSION: Long term prognosis is unknown for AFM. Steroids and plasmapheresis have not shown any benefit. IVIg may have a potential beneficial role in these patients.

THIAMINE DEFICIENCY MASQUERADING AS ACUTE MOTOR AND SENSORY AXONAL NEUROPATHY (AMSAN) IN THE SETTING OF HEAVY ALCOHOL USE

Parthkumar Patel (Washington, DC), Jenny Patel (Washington, DC), Michelle Offit (Washington, DC), Yasir Al-Khalili (McLean, VA)

INTRODUCTION/BACKGROUND: Thiamine (vitamin B1) deficiency is a rare cause of polyneuropathy, often observed in the United States with chronic alcoholism, post-gastrectomy, or anorexia nervosa. Neuromuscular manifestations of thiamine deficiency are a diagnostic challenge. We present a case of a patient with chronic alcoholism and known thiamine deficiency presenting with acute ascending weakness.

CASE REPORT: Patient is a 29-year-old female who presented with 3 weeks of bilateral lower extremity paresthesia and weakness that gradually progressed to bilateral upper extremity numbness and weakness, and eventual gait disturbance leading to dependence on walker. Physical exam remarkable for bilateral 4+/5 deltoids, 4/5 wrist flexion/extension, 4+/5 dorsiflexion, length dependent sensory loss, and trace reflexes throughout. Initial workup remarkable for thiamine level 89, GD1a Ab positivity, and unremarkable MRI brain and spinal cord. The initial EDX study showed diffuse sensory-motor polyneuropathy, primary axonal with marked ongoing denervation of the distal muscles bilaterally. She was then seen eight weeks after the initial presentation and noted to have significant improvement in motor strength, though still with sensory deficits and areflexia. The patient was initially treated with intravenous immunoglobulin (IVIg) for 5 days due to concern for acute motor and sensory axonal neuropathy and high dose thiamine.

SUMMARY/CONCLUSION: It is important to consider nutritional neuropathies when dealing with a patient who has chronic alcoholism. In case of an acute presentation of ascending neuropathy, it is necessary to prioritize thiamine as a possible cause, along with Guillain-Barré syndrome and its variants, as the treatment, prognosis and disease course differ among them.

ASSESSING THE SUITABILITY OF THE NEURO-QOL FATIGUE TO EVALUATE FATIGUE IN PATIENTS WITH MYASTHENIA GRAVIS

Sheryl Pease (Raritan, NJ), Kayla Scippa (Raritan, NJ)

INTRODUCTION: Generalized myasthenia gravis (gMG) is a rare, chronic, autoantibody-mediated neuromuscular disease characterized by fatigable muscle weakness.

OBJECTIVE: The objectives of this research were to identify an appropriate patient-reported outcome (PRO) measure to assess fatigue in patients living with gMG and to conduct patient interviews to evaluate the content validity of the measure.

METHODS: A literature review identified the Neuro-QoL Fatigue as a suitable candidate PRO to assess fatigue in gMG. Twenty-three interviews were conducted with adults living with gMG. All participants were recruited from the United States via research partners following internal review boardapproval. Each interview explored the symptoms and impacts of gMG on participants' daily lives. The final eight interviews included cognitive debriefing of the Neuro-QoL Fatigue to determine its appropriateness for use in gMG.

RESULTS: All participants reported experiencing fatigue as part of their experience with gMG and that fatigue impacted their ability to participate and carry out daily activities. Among those asked to provide bothersome ratings, 80% (n=12 of 15) reported that fatigue was their most bothersome symptom. The debriefing exercise demonstrated that nearly all participants interpreted the Neuro-QoL Fatigue instructions, items, and recall period as intended.

SUMMARY/CONCLUSION: Fatigue is a bothersome symptom of gMG that limits patients' abilities to participate in daily life. The interview insights support the content validity of the Neuro-QoL Fatigue in gMG patients. Future research will focus on evaluating the psychometric properties of the Neuro-QoL Fatigue in the gMG patient population.

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Kayla Scippa - employed by, and may hold stock or stock options in Johnson & Johnson.

RADIAL CONDUCTION BLOCK AND POSTERIOR INTEROSSEOUS NERVE: STAY ATTUNED WITH MULTIFOCAL MOTOR NEUROPATHY

Jose Pedro Soares Baima (São Paulo, Brazil), Carlos Heise (São Paulo, Brazil)

INTRODUCTION: Multifocal motor neuropathy (MMN) is a progressive asymmetric motor neuropathy with the main involvement of the upper limbs. Wrist drop or wrist extension weakness is a common presentation of either posterior interosseous nerve (PIN) or multifocal motor neuropathy, but treatment differs in these two conditions.

METHODS: We reviewed the charts and EDX studies of patients from 2014-2022, with a clinical diagnosis of MMN or PIN syndrome. Parameters included in the analysis were motor conduction velocity, the presence and magnitude of conduction block, motor distal latencies, and the amplitude of the affected radial nerve. Statistical significance was calculated with the Fisher test and U Mann-Whitney.

RESULTS: We found 12 patients with MMN and 16 patients with posterior interosseous syndrome. Six patients were excluded (four MMN and two PIN syndrome). A total of 43 radial NCS were included. Conduction block in the radial nerve was present in all patients with MMN and in two patients with PIN syndrome ($p < 0.05$). Axonal degeneration was present in four patients with MMN and in all patients with PIN syndrome ($p < 0.05$). Differences in distal motor latency or motor conduction velocity of the radial nerve were not statistically significant.

SUMMARY/CONCLUSION: Patients presenting clinically with selective radial involvement are at risk of misdiagnosis of PIN syndrome. When evaluating patients with suspected PIN syndrome, the presence of conduction block or the absence of distal compound muscle action potentials (CMAP) amplitude reduction should warn the EDX physician that MMN should be considered.

MYOPATHIC CHANGES IN ULTRASOUND AND EMG IN SYSTEMIC SCLEROSIS: CASE REPORT

Laura Pinzón (Bogotá D.C, Colombia), David Eliécer Rodríguez Rodríguez (Bogotá D.C., Colombia), Jorge Arturo Diaz Ruiz (Bogotá D.C., Colombia)

INTRODUCTION/BACKGROUND: Myopathy is a common musculoskeletal manifestation of systemic sclerosis (SSc). Scleromyositis is emerging as an entity in the spectrum between SSc and inflammatory myopathies. Although there is no specific case definition, it is described that up to 95% of patients may have symptoms related to weakness and myalgia.

CASE REPORT: A 39-year-old male diagnosed with SSc 7 years ago, presents with a 1-year history of generalized muscle weakness. Examination demonstrated, symmetric proximal weakness in the upper and lower extremities, and atrophy of the abductor pollicis brevis and first dorsal interosseous muscles. EDX testing was consistent with median neuropathy at the wrist bilaterally, in addition to low-amplitude compound motor unit potentials of the right peroneal and bilateral ulnar nerves. Conventional and quantitative interference pattern analysis (IPA) EMG showed units with myopathic characteristics and rapid recruitment in proximal muscles. There were signs of membrane instability proximally and some neuropathic units in distal muscles. The ultrasound scan showed increased echogenicity in muscles such as the biceps and tibialis anterior. The cross sectional areo of the median nerve was normal on both sides. The study was considered compatible with an inflammatory myopathy.

SUMMARY/CONCLUSION: Scleromyositis in an emerging entity. It is associated with a worse functional prognosis of the patient with SSc. At the EMG level, it is characterized by myopathic units with signs of membrane instability; Neuropathic patterns are also described. Quantitative EMG by IPA and neuromuscular ultrasound are complementary tools in unclear cases.

DOUBLE CRUSH MECHANISM DETECTED ON ULTRASOUND IN A PATIENT WITH DIABETES MELLITUS

Laura Pinzón (Bogotá D.C, Colombia), Liliana Rodriguez (Bogotá D.C., Colombia)

INTRODUCTION/BACKGROUND: The double crush phenomenon classically describes the entrapment of a peripheral nerve in different places along its path. Currently it is also used to describe the concomitant presence of other entities such as polyneuropathy or radiculopathy together with compressive neuropathy.

CASE REPORT: The case of a 67-year-old male patient with a 25-year history of diabetes mellitus is described. He is referred to the EMG laboratory for paresthesia, hypoesthesia, distal weakness, and areflexia. His presentation was consistent with multiple entrapment neuropathies and length dependent polyneuropathy. Nerve conduction testing demonstrated absent motor and sensory potentials in all four extremities. As EDX testing was inconclusive for entrapment neuropathy, neuromuscular ultrasound (NMUS) was performed. NMUS demonstrated focal increase of the cross-sectional area of the right median and ulnar nerves at the wrist and elbow respectively, as well as the right peroneal nerve under the head of the fibula. At non-entrapment sites, the peripheral nerves had homegenously decreased fascicular pattern and echogenicity, findings compatible with chronic axonal involvement of the peripheral nerve.

SUMMARY/CONCLUSION: The neuropathy associated with diabetes mellitus can vary from compressive neuropathies, multifocal neuropathy to sensory-motor polyneuropathy. It is common to find these entities together acting under a double crush mechanism. NMUS is a complementary diagnostic tool in the evaluation of the peripheral nerve, allowing simultaneous alterations to be found in patients with no response in the conventional EDX study.

CONCENTRIC NEEDLE BENDING DURING ROUTINE EXTENSOR HALLUCIS LONGUS ELECTROMYOGRAPHY

Michael Platto (Washington, PA), George Small (Pittsburgh, PA), Carol Schramke (Pittsburgh, PA)

INTRODUCTION: Concentric needle electrode bending during EMG occurs occasionally. One of the authors (MP) has observed that bent needles (BN) are more common with extensor hallucis longus (EHL) EMG. Others have suggested examiner handling, inferior manufacture, or excessive force is causative. We propose patient characteristics may predict BN.

OBJECTIVE: To test for a relationship between BN and specific patient characteristics during EMG.

METHODS: EMGs of 115 patients were performed by MP, who has over 34 years EMG experience. Data were collected during lower extremity EMG. Age, sex, and diagnosis were recorded.

RESULTS: BN was observed in 25% of our sample. Comparing BN and non-bent needle (NBN) groups, BN patients were older (mean age=69 versus 58), were less likely to be female (36% versus 57% male) and were less likely to have normal results (8% normal, 71% polyneuropathy, and 21% radiculopathy for BN versus 45% normal, 38% polyneuropathy, and 16% radiculopathy in NBN). Regression analysis suggested the model was significant ($p<.001$) with increasing age being a significant predictor of BN ($p=.007$). Gender and EMG result were not significant predictors ($p=.071$ and $p=.082$).

SUMMARY/CONCLUSION: BNs were more common with increased age and more frequent in males with abnormal studies, but these differences were not statistically significant. Examiner and needle characteristics appear less likely to be causative as BNs were rare in younger patients with normal studies. Poor sensory feedback in older patients with radiculopathy or polyneuropathy may lead to jerking, with a resulting BN versus smooth voluntary EHL contraction which does not bend the needle.

RISK OF SERIOUS INFECTIONS AND MALIGNANCIES IN ADULT MYASTHENIA GRAVIS PATIENTS: A US CLAIMS DATABASE STUDY

Jana Podhorna (Ghent, Belgium), Charlotte Ward (Evanston, IL), Ikjae Lee (New York, NY), Yuebing Li (Cleveland, OH), Tobias Ruck (Düsseldorf, Germany), Elizabeth Teperov (Ghent, Belgium), Ami Shah (Ghent, Belgium), Jeffrey Guptill (Ghent, Belgium)

INTRODUCTION: Autoimmune disorders such as myasthenia gravis (MG) and their immunosuppressive treatments may increase the risk of infections and certain malignancies.

OBJECTIVE: To characterize the risk of serious infections and malignancies among adult MG patients compared to matched controls.

METHODS: Using Optum's de-identified Market Clarity claims dataset (2015-2018), this study assessed incidence rate (IR) and incidence rate ratio (IRR) for infections and malignancies between MG patients and non-MG controls.

RESULTS: Among 5,004 MG patients and 3,818 matched controls, MG patients were more likely to experience serious infections compared to controls (IRR = 1.83, 95% confidence interval (CI) [1.54, 2.16]), especially sepsis (IRR = 1.84, 95% CI [1.38, 2.46]), pneumonia (IRR = 1.48, 95% CI [1.08, 2.02]), cellulitis (IRR = 1.84, 95% CI [1.12, 3.04]), and urinary tract infections (IRR = 1.79, 95% CI [1.17, 2.72]). They were also more likely to experience fatal infections (IRR = 2.57, 95% CI [1.29, 5.10]), and infections with Candida (IRR = 1.52, 95% CI [1.26, 1.82]), Herpes zoster (IRR = 1.66, 95% CI [1.27, 2.17]), Klebsiella (IRR = 2.93, 95% CI [1.65, 5.22]), and Pseudomonas (IRR = 2.53, 95% CI [1.41, 4.54]). MG patients had an increased rate of some malignancies including thymic (IRR = 79.5, 95% CI [4.91, 1287.63]), skin (IRR = 1.46, 95% CI [1.19, 1.79]), male genital organs (IRR = 1.54, 95% CI [1.01, 2.33]), and CNS (IRR = 5.76, 95% CI [1.54, 21.51]).

SUMMARY/CONCLUSION: There is an increased risk of serious infections, opportunistic infections, infection-related death, and certain solid malignancies in patients with MG.

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Elizabeth Teperov - is an employee of argenx.

Ami Shah - is an employee of argenx.

Jeffrey Guptill - is an employee of argenx.

CLINICAL, ELECTROPHYSIOLOGICAL AND MR NEUROGRAPHY PROFILE OF PARAPROTEINEMIC NEUROPATHY – A SINGLE CENTRE EXPERIENCE FROM SOUTH INDIA

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INTRODUCTION: Paraproteinemic neuropathies (PPN) are acquired heterogenous disorders, the paucity of data led to the study

OBJECTIVE: To study the clinical spectrum of PPN and their electrophysiologic and imaging correlates.

METHODS: Newly diagnosed patients of PPN presenting to the neurology department, NIMHANS from Jan 2017 to Jan 2023 that satisfied the inclusion criteria were included in this retrospective descriptive study.

RESULTS: Thirty-one patients (24 males, 7 females) with mean age at presentation 49.43±12.5, years and a mean duration of follow-up of 23 months were identified. Of those, 16 (51.6%)had a typical chronic inflammatory demyelinating polyneuropathy (CIDP) presentation,10 (32.2%) distal acquired demyelinating symmetric neuropathy (DADS), and 5 (16.1%) sensorimotor axonal polyneuropathies. NCS showed demyelination in 20 (64.5%) and 11 (35.5%) had axonal changes. The median and ulnar terminal latency index (TLI) were 0.55 and 0.65 respectively. The most common was IgG lambda 9/21 (42.8%) followed by Ig A lambda 5/21 (23.8%). The hematological classification 16 (51.6%) monoclonal gammopathy of undetermined significance, 7 (22.6%) with polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes., 6 (19.4%) had multiple myeloma and 1 each had AL amyloidosis and solitary plasmacytoma. The mean cerebrospinal fluid protein levels were 143.2 (22/31). The mean brachial and lumbar cross-sectional areas (CSA) were 0.24±0.07 cm2 (17/31) and 0.35 ±0.17 cm2 respectively. Neurography showed diffuse symmetric thickening of roots 94.1% (16/17), one had asymmetric. The fascicular architecture and perineural fat integrity were maintained in majority, disrupted in 17.6% and 11.8% respectively. No significant associations between hematology syndrome, paraprotein elevation with clinical, electrophysiology or radiology

SUMMARY/CONCLUSION: The main phenotypic presentation was CIDP followed by DADS. TLI need not be low even in DADS subgroup. Magnetic resonance neurography revealed diffuse thickening of roots.

SAFETY, PULMONARY FUNCTION, AND MOTOR FUNCTION IN AMBULATORY AND NONAMBULATORY PARTICIPANTS WITH DUCHENNE MUSCULAR DYSTROPHY TREATED WITH VILTOLARSEN: RESULTS FROM THE GALACTIC53 CLINICAL TRIAL

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INTRODUCTION: Pulmonary decline is concerning in Duchenne muscular dystrophy (DMD). Viltolarsen is indicated for the treatment of DMD patients amenable to exon 53 skipping. Previously, viltolarsen demonstrated increased dystrophin production, stabilized motor function, and was well tolerated; pulmonary and upper limb function were not evaluated.

OBJECTIVE: To evaluate safety and pulmonary and motor function in DMD participants treated with viltolarsen.

METHODS: In this Phase 2, 48-week study, ambulatory (n=10) and nonambulatory (n=10) participants aged ≥8 years were treated with viltolarsen 80 mg/kg/week (NCT04956289). Least square mean change from baseline ± standard error (SE) in percent predicted forced vital capacity (FVC%p) and peak cough flow (PCF) in participants receiving viltolarsen were compared with CINRG Duchenne Natural History Study (DNHS) controls (N=48) who were matched for multiple variables. Performance of Upper Limb (PUL) 2.0 was evaluated.

RESULTS: Baseline characteristics were well-matched between viltolarsen and DNHS cohorts. Nineteen viltolarsen participants reported treatment-emergent adverse events (AEs; 4 treatment-related). No serious adverse events (AEs) were reported, and no participants discontinued. FVC%p was higher at Week 49 for viltolarsen versus DNHS control (ambulatory: 8.3±3.3% versus 1.2±2.1%, respectively; nonambulatory: 1.6±3.0% versus -3.2±2.0%, respectively). PCF for ambulatory and nonambulatory participants was higher for viltolarsen versus DNHS control at Week 49. PUL 2.0 scores were stable with treatment.

SUMMARY/CONCLUSION: The safety of viltolarsen is consistent with previous trials. This is the first study of viltolarsen evaluating pulmonary and upper limb function and included ambulatory and nonambulatory participants. These results suggest benefit of viltolarsen on respiratory and motor function for boys and older males with DMD amenable to exon 53 skipping.

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AXONAL POLYNEUROPATHY SECONDARY TO AUTOINMUNE VASCULITIS, DIAGNOSTIC APPROACH WITH ULTRASONOGRAPHY

Daniela Andrea Puerto Avila (Bogotá, Colombia), Liliana Elizabeth Rodriguez Zambrano (Bogotá, Colombia), Jorge Arturo Diaz Ruiz (Bogotá, Colombia), Jorge Nicolás Muñoz (Bogotá, Colombia)

INTRODUCTION/BACKGROUND: Granulomatosis with polyangiitis is a systemic necrotizing vasculitis associated with atineutrophil cytoplasmic antibodies, which can affect the peripheral nervous system. A case of axonal polyneuropathy with predominantly sensory symptoms secondary to this vasculitis is presented.

CASE REPORT: A remale patient presented with a history of granulomatosis with polyangiitis, paresthesias in hands and feet, and mild global hyporeflexia. The EDX study reported an absence of sensory response in the peroneal and sural nerves, as well as prolonged sensory latency in the median, ulnar, and radial nerves. Ultrasonographic exploration revealed a slight increase in the cross-sectional area of the sural and median nerves. Therefore, the diagnosis was established as axonal sensory polyneuropathy.

SUMMARY/CONCLUSION: Granulomatosis with polyangiitis can lead to a pattern of sensorimotor axonal polyneuropathy with paresthesias in the distal portions of the limbs in early stages, progressing to muscle weakness and atrophy. It is believed that an increase in the cross-sectional area is more useful for diagnosing the demyelinating variant, as studies show significant increases in this measurement. However, in this case, it is evident that even in the axonal variant, albeit mild, changes can be observed. Early ultrasound may be used as a risk marker for muscle atrophy and to optimize rehabilitation and immunotherapy strategies.
When studying axonal polyneuropathies secondary to autoimmune vasculitis, the use of EDX tools and ultrasonography is valuable for taking preventive measures against physical deterioration, monitoring disease progression, and assessing prognosis.

READABILITY ANALYSIS ASSESSING READABILITY IN ONLINE HEALTH INFORMATION FOR PEDIATRIC NEUROMUSCULAR DISORDERS: A FOCUS ON CEREBRAL PALSY AND MYELODYSPLASIA

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INTRODUCTION: Pediatric neuromuscular disorders pose significant challenges in global health, especially as individuals increasingly seek health information online in the digital era making it crucial to evaluate the readability of online content.

OBJECTIVE: This study aims to assess the readability of information related to pediatric neuromuscular disorders, focusing on prevalent conditions such as cerebral palsy and myelodysplasia, on reputable health websites.

METHODS: Careful consideration was given to selecting websites based on authority and prevalence using Google, the most popular search engine. Employing the neutral term "pediatric neuromuscular disorders" we began a comprehensive sample of websites. Common domains within the top search results were identified, sorted, and saved for analysis. Various readability formulas were applied using Python, including the Flesch Reading Ease Score (FRES), Flesch-Kincaid grade level (FKGL), Simple Measure of Gobbledygook (SMOG), Gunning Fog (GFOG), Coleman-Liau score (CL), automated readability index (ARI), and Linsear Write (LW).

RESULTS: Comparing our readability results to the recommended sixth-grade level by reputable medical organizations, such as the American Medical Association and the National Insititute of Health, revealed that the scores exceeded the recommended level. Notably, publicly accessible data related to pediatric neuromuscular disorders tends to be presented at a higher reading level than recommended for general comprehension, posing critical implications for patient education and health literacy within the context of these disorders.

SUMMARY/CONCLUSION: This study provides valuable insights into the readability landscape of reputable health websites, revealing a potential gap between the complexity of information and the general public's reading ability in the context of these disorders.

INTERIM RESULTS FOR MYASTHENIA GRAVIS-RESOURCE UTILIZATION, EPIDEMIOLOGY, SURVIVAL & TREATMENT PATTERNS (MG-REST) STUDY IN ONTARIO, CANADA

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INTRODUCTION: Reliable real-world data on the burden of myasthenia gravis (MG) is needed to inform Canadian clinical and policy decisions in the era of new MG therapeutics, including FcRn inhibitors. Given the lack of recent Canadian data on MG disease burden, the MG-REST.

OBJECTIVE: Study aims to estimate the clinical burden of MG in Ontario.

METHODS: Ontario administrative data from ICES were utilized for a retrospective population-based cohort study of adults with MG identified through a validated algorithm (April 2013-March 2019) and followed for up to7 years (March 2020) to determine myasthenic crisis characteristics and overall survival (OS).

RESULTS: The MG cohort (n=2,601) had an average age of 65.7 years and 53.3% were males. Incidence of first myasthenic crisis was 9%, with 87% of events occurring at/after diagnosis. MG OS was 89%, 85% and 75% at 1-year, 2-years and 5-years, respectively, while OS after first crisis was 60%, 52%, and 39% for the same years.

SUMMARY/CONCLUSION: Despite the availability of conventional therapies throughout the study, MG crisis remains a serious, common complication of MG, with decreased survival at 1-year post-crisis (29% difference versus 1-year OS following MG diagnosis). Study highlights MG burden and unmet need for new effective therapies for MG treatment.

Disclosures:

Carolina Barnett - has served as member of the advisory board for argenx, Alexion, UCB and Janssen. She has been a consultant for argenx, Janssen and UCB. She has received research support from US Department of Defense, Muscular Dystrophy Canada and MGNet. Grifols and Octapharma. She is the primary developer of the MGII and may receive royalties.

Kobina Quansah - is an employee of Janssen Canada Inc.

Aysegul Erman - is an employee with Janssen Canada Inc.

Ryan Ng - is a full-time employee of IQVIA Solutions Canada Inc.

Nikhil Nath - is a full-time employee of IQVIA Solutions Canada Inc.

Arushi Sharma - is a full-time employee of IQVIA Solutions Canada Inc.

A CASE OF SPONTANEOUS REGRESSION OF THYMOMA IN ACH-R ANTIBODY POSITIVE MYASTHENIA GRAVIS

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INTRODUCTION/BACKGROUND: Myasthenia gravis (MG) is characterized by autoantibodies targeting post-synaptic acetylcholine receptors (AChR) at the neuromuscular junction, resulting in motor weakness. While its precise etiology remains uncertain, genetic factors and thymoma association are documented in literature, with spontaneous regression of thymoma being exceedingly rare. Here, we present a case of temporary spontaneous regression of thymoma in a female with anti-AChR antibody-positive MG, anti-muscle specific kinase negative and biopsy-confirmed thymoma, discussing its epidemiology and potential regression mechanisms.

CASE REPORT: A 69-year-old female with a history of deep vein thrombosis on apixaban, initially received treatment for MG including prednisone, mycophenolate, pyridostigmine, and intravenous immunoglobulin (IVIg). Her initial MG Activities of Daily Living (MG-ADL) was five. Positron emission tomography computed tomography at 3 months revealed significant thymoma reduction, and interval CT 5 months later displayed residual mass. The patient received no medical nor surgical therapy to explain this. Chest CT 6 months later demonstrated mass recurrence, suggesting only temporary thymoma involution. Contrast MRI is pending for further investigation. During thymoma involution, her MG-ADL Score improved to 1. Her current medication regimen has been de-escalated and she no longer requires IVIg.

SUMMARY/CONCLUSION: Evidence of spontaneous thymoma regression is limited to case reports and the mechanism is not established. Suggested mechanisms include ischemia, as the tumor outgrows its blood supply, and (micro)thromboses occluding tumor blood supply. Furthermore, we address the epidemiology of thymoma spontaneous regression, inconsistent with this patient's unique demographic, emphasizing further investigation to explain risk factors, predictive factors for outcomes, treatment methods, and other possible mechanisms of spontaneous thymoma regression.

ALNYLAM ACT®: EFFECTIVENESS OF GENETIC TESTING IN ESTABLISHING A DIAGNOSIS IN PATIENTS WITH SUSPICION OF HEREDITARY TRANSTHYRETIN AMYLOIDOSIS

Steven Roblin (Boston, MA), John Garcia (San Francisco, CA), Ana Morales (San Francisco, CA), John Wyatt (Boston, MA)

INTRODUCTION: Alnylam Act® offers third-party genetic testing for individuals ≥18 years with suspected diagnosis or confirmed family history of hereditary transthyretin amyloidosis (hATTR), a progressive, fatal disease caused by mutations in the transthyretin (TTR) gene.

OBJECTIVE: To describe the effectiveness of genetic testing in identifying patients suspected of hATTR.

METHODS: Testing is performed using panels for neuropathies (82 genes), cardiomyopathy (102 genes), or a single-gene TTR test, individually or in combination. Descriptive analyses were performed (August 2017-May 2023).

RESULTS: Overall, 89,760 patients were tested (average age 60.5 years; 14.3% Black, 63.9% White; 57.1% male). Specialties utilizing the program were 29.1% cardiology, 31.5% neurology, 4.3% genetics, and 35.1% unknown/other. Among patients tested, 12.4% (11,149) had a positive result for any gene in a panel and 4.79% (4,297) were specifically positive for a pathogenic or likely pathogenic DNA variant in TTR. Of TTR-positive patients, 82.2% (3,533) were probands with suspected hATTR diagnosis vs 17.8% (764) with only family history of hATTR. Average age at testing was 65.6; 61.4% (2,640) were Black, 98.1% (2,590) of whom had the V142I variant. Commonly reported signs and symptoms in TTR-positive patients were 64.0% (2,748) cardiac, 27.8% (1,195) neurologic, and 11.2% (482) autonomic. TTR variant positivity rate varied by provider specialty (genetics, 11.5%; cardiology, 10.4%; neurology, 1.11%) and test type (single-gene TTR, 15.6%; cardiomyopathy panel, 5.10%; neuropathies panel, 0.77%).

SUMMARY/CONCLUSION: A genetic testing program is an effective approach for confirming diagnosis in patients suspected of hATTR. Presenting signs and symptoms, provider specialty, and test type influence positivity rate.

Disclosures:

Steven Roblin - is an employee of Alnylam Pharmaceuticals.

John Garcia - is a full time employee of Invitae.

Ana Morales - is an employee and shareholder at Invitae Corporation.

John Wyatt - is an employee of Alnylam Pharmaceuticals and I own equity in Alnylam Pharmaceuticals.

EARLY DIAGNOSIS OF FAMILIAL AMYLOID POLYNEUROPATHY: A CASE REPORT

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INTRODUCTION/BACKGROUND: Familial amyloid polyneuropathy due to hereditary transthyretin (TTR-FAP) is a progressive, irreversible, and systemic disease with insidious onset involving sensory, motor, and autonomic nerves. Although rare, it can be highly disabling. FAP is autosomal in transmission and is due to a mutation in the transthyretin gene (TTR), typically Val142Ile in Colombia, although hundreds of other gene mutations have been reported. The age of onset varies as well as the time to diagnosis, depending on the presence or absence of positive family history.

CASE REPORT: A 22-year-old asymptomatic man with a family history (father and siblings) of amyloidosis. Genetic studies revealed that he was a carrier of the Val142Ile variant. Neither conventional EDX studies nor small fiber evaluation showed abnormalities. However, neuromuscular ultrasound (NMUS) study showed an increase in cross-sectional area of nerves, especially median and ulnar nerves at the arm (22 mm2 and 26 mm2, respectively), as well as fibular nerve at the knee (22 mm2) and tibial nerve at the ankle (25 mm2), with an ultrasound pattern sub-score A of 8.

SUMMARY/CONCLUSION: NMUS is an important tool in detecting structural alterations of peripheral nerves, which may even precede symptoms or electrophysiological findings. Thus, NMUS can be considered as a tool to optimize early detection of FAP. This could be of importance for timely treatment in disease carriers.

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EFFECTIVENESS OF EFGARTIGIMOD IN PATIENT WITH MYASTHENIA GRAVIS AND TUMOR: A SINGLE CENTER EXPERIENCE

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INTRODUCTION: This study aims to observe the effectiveness and safety of efgartigimod in special myasthenia gravis (MG) patients.

OBJECTIVE: Though efgartigimod has been approved for acetylcholine receptor antibody positive (AChR+) adult MG patients, its safety and efficacy in MG patients with tumors are undetermined.

METHODS: In this prospective cohort, patients with MG were classified into tumor and non-tumor groups. The efgartigimod treatment regimen was 10 mg/Kg/infusion, administered weekly for 4 weeks, followed by a medication-free observation phase for a total of 8 weeks. Clinical assessment was conducted before each infusion and week 8. Primary efficacy was gauged by the change in MG activities of daily living (MG-ADL) scores from baseline, while safety measures included any reported adverse events. Repeated measures data were analyzed using a mixed-effects model.

RESULTS: The study comprised 15 eligible patients, with 5 having concurrent tumors, including invasive thymoma (1), unresected thymoma (2), lung cancer (1), and prostate cancer (1), with the remaining 10 patients as controls. Baseline attributes and disease severity were statistically equivalent between groups. Post-efgartigimod treatment, both groups showed a significant initial decline in MG-ADL scores (adjusted mean -3.26 and -3.27) in week 1, with further downward trends observed over time. By week 8, respective adjusted mean MG-ADL score reductions were -5.4 and -5.3, with no significant inter-group difference (P=0.37). Only one patient reported a mild upper respiratory tract infection.

SUMMARY/CONCLUSION: Efgartigimod rapidly ameliorates symptoms in AChR+ MG patients, and its safety and efficacy remain consistent in generalized MG patients with concurrent tumors, comparable to the non-tumor group.

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REAL-WORLD REDUCTION IN ORAL CORTICOSTEROID UTILIZATION FOLLOWING EFGARTIGIMOD INITIATION

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INTRODUCTION: Reducing or tapering oral corticosteroids (OCS, prednisone equivalent), a common treatment used in generalized myasthenia gravis (gMG), can alleviate risk related to long-term OCS usage.

OBJECTIVE: To evaluate OCS usage following efgartigimod initiation.

METHODS: In this retrospective study, patients with gMG using OCS who initiated efgartigimod were identified from a United States medical and pharmacy claims database (based on information licensed from IQVIA: Longitudinal Access and Adjudication Data [LAAD] for the period April 2016−November 2023, reflecting estimates of real-world activity [all rights reserved]). Mean (SD) average daily dose (ADD) of OCS was evaluated during the 3 months prior to, and at 3 and 6 months post-efgartigimod initiation. Any patients enrolled in the “My VYVGART Path” patient support program that had baseline and follow-up myasthenia gravis activities of daily living (MG-ADL) scores available were identified to assess score change.

RESULTS: Among 842 patients who initiated efgartigimod by December 31, 2022, and continued efgartigimod for ≥6 months, 316 (38%) were using OCS at baseline. Mean standard deviation (SD) OCS ADD was significantly reduced at 3 months (15.4 [14.9] mg/day, P=7x10-5) and 6 months (13.5 [14.6] mg/day, P=3x10-10) post-efgartigimod initiation compared with baseline (18.6 [15.0] mg/day). A subset of 109 patients (35%) had MG-ADL scores available both before and during the 6 months following efgartigimod initiation. Among them, significant reduction was observed in best follow-up mean SD MG-ADL (from 8.7 [3.7] to 4.3 [3.2], P<0.0001).

SUMMARY/CONCLUSION: OCS usage was significantly reduced over 6 months post-efgartigimod initiation, while improving patient MG-ADL response.

Disclosures:

Tobias Ruck - received honoraria and/or research support from Alexion, argenx, Biogen, Merck, Novartis and Roche.

Glenn Phillips - is an employee of argenx.

Neelam Goyal - has served as a paid consultant for argenx, UCB Pharma, Janssen, and Alexion, and has grant support from argenx.

Cynthia Qi - is an employee of argenx.

John Stone - has consulted for argenx on glucocorticoid toxicity.

Deborah Gelinas - is an employee of argenx.

Matthew Jefferson - is an employee of argenx.

Tharun Balaji Suthagar - is an employee of ZS Associates (Evanston, IL, USA) and serves as a paid consultant for argenx.

Rohit R Menon - is an employee of ZS Associates (Evanston, IL, USA) and serves as a paid consultant for argenx.

Mai Sato - is an employee of ZS Associates (Evanston, IL, USA) and serves as paid consultant for argenx.

CHRONIC STEROID TOXICITY IN ADULTS WITH MYASTHENIA GRAVIS IN THE UNITED STATES BASED ON ELECTRONIC HEALTH RECORDS

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INTRODUCTION: While benefits/risks of steroids in myasthenia gravis (MG) have been studied, quantifying steroid toxicity is challenging using real-world data.

OBJECTIVE: To examine toxicity associated with chronic steroid use in MG.

METHODS: Adults with MG (≥2 MG diagnoses 30-730 days apart) were identified in United States (US)-based Optum® de-identified Electronic Health Record data set (Optum® EHR) (Jan 2013-Dec 2022). Index dates were defined as first steroid prescription (for steroid initiators [MG-SI]) or assigned after age/gender match (for steroid-naïve [MG-SN]). Patients with available lab measures for main criteria of the Glucocorticoid Toxicity Index-Metabolic Domains (GTI-MD) were included. GTI-MD scores (Aggregate Improvement Score [AIS] and Cumulative Worsening Score [CWS], higher scores represent higher toxicity) were compared between MG-SI vs. MG-SN cohorts. Multivariate regression assessed the relationship of steroid usage, strength, and timing of follow-up assessment to GTI-MD.

RESULTS: Among 27,157 patients with MG, 377 and 305 were included in the MG-SI and MG-SN cohorts, respectively. 30% of the MG-SI cohort had multiple steroid prescriptions, and ≥20mg/day prescription at index. GTI-MD (SD) scores were higher in MG-SI compared with MG-SN (AIS: 4.9 [34.5] vs. 1.9 [34.3], P=0.27; CWS: 22.6 [22.8] vs. 18.7 [21.2], P=0.023). Regression results showed MG-SI patients with ≥2 records and ≥20mg/day at index had an average AIS 10.2 higher than MG-SN (P=0.01). Each additional month of follow-up since index was associated with a decrease of 1.5 AIS (P<0.001).

SUMMARY/CONCLUSION: Our results demonstrated steroid toxicity is significantly higher in patients with higher strength and repeated steroid usage. Patients experienced consistent elevation in steroid toxicity over time.

Disclosures:

Tobias Ruck - received honoraria and/or research support from Alexion, argenx, Biogen, Merck, Novartis, and Roche.

Dakshinamoorthy Amirthaganesan - is an employee of ZS Associates and serve as a paid consultant for argenx.

Rucha Kulkarni - is an employee of ZS Associates and serve as a paid consultant for argenx.

Albert Whangbo - is an employee of ZS Associates and serve as a paid consultants for argenx.

Neelam Goyal - has served as a paid consultant for argenx, UCB Pharma, and Alexion

Michael Hehir - is a paid consultant for Alexion, argenx, UCB, Janssen, and Immunovant; has received honorarium as Associate Editor of MedLink Neurology, educational speaker for Medscape, and a Guest Editor of Continuum

Glenn Phillips - is an employee of argenx.

John H Stone - has consulted for argenx on glucocorticoid toxicity.

Cynthia Qi - is an employee of argenx.

Martha Stone - is Chief Executive and Majority Owner of Steritas.

Deborah Gelinas - is an employee of argenx.

Anthony Chamberas - is a consultant to Steritas.

COMPLIANCE TO DAILY SELF-ADMINISTERED SUBCUTANEOUS ZILUCOPLAN IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: A POST HOC ANALYSIS OF THE RAISE-XT STUDY

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INTRODUCTION: Zilucoplan is the first complement component 5 inhibitor that is self-administered as a once-daily subcutaneous injection for the treatment of adults with acetylcholine receptor autoantibody-positive generalized myasthenia gravis (gMG).

OBJECTIVE: To evaluate compliance to self-administered, once-daily subcutaneous injections of zilucoplan among patients with gMG in the ongoing Phase 3, open-label extension study, RAISE-XT (NCT04225871).

METHODS: Adults with gMG who completed a qualifying double-blind study (NCT04115293/NCT03315130) could enter RAISE-XT to receive once-daily subcutaneous zilucoplan 0.3 mg/kg by self-injection (data cutoff: November 11, 2023). The primary endpoint of RAISE-XT was incidence of treatment-emergent adverse events (TEAEs). The duration of zilucoplan exposure was assessed. The percentage of medication taken was analyzed post hoc for the overall population and subgroups of age (<65 and ≥65 years), sex (male and female), disease duration (< median and ≥median) and baseline Myasthenia Gravis Activities of Daily Living (MG-ADL) score (≤9 and ≥10). All analyses were descriptive.

RESULTS: Overall, 200 patients were enrolled in RAISE-XT; 97.0% (194/200) of patients experienced a TEAE. Compliance data were analyzed for 199 patients. Over a median (range) exposure to zilucoplan of 2.2 (0.1-5.6) years, 95.0% (189/199) of patients reported taking >95% of their medication. In total, patients reported taking a mean percentage of 99.2% of their medication. Data for the subgroups of age, sex, disease duration and baseline MG-ADL score were consistent with those of the overall population (mean percentage of medication taken for all subgroups was ≥98.4% of doses).

SUMMARY/CONCLUSION: Long-term compliance to subcutaneous, self-administered, daily injection with zilucoplan was high.

Disclosures:

Katherine Ruzhansky - has served as a paid Consultant for argenx, Alexion Pharmaceuticals, UCB Pharma and Immunovant. She has received research support from Alexion Pharmaceuticals, UCB Pharma, Janssen Pharmaceuticals and Immunovant.

Fiona Grimson - is an employee and shareholder of UCB Pharma.

Natasa Savic - is an employee and shareholder of UCB Pharma.

James F. Howard Jr. - has received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention (Atlanta, GA, USA), the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health (including the National Institute of Neurological Disorders and Stroke and the National Institute of Arthritis and Musculoskeletal and Skin Diseases), PCORI and UCB Pharma; honoraria from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-La Roche, Medscape CME, Merck EMD Serono, NMD Pharma, Novartis, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, UCB Pharma, Regeneron Pharmaceuticals, Sanofi US, Horizon Therapeutics (now Amgen) and Zai Labs; non-financial support from Alexion AstraZeneca Rare Disease, argenx, UCB Pharma and Toleranzia AB.

Miriam Freimer - has served as a paid Consultant for argenx, UCB Pharma and Alexion Pharmaceuticals. She receives research support from the NIH, UCB Pharma, Janssen Pharmaceuticals, Alnylam, Avidity and Fulcrum.

M. Isabel Leite - is funded by the NHS (Myasthenia and Related Disorders Service and National Specialised Commissioning Group for Neuromyelitis Optica, UK) and by the University of Oxford, UK. She has been awarded research grants from the UK association for patients with myasthenia (Myaware) and the University of Oxford. She has received speaker honoraria or travel grants from Biogen, Novartis, UCB Pharma and the Guthy-Jackson Charitable Foundation. She serves on scientific or educational advisory boards for UCB Pharma, argenx and Viela Bio (now Horizon Therapeutics).

Angelina Maniaol - has received payment for travel, meeting attendance, consulting honoraria or advisory board participation from CSL Behring, Novartis, Biogen, argenx and UCB Pharma.

Renato Mantegazza - has received funding for travel and meeting attendance or advisory board participation from Alexion Pharmaceuticals, argenx, BioMarin, Catalyst, Sanofi, Regeneron Pharmaceuticals and UCB Pharma.

Kimiaki Utsugisawa - has served as a paid Consultant for UCB Pharma, argenx, Janssen Pharmaceuticals, Viela Bio (now Horizon Therapeutics), Chugai Pharmaceutical, HanAll Biopharma, Merck and Mitsubishi Tanabe Pharma; he has received speaker honoraria from argenx, Alexion Pharmaceuticals, UCB Pharma and the Japan Blood Products Organization.

Tuan Vu - is the USF Site Principal Investigator for MG clinical trials sponsored by Alexion/Astra Zeneca, argenx, UCB Pharma, Amgen, Immunovant, Regeneron, Johnson & Johnson, Remegen, Dianthus, and Cartesians Therapeutics. He has served as a speaker for Alexion, argenx, CSL Behring, and Allergan/Abbvie. He performed consulting work for argenx, Alexion/Astra Zeneca, Dianthus, Remegen, ImmunAbs, and UCB Pharma.

Michael D. Weiss - has received honoraria for serving on scientific advisory boards for Alexion Pharmaceuticals, Immunovant, Ra Pharmaceuticals (now UCB Pharma), argenx, Biogen, Mitsubishi Tanabe Pharma and Amylyx, consulting honoraria from Cytokinetics and CSL Behring and speaker honoraria from Soleo Health. He also serves as a special government employee for the Food and Drug Administration.

Babak Boroojerdi - is an employee and shareholder of UCB Pharma.

HIRAYAMA DISEASE (MONOMELIC AMYOTROPHY) INITIALLY DIAGNOSED AND MANAGED WITH MULTIFOCAL MOTOR NEUROPATHY, CASE REPORT

Camilo Salazar (Bogotá, Colombia)

INTRODUCTION/BACKGROUND: Monomelic amyotrophy, also known as Hirayama disease, is a rare lower motor neuron syndrome due to localized lower motor neuron loss in the spinal cord at the cervical level.

CASE REPORT: We present a 25-year-old man with a 2-year history of slowly progressive unilateral weakness and atrophy of his right-hand muscles. Neurological examination revealed weakness and atrophy in his intrinsic hand muscles, with sparing of the abductor pollicis brevis muscle. Also, mild atrophy of the ulnar aspect of the forearm was detected with sparing of the brachioradialis muscle. EMG showed active and chronic neurogenic changes affecting C8 and T1 myotomes, with mild chronic neurogenic changes on C7 myotome. After several treatments carried out under an initial diagnosis of multifocal motor neuropathy, and due to the non-response to these treatments. It is decided to request diagnostic images Magnetic resonance imaging of his cervical spine revealed spinal cord atrophy involving C5 to C7 segments, associated with forward displacement of the posterior wall of the dura in cervical spine flexion.

SUMMARY/CONCLUSION: The clinical characteristics associated with the electrophysiological and imaging findings support the diagnosis of monomelic amyotrophy, changing the patient's diagnosis and avoiding further inappropriate treatments.

THE DUKE MG PATIENT REGISTRY: III. THE COMPARATIVE EFFECTIVENESS OF AZATHIOPRINE AND MYCOPHENOLATE MOFETIL IN MYASTHENIA GRAVIS, A RETROSPECTIVE SINGLE CENTER REVIEW

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INTRODUCTION: The Duke Myasthenia Gravis (MG) Clinic Registry contains comprehensive physician- and patient-derived data on patients seen in the Duke MG Clinic since 1980.

OBJECTIVE: To report outcomes in patients treated with azathioprine (AZA) or mycophenolate mofetil (MMF) in the Duke MG Clinic according to the consensus guidance statements.

METHODS: This is a retrospective cohort study of patients initially seen after 1980 and followed for at least 2 years in the Clinic. The Treatment Goal (TG) was defined as achieving MGFA Post-Intervention Status (PIS) Minimal Manifestations (MMS) or better; PIS was determined by the treating neurologist at each clinic visit. Time-to-event analysis, including Cox proportional hazards modeling, was performed. Censoring was based on the date that drug treatment ended or last clinic visit.

RESULTS: Among 633 patients with ocular or generalized MG (gMG), 342 were treated with recommended doses of AZA and 291 with MMF for at least 90 days. Of these, 51% treated with AZA achieved TG at a median time of 1,398 days; 56% treated with MMF achieved TG, median time 882 days (p=0.0003). Subgroup analysis was performed for gMG, concomitant treatments, sex, antibody status, onset age, and disease duration and severity.

SUMMARY/CONCLUSION: Approximately half of patients with MG treated with recommended doses of AZA or MMF achieved MMS or better, and those on MMF did so more quickly.

QUALITY OF LIFE IN GENERALIZED MYASTHENIA GRAVIS: RESULTS FROM A GLOBAL REGISTRY OF ECULIZUMAB AND RAVULIZUMAB TREATMENT

Christopher A. Scheiner (Knoxville, TN), Nan Jiang (Birmingham, AL), Gary Cutter (Birmingham, AL), Pushpa Narayanaswami (Boston, MA), Rup Tandan (Burlington, VT), Lida Zeinali (Toronto, Canada), Ema Rodrigues (Boston, MA), Ashley Yegin (Boston, MA), Andrew J. Gordon (Lake Barrington, IL)

INTRODUCTION: Complement C5 inhibitor therapies (C5ITs) eculizumab and ravulizumab are approved in the US and EU for anti-acetylcholine receptor antibody positive (AChR+) generalized myasthenia gravis (gMG). The global MG SPOTLIGHT Registry enrolled patients receiving C5ITs in clinical practice to assess eculizumab and ravulizumab safety and effectiveness in patients with gMG.

OBJECTIVE: This analysis examined quality of life (QOL) changes after C5IT initiation using Myasthenia Gravis Quality of Life 15-revised (MG-QOL15r) scores.

METHODS: Enrolled registry patients were included if they had MG-QOL15r assessments before and after C5IT initiation. Descriptive statistics were performed and are presented as mean standard deviation (SD). Safety was assessed by evaluating frequency and type of serious adverse events.

RESULTS: The 47/204 (23%) enrolled registry patients with available data were 60% male (aged 46.5 [20.3] years at MG diagnosis). In eculizumab-only treated patients (n=30), the MG-QOL15r score before eculizumab initiation, 18.2 (6.9), improved to 12.2 (8.5) after 30.9 (16.1) months of eculizumab treatment. Among eculizumab-to-ravulizumab switched patients (n=10), the MG-QOL15r score of 18.2 (7.9) before C5IT initiation improved to 11.2 (10.6) after 29.6 (25.4) months of eculizumab and to 8.7 (9.0) after 4.6 (3.1) months of ravulizumab. The C5IT safety profile within this patient cohort was similar to previous analyses, including clinical trial data. Limitations include the lower number of patients with MG-QOL15r data in routine clinical use and lack of adjustment for potential confounders.

SUMMARY/CONCLUSION: These initial results underline clinically meaningful QOL improvements in patients with AChR + gMG treated with C5ITs in clinical practice. Patients transitioned from eculizumab experienced further slight QOL improvements with ravulizumab.

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Ema Rodrigues - is an employee of Alexion, AstraZeneca Rare Disease, and holds stock options in AstraZeneca.

Ashley Yegin - is an employee of Alexion, AstraZeneca Rare Disease, and holds stock options in AstraZeneca.

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LUMBOSACRAL RADICULOPLEXUS NEUROPATHY WITH THORACIC WALL INVOLVEMENT - RECOGNIZING A RARE PERIPHERAL NERVOUS SYSTEM DISORDER

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INTRODUCTION/BACKGROUND: LRPN is a rare disease with annual incidence of 4.2 per 100,000. Although commonly characterized clinically by proximal muscle pain and weakness, the highly variable presentation and course may result in delayed diagnosis.

CASE REPORT: A 70-year-old nondiabetic, ambulatory woman presents with subacute paretic right leg, associated with significant burning pain and paresthesias in the proximal right leg. MRI of the lumbar spine demonstrated severe neural foraminal narrowing at L4-L5, however no explanatory lesions more superiorly. EMG/NCS was consistent with femoral and tibial axonal mononeuropathies, and polyradiculopathy. The right leg symptoms improved over 9 months; approximately 1 year later, she developed swelling in the right thorax, and pain sans herpetic rash. She also developed weakness of the left leg in a similar pattern to the right. She underwent a muscle and nerve biopsy indicating neurogenic change without vasculitis. Her pain was managed with pregabalin and hydrocodone, with weakness plateauing.

SUMMARY/CONCLUSION: LRPN is a heterogenous disorder affecting primarily the lumbosacral plexus and spinal roots. Approximately 67% of cases are diabetic in etiology, with the remainder idiopathic. Pathophysiology of LRPN is hypothesized to be microvasculitic nerve injury. Typical course involves debilitating painful weakness unilaterally and focally in the proximal leg, with subsequent spread to other regions ipsilaterally or contralaterally. A minority of patients develop arm involvement, which may manifest as multiple mononeuropathies or a partial brachial plexopathy. Involvement of the thoracic wall, as in this case, implies a thoracic radiculopathy, seen in ~10% of cases.

ISOLATED ANARTHRIA: AN ATYPICAL PRESENTATION OF MYASTHENIA GRAVIS

Amanda Sellers (Hollywood, FL), Sean Kenniff (Hollywood, FL), Mary DesRosiers (Hollywood, FL)

INTRODUCTION/BACKGROUND: Myasthenia gravis (MG) is a well-known autoimmune disorder affecting the neuromuscular junction, commonly presenting with ocular muscle weakness but exhibiting a wide range of manifestations often involving bulbar, extremity, and respiratory muscles. In our literature review, we were unable to identify any reported cases of MG presenting as isolated anarthria. Thus, we describe the case of a 77-year-old male presenting with an exceedingly rare initial manifestation of MG.

CASE REPORT: We present the case of a 75-year-old male with a history of hyperlipidemia, type II diabetes mellitus, hypertension, macular degeneration, and chronic medical marijuana use, who presented with intermittent anarthria, described as a total inability to articulate words. The onset was 3 months ago with recent progression. He also reported thick secretions that he attributed to daily marijuana use; however, he denied any additional symptoms classically associated with MG. Initial investigations, including basic laboratory workup and imaging with MRI of the brain and magnetic resonance angiography of the brain and neck, were unremarkable. However, extended serological testing revealed strongly positive acetylcholine receptor binding and modulating antibodies, confirming the diagnosis of MG.

SUMMARY/CONCLUSION: Our patient’s case highlights the importance of considering MG in the differential diagnosis of atypical bulbar presentations, thereby facilitating timely diagnosis, and minimizing morbidity and mortality.

ADVERSE PREGNANCY OUTCOMES IN MYASTHENIA GRAVIS: A RETROSPECTIVE COHORT STUDY IN A US HEALTH INSURANCE CLAIMS DATABASE

Melanie H. Jacobson (New York City, NY), Rupa Makadia (Union City, NJ), John Sheehan (Pennington, NJ), Nathan Hall (Union city, NJ), Jill Hardin (Hollis, NH), Sicong Huang (Titusville, NJ), Ran Sun (Raritan, NJ), Rebecca Zaha (Raritan, NJ), Alexis A. Krumme (Raritan, NJ)

INTRODUCTION: Pregnancy is common among individuals with autoantibody conditions and adverse perinatal outcomes have been documented. However, previous studies in myasthenia gravis (MG) have produced mixed results

METHODS: We conducted a retrospective cohort study in the United States (US) MarketScan Commercial Claims and Encounters database between 2000-2022. Pregnancies in females aged 18-49 were identified and among live births, maternal and infant records were linked. MG was defined by ≥1 inpatient or ≥2 outpatient diagnoses within a 365-day period, with ≥1 diagnosis required before pregnancy end. The prevalence of six perinatal outcomes was calculated in the MG and total populations: live birth, spontaneous abortion, Cesarean section, preeclampsia, preterm birth, and small for gestational age (SGA). Outcome prevalence in the total population was standardized to the MG population age distribution

RESULTS: A total of 694 individuals with MG had 900 pregnancies and 3,928,256 individuals in the total population had 5,185,726 pregnancies. The prevalence of live birth (75.0% vs. 73.9%) and spontaneous abortion (20.4% vs. 20.8%) was similar in the MG and age-adjusted total population, respectively. Preeclampsia and cesarean section were more frequent among MG than the total population (10.7% vs. 7.1%; 42.9% and 35.0%, respectively). The largest differences were noted for preterm birth and SGA, which were more prevalent among MG than the total population (18.0% vs. 9.7%; 4.3% vs. 1.7%, respectively)

SUMMARY/CONCLUSION: MG was associated with a greater burden of certain adverse perinatal outcomes, occurring in both mother and infant. Further research is needed to understand drivers of pregnancy outcomes in MG.

Disclosures:

Melanie H. Jacobson - This study was conducted by Janssen Research & Development, LLC. The author is employed by, and may hold stock or stock options in Johnson & Johnson.

Rupa Makadia - This study was conducted by Janssen Research & Development, LLC. The author is employed by, and may hold stock or stock options in Johnson & Johnson.

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Alexis A. Krumme - This study was conducted by Janssen Research & Development, LLC. The author is employed by, and may hold stock or stock options in Johnson & Johnson.

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PERINATAL TREATMENT PATTERNS IN MYASTHENIA GRAVIS

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INTRODUCTION: Clinical management of myasthenia gravis (MG) during pregnancy is complex, as both the disease and available treatments may have adverse effects on the mother and/or infant. Although clinical guidelines have been established, few studies of real-world medication utilization have been conducted in this population.

METHODS: We conducted a retrospective cohort study in the United States (US) Marketscan Commercial Claims and Encounters database between 2000-2022. Pregnancies in females aged 18-49 were identified. MG was defined by ≥1 inpatient or ≥2 outpatient diagnoses within a 365-day period, with ≥1 diagnosis required before pregnancy end. Prescription fills were summarized at the class level in preconception, pregnancy, and postpartum and included corticosteroids, rapid-acting immunotherapies, acetylcholinesterase inhibitors, steroid-sparing immunosuppressants, and monoclonal antibodies

RESULTS: Among 647 women with MG, 54.3% were untreated in the 6 months before pregnancy, 61.2% in pregnancy (69.2% in the first trimester), and 58.0% in the 6 months postpartum. The most common medication class was acetylcholinesterase inhibitors (31.2% before pregnancy, 26.9% in pregnancy, and 26.7% in postpartum) followed by corticosteroids (24.4%, 19.6%, and 24.0%, respectively). Those taking acetylcholinesterase inhibitors or corticosteroids before pregnancy were more likely to continue a medication in the class during pregnancy (67.3% and 53.8%, respectively) than those taking steroid-sparing immunosuppressants before pregnancy (42.5%). Of those taking acetylcholinesterase inhibitors or corticosteroids in pregnancy, 21.8% and 33.1% of them had not been taking them before pregnancy, respectively.

SUMMARY/CONCLUSION: Though most patients with MG did not receive treatment in the perinatal period, those who did showed dynamic patterns.

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Anna Ostropolets - This study was conducted by Johnson & Johnson. All authors are employed by, and hold stock in, Johnson & Johnson.

John Sheehan - This study was conducted by Johnson & Johnson. All authors are employed by, and hold stock in, Johnson & Johnson

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A NOVEL CASE OF ADENOVIRUS ENCEPHALITIS AND ACUTE INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY IN AN IMMUNOCOMPROMISED ADULT

Ashish Shrestha (Allentown, PA), Alison Walsh (Allentown, PA), Brian Harte (Allentown, PA)

INTRODUCTION/BACKGROUND: Human adenovirus is a double-stranded DNA virus that is a common cause of respiratory and gastrointestinal infections. Rarely, adenovirus causes infection of the central nervous system, particularly in adults. We describe a novel case of an adult with adenovirus encephalitis and acute inflammatory demyelinating polyradiculoneuropathy (AIDP).,

CASE REPORT: A 64-year-old woman with relapsing-remitting multiple sclerosis, being treated with diroximel fumarate, presented to the emergency department with persistent nausea, vomiting, and diarrhea. Stool sample was positive for adenovirus. A week after initial presentation, patient began experiencing encephalopathy and decreased responsiveness with progressive lower extremity weakness requiring transfer to ICU. Mental status examination displayed disorientation, poor attention, and impaired memory. Motor examination demonstrated bilateral, proximal greater than distal, weakness in the upper and lower extremities. Deep tendon reflexes were absent. MRI of the brain, cervical, and thoracic spine, with and without gadolinium, did not show evidence of active demyelination. EEG showed diffuse slowing consistent with encephalopathy. Cerebrospinal fluid studies revealed elevated white blood cells (87/mm3) with monocytic predominance, elevated protein (177 mg/dl), and normal glucose (45 mg/dl). Ganglioside antibodies were unremarkable. EDX studies revealed severe sensorimotor polyneuropathy with demyelinating features and axonal involvement.

Patient was treated with intravenous immunoglobulin (IVIg) (2g/kg) with gradual improvement in strength.

SUMMARY/CONCLUSION: We report a rare case of encephalitis and AIDP caused by adenovirus in an immunocompromised adult. Concomitant acute neurologic manifestations are unusual but not infrequent and having a high index of suspicion in assessing the immunocompromised patient is essential to direct timely diagnosis and treatment.

RICHE-CANNIEU ANASTOMOSIS WITH DEEP ULNAR PALMAR MOTOR NEUROPATHY MIMICKING A SEVERE MEDIAN CONDUCTION BLOCK AT THE WRIST

Chaichana Sinthuwong (Cleveland, OH), Hemani Ticku (Cleveland, OH), Bashar Katirji (Cleveland, OH), Kamal Chémali (Shaker Heights, OH)

INTRODUCTION/BACKGROUND: Riche-Cannieu anastomosis (RCA) is an anomalous connection between the ulnar and median motor nerves in the palm, complicating the assessment of median nerve during routine EDX study. This complexity is further compounded if concurrent injuries occur in the hand.

CASE REPORT: A 41-year-old woman reported right palmar pain, numbness in the right middle and ring fingers, and difficulty grasping objects for 4 months. Examination revealed mild weakness in right thumb abduction and handgrip. Median compound muscle action potential (CMAP) recording abductor pollicis brevis (APB) showed markedly low amplitude upon wrist and elbow stimulations but was normal upon mid-palm stimulation. Median sensory nerve action potential (SNAP) showed reduced amplitude and prolonged latency. Ulnar CMAP recording abductor digiti minimi and SNAP were normal, suggesting severe CTS with distal conduction block.

However, needle electrode examination revealed normal APB recruitment but showed active denervation in the first and second dorsal interossei with neurogenic firing pattern and normal in third and fourth interossei, suggesting a deep palmar ulnar neuropathy.

Additional ulnar CMAP recording APB was robust, confirming the presence of RCA. Ulnar CMAP recording first dorsal interosseous showed reduced amplitude. This changed the final diagnosis to deep palmar ulnar neuropathy with RCA and mild CTS.

SUMMARY/CONCLUSION: This case highlights a complex scenario of deep palmar ulnar neuropathy associated with RCA and a mild CTS, manifesting as distal median pseudo-block on routine NCS. Awareness of RCA is crucial to prevent overestimation of CTS severity. Clinicians should suspect RCA when there is a discrepancy between median sensory, median motor, and needle EMG studies of APB or when the clinical presentation is atypical for CTS.

PAIN-RELATED SOMATOSENSORY EVOKED POTENTIALS AS A TOOL IN EVALUATING SMALL-FIBER NEUROPATHY IN HATTR AMYLOIDOSIS

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INTRODUCTION/BACKGROUND: Routine NCS do not evaluate small fibers. New protocols should be sought to improve detection of small-fiber neuropathy, especially in developing countries, where gold standard tests are not easily available. Hereditary amyloidosis is endemic in Brazil, and the classic form presents initially with small-fiber neuropathy. We present two cases on genetically confirmed hATTR with normal NCS in which pain-related Evoked potential (PREP) was able to identify small-fiber pathology.

CASE REPORT: Case 1: A 45-year-old female with a 3-year history of progressive sensory symptoms on the feet. She complained of transient lipothymia, and a tilt test showed a vasodepressor response. Neurological examination was remarkable for painful hypoesthesia. Neuropathy impairment score (NIS) was 04. NCS were within normal range. A tilt test showed a vasodepressor response. She was submitted to PREP that revealed a normal response in upper limbs, but an absent response on lower limb, suggesting a length-dependent small-fiber neuropathy. Genetic test performed identified a p.Val50Met variant on TTR gene.

Case 2: A 54-year-old female patient with a history of a TTR-related cardiomyopathy with a p.Val142Ile variant. She reported painful paresthesias on feet for over a year. NIS was 02. NCS was within normal range. PREP showed a normal response on upper limb with an absent response in upper limb, also suggesting small-fiber neuropathy.

SUMMARY/CONCLUSION: PREP was able to identify small-fiber neuropathy on both cases. Although further studies are needed, PREP could be a tool in care of TTR-related pathology and enable earlier diagnosis.

THE SAFETY AND EFFICACY PROFILE OF ECULIZUMAB IN MYASTHENIC CRISIS: A PROSPECTIVE SMALL CASE SERIES

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INTRODUCTION: Eculizumab brought a better recovery from ventilatory support in case reports with myasthenic crisis (MC). However, the safety and efficacy profiles from prospective studies are still lacking.

OBJECTIVE: To explore the safety and efficacy profile of eculizumab in a prospective case series with refractory MC.

METHODS: The current study followed a case series with acetylcholine receptor (AChR) subtype MG who was given eculizumab as an add-on therapy for 12 weeks during MC to promote the weaning process or lower disease activity. Serum anti-AChR antibodies and peripheral immune molecules associated with the complement pathway were evaluated before and after eculizumab administration.

RESULTS: Compared with the baseline MGFA-quantitative MG test (MGFA-QMG) (22.25±4.92) and MG-activities of daily living (MG-ADL) (18.25±2.5) at crisis, improvement was observed from 4 weeks (14.5±10.47 and 7.5±7.59, respectively) through 12 weeks (7.5±5.74 and 2.25±3.86, respectively) after eculizumab treatment. Muscle strength was regained consistently across ocular, bulbar, respiratory, and limb/gross domain groups. One case died of cardiac failure at 16 weeks. Three cases remained in remission at 24 weeks with a mean quantitative MG score of 2.67±2.89 and ADL score of 0.33±0.58. No significant side effects were reported. Serum CH 50 and soluble C5b-9 levels significantly declined, while there were no significant changes in serum anti-AChR antibody levels, C1q, C5a levels, and peripheral lymphocyte proportions.

SUMMARY/CONCLUSION: Eculizumab was well-tolerated and efficacious in patients with MC in this case series. Large prospective cohort studies with a long follow-up period are expected to explore the safety and efficacy profile in real-world practice.

SAFETY AND EFFECTIVENESS OF NIPOCALIMAB IN ADOLESCENT PARTICIPANTS IN THE OPEN LABEL PHASE 2/3 VIBRANCE-MG CLINICAL STUDY

Jonathan Strober (San Francisco, CA), Shawn Black (Spring House, PA), Sindhu Ramchandren (Titusville, NJ), Saunder Bernes (Phoenix, AZ), Akiyuki Uzawa (Chiba, Japan), Yasuhiro Kimoto (Miyazaki, Japan), Keiko Ishigaki (Tokyo, Japan), Tuan Vu (Tampa, FL), Dan Huang (Neuss, Germany), Yaowei Zhu (Spring House, PA), Hong Sun (Titusville, NJ)

INTRODUCTION: Nipocalimab is a fully human, effectorless IgG1 anti-neonatal Fc receptor (FcRn) monoclonal antibody. Nipocalimab may ameliorate generalized myasthenia gravis (gMG) disease manifestations by selectively targeting FcRn IgG recycling and lowering IgG, including pathogenic autoantibodies in gMG.

OBJECTIVE: To evaluate the effectiveness and safety of intravenous nipocalimab added to background standard-of-care therapy in adolescents with gMG.

METHODS: Seropositive patients (12-<18 years) with gMG (MGFA Class II-IV) on stable therapy but inadequately controlled, were enrolled in a 24-week open label study. Nipocalimab was administered as a 30 mg/kg IV loading dose followed by 15 mg/kg IV every 2 weeks. The primary endpoint was change in total serum IgG. Secondary endpoints included change in MG-Ativities of Daily Living (MG-ADL) and quantitiatve MG(QMG) scores. Safety was assessed.

RESULTS: Seven adolescents were enrolled, five have completed 24 weeks. Mean standard deviation (SD) age was 14.1 (1.86) years; seven were anti-AChR+, six were female. Mean (SD) baseline scores were 4.29 (2.430) for MG-ADL, and 12.50 (3.708) for QMG. Nipocalimab showed a statistically significant reduction in total serum IgG at week 24; the mean (SD) percent change from baseline to week 24 for total serum IgG was -68.98% (7.561). The mean (SD) change at week 24 in MG-ADL was -2.40 (0.418) and in QMG was -3.80 (2.683); four of five patients achieved minimum symptom expression (MG-ADL score 0-1) by week 24. Nipocalimab was well-tolerated; there were no serious adverse events and no discontinuations due to an adverse event.

CONCLUSION: Nipocalimab demonstrated efficacy and safety in this 6-month trial in seropositive adolescents with gMG.

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Yaowei Zhu - employee of Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

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AGE-ASSOCIATED B CELLS IN MYASTHENIA GRAVIS AND THE INFLUENCE OF BRUTON'S TYROSINE KINASE ON THEIR DIFFERENTIATION AND FUNCTION

Manqiqige Su (Shanghai, China), Jie Song (Shanghai, China), Sushan Luo (Shanghai, China), Chongbo Zhao (Shanghai, China)

INTRODUCTION: The prognosis of myasthenia gravis (MG) is related to the activation of autoreactive B cells, which are challenging to track and target. Recently, a novel subset of B cells, known as age-associated B cells (ABCs), has been described with growing interest.

OBJECTIVE: This study investigates the characteristics of ABCs in naive MG patients and explores the potential of Bruton's tyrosine kinase (BTK) as a therapeutic target.

METHODS: Generalized acetylcholine receptor (AChR)-antibody positive MG patients without any prior immunotherapy were enrolled from Jan 2022 to May 2024 at Huashan Hospital. Single-cell transcriptomic sequencing, B cell receptor sequencing, and flow cytometry were employed to analyze the amplification and characteristics of ABCs in peripheral blood. BTK expression and phosphorylation levels were assessed using flow cytometry.

RESULTS: Peripheral ABCs were significantly elevated in MG patients compared to healthy controls, exhibiting phenotypic and immunoglobulin repertoire characteristics intermediate between naive and memory B cells. FPR1 and PLEK genes were notably upregulated in patinet ABCs relative to other B cell subsets. Under the in-vitro stimulation, patient ABCs significantly differentiated into antibody-secreting cells (ASC), producing IgG and higher levels of IL-6. Compared to controls and other B cell subsets in patients, BTK activation in ABCs was abnormally activated with higher expression and phosphorylation levels. In-vitro evobrutinib significantly reduced the proportion of ASCs and ABCs and the level of IgG, and significantly reduced T-bet level.

SUMMARY/CONCLUSION: This is the first study to elucidate the abnormal amplification and characteristics of peripheral ABCs in naive MG patients. These findings provide effective ideas for single drug application or multi-drug combination for the clinical treatment of MG patients.

THE APPLICATION OF DROPLET DIGITAL PCR AND METAGENOMIC NEXT-GENERATION SEQUENCING IN PATHOGENS IDENTIFICATION OF PNEUMONIA IN PATIENTS WITH MYASTHENIA GRAVIS: A PROSPECTIVE COHORT STUDY

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INTRODUCTION: Myasthenia gravis (MG) is an autoimmune disease affecting neuromuscular junctions. With long-term use of immunosuppressive therapies, MG patients are vulnerable to infections, in particular, pneumonia. Timely diagnostic investigation to establish the microbial etiology of pneumonia is essential for directing early intervention and improving clinical outcomes.

OBJECTIVE: This is the first prospective head-to-head study utilizing droplet digital polymerase chain reaction (ddPCR) and metagenomic next-generation sequencing (mNGS) to identify pathogens of pneumonia in MG patients

METHODS: We enrolled 22 MG inpatients diagnosed with pneumonia in the Department of Neurology, Huashan Hospital Affiliated to Fudan University from February 2023 to June 2023. A total of 23 sputum or bronchoalveolar lavage fluid (BALF) and three blood samples were detected synchronously by traditional culture, ddPCR, and mNGS.

RESULTS: The positive detection rate of pathogens detection was 88.46% (23/26) using culture, 96.15% (25/26) using mNGS, and 100% (26/26) using ddPCR. In the ddPCR-targeted 18 pathogens in spectrum, the positive detection rate by ddPCR was significantly higher than that by mNGS ($P<0.001$). We also detected antimicrobial resistance (AMR) genes using both ddPCR and mNGS tests. OXA gene was only identified by mNGS ($P=0.001$).

SUMMARY/CONCLUSION: The detection of ddPCR was more sensitive and rapid than that of mNGS in the target pathogens in spectrum, which can be conducive for early diagnosis. The evidence presented in our study concludes that the optimized ddPCR test alone or combined with mNGS could improve the precise and rapid diagnosis of pathogens in MG patients with pneumonia.

A CASE REPORT OF A GENETIC SYNDROME (CANVAS) PRESENTING WITH ATAXIA, NEUROPATHY, AND CHRONIC COUGH

Rani Priyanka Vasireddy (Lexington, KY), Yuyao Sun (Lexington, KY)

INTRODUCTION: Cerebellar ataxia, neuropathy, and vestibular areflexia syndrome (CANVAS) is an underdiagnosed cause of genetic neuropathy. Besides the classic triad of ataxia, neuronopathy, and vestibulopathy, patients often exhibit chronic cough, dysautonomia, and neuropathic pain. CANVAS is an autosomal recessive condition due to biallelic AAGGG expansion in the replication factor complex subunit 1 (RFC1) gene.

CASE REPORT: We report a 68-year-old man who experienced bilateral lower extremity numbness in his 50s which progressively worsened with resultant gait and balance difficulties. He developed progressive sequential bilateral hearing loss in his 60s. EDX testing was consistent with sensory neuropathy. The genetic neuropathy panel revealed a heterozygous pathogenic mutation of the POLG gene, associated with an autosomal recessive progressive sclerosing poliodystrophy, which does not explain his phenotype. Due to the hearing loss, he was treated for a presumed mitochondrial disorder, however, no clinical improvement was observed. Upon further inquiry, the patient reported falls, dizziness, clumsiness, dysphagia, and chronic cough. Physical exam was notable for bilateral hearing loss, sensory impairment in all modalities in bilateral lower extremities, diffuse areflexia, positive Romberg test, and ataxia. Given the combination of neuropathy, ataxia, and chronic cough, CANVAS was suspected and subsequently confirmed through genetic testing.

SUMMARY/CONCLUSION: We emphasize the importance of expanding genetic testing to include the RFC1 gene in cases of ataxia, neuropathy, and chronic spasmodic cough, as CANVAS is an underdiagnosed novel genetic disorder that is not covered by routine sponsored gene panels.

SUBCUTANEOUS EFGARTIGIMOD PH20 IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY: KEY SECONDARY OUTCOMES FROM THE ADHERE TRIAL

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INTRODUCTION: Efgartigimod, a human immunoglobulin G (IgG)1 antibody Fc fragment, blocks the neonatal Fc receptor, reducing IgG levels, including pathogenic autoantibodies. Multistage, double-blind, placebo controlled ADHERE assessed efficacy/safety of subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20) in chronic inflammatory demyelinating polyneuropathy (CIDP).

OBJECTIVE: To report new analyses related to ADHERE key secondary outcomes.

METHODS: Participants with active CIDP disease (off treatment/on standard treatments withdrawn during run-in) received weekly efgartigimod PH20 SC 1000 mg (stage A). Responders were randomized (1:1) to weekly efgartigimod PH20 SC 1000 mg or placebo (stage B). Key secondary endpoints included change from baseline (CFB) to last assessment in adjusted Inflammatory Neuropathy Cause and Treatment (aINCAT) score, Inflammatory Rasch-built Overall Disability Scale (I-RODS) score, mean grip strength (dominant hand), and safety (stages A/B).

RESULTS: In stage A, mean standard deviation (SD) CFB in aINCAT score, I RODS score, and grip strength was –0.9 (1.71), 7.7 (15.48), and 12.3 (18.68) kPa, respectively. In stage B, reduced risk of relapse with efgartigimod was observed regardless of aINCAT score change in stage A (≥1-point decrease: HR: 0.42 [95% CI,0.25–0.70]; no decrease: HR: 0.34 [95% CI,0.14–0.82]). In stage B, mean (SD) CFB in aINCAT score, I RODS score, and grip strength for efgartigimod vs placebo was 0.1 (1.08) vs 0.9 (1.98), 0.8 (12.33) vs –7.0 (19.10), and 2.1 (13.29) vs –8.2 (20.69) kPa, respectively. Efgartigimod was well tolerated; most adverse events were mild/moderate in severity.

SUMMARY/CONCLUSION: Clinical benefit across secondary endpoints in stage A was maintained with efgartigimod in stage B, but (partially) lost with placebo.

Disclosures:

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CARDIOVASCULAR COMORBIDITIES AND MYASTHENIA GRAVIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disorder characterized by varying degrees of skeletal muscle weakness. While primarily manifesting through ocular and generalized muscle weakness, its impact extends beyond these symptoms, influencing both the quality of life and morbidity spectrum including cardiovascular diseases.

OBJECTIVE: This systematic review and meta-analysis uses current evidence from primary studies on cardiovascular comorbidities in MG patients, providing a comprehensive overview of their cardiovascular risk profile.

METHODS: PubMed, Scopus, and Web of Science databases were searched through March 2024. Twelve observational studies encompassing 7,218 MG patients were included. Prevalence rates and corresponding sample sizes were extracted from eligible studies. The meta-analysis was conducted using the 'meta' package in R version 4.4.3. Meta-analysis was performed to estimate pooled prevalence rates for coronary artery disease (CAD), congestive heart failure (CHF), cerebrovascular diseases (CVDs), hypertension (HTN), and myocardial infarction (MI).

RESULTS: The meta-analysis revealed varied prevalence rates of cardiovascular conditions among MG patients. The pooled prevalence estimates (95% CI) were as follows: CVDs 21% (14% - 29%) [based on data from 3,104 patients], HTN 21% (11% - 35%) [based on data from 2,537 patients], CAD 8% (3% - 19%) [based on data from 538 patients], CHF 2% (1% - 4%) [based on data from 3,693 patients], and MI 5% (2% - 9%) [based on data from 3,344 patients].

SUMMARY/CONCLUSION: A significant burden of cardiovascular comorbidities exist among MG patients. These findings underscore the importance of comprehensive cardiovascular risk assessment and management in this population. Interventions targeting cardiovascular outcomes in MG are warranted.

TRANSCRIPTOMIC SIGNATURE INDUCED BY EDARAVONE IN MOTOR NEURONS FROM AN ALS PATIENT WITH A TDP-43 MUTATION

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INTRODUCTION: ALS is a fatal neurodegenerative disease characterized by progressive motor function loss. RADICAVA IV (edaravone) was United States FDA-approved for ALS treatment in 2017. In preclinical studies, edaravone reduced phenotypes in mouse models with a SOD1 mutation and in SOD1 mutation carrier-derived induced pluripotent stem cells (iPSCs). The broader applicability of edaravone in ALS treatment, particularly for non-SOD1 mutations, remains unclear.

OBJECTIVES: To investigate edaravone’s effect on spinal motor neurons derived from an ALS patient with a TDP-43 mutation.

METHODS: iPSCs from an ALS patient with the TDP-43 A382T mutation were differentiated into spinal cholinergic neurons and treated with 30 μM edaravone for intervals of 6, 12, and 24 hours after 1 week of culture. Neuronal cell death assays, immunocytochemistry, and RNA sequencing were conducted to evaluate treatment effects.

RESULTS: Edaravone demonstrated neuroprotective effects and corrected TDP-43 mislocalization in iPSC-derived motor neurons from an ALS patient with the TDP-43 mutation. Transcriptomic analysis revealed over 1000 differentially expressed genes (DEGs) in edaravone-treated neurons, with gene ontology and pathway analyses linking these DEGs to neuronal survival and stress resilience. These findings suggest edaravone operates through a unique mechanism distinct from other antioxidants in ALS.

SUMMARY/CONCLUSION: Our findings provide evidence suggestive of edaravone’s capacity to induce transcriptomic changes that confer neuroprotection in ALS models with TDP-43 pathology. Our iPSC data from the A382T mutation in a TDP-43 ALS case support edaravone’s therapeutic value in ALS and highlighting the possibility of modulating TDP-43-related pathways in treatment strategies.

Disclosures:

Satsuki Mikuriya - is an employee of Mitsubishi Tanabe Pharma America, Inc.

Abduqodir Toychiev - is an employee of Mitsubishi Tanabe Pharma America, Inc.

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LONG-TERM FOLLOW-UP STUDY OF RISDIPLAM IN PARTICIPANTS WITH SPINAL MUSCULAR ATROPHY (WeSMA)

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INTRODUCTION: Spinal muscular atrophy (SMA) is a genetic, progressive neuromuscular disease. Risdiplam (EVRYSDI®), an oral survival of motor neuron 2 (SMN2) pre-mRNA splicing modifier, is an FDA-approved treatment for pediatric and adult individuals with SMA.

OBJECTIVE: This Phase 4, multi-center, longitudinal, prospective, non-comparative study (WeSMA; NCT05232929) will investigate risdiplam's long-term safety and effectiveness in individuals with all SMA types.

METHODS: Individuals with SMA receiving risdiplam are eligible. Exclusion criteria include risdiplam hypersensitivity or participation in another risdiplam trial. Enrollment of ≤500 individuals is planned. Follow-up is ≤5 years from enrollment or until consent withdrawal, loss to follow-up, or death. Primary outcomes are adverse event (AE) rates, AEs of special interest and serious AEs. The secondary outcome is the percentage of participants improved on the Clinical Global Impression-Change scale. Exploratory outcomes are changes in motor, respiratory and bulbar functions; hospitalizations; survival in infants aged <2 years with Type 1 SMA; and patient- and caregiver-reported outcomes.

RESULTS: This interim analysis included 198 individuals (data cut-off: January 17, 2024). The sample size and calculated percentages were dependent on available data. Mean (standard deviation (SD)) age at enrollment and diagnosis were 21.2 (17.1) and 5.0 (11.3) years, respectively. At study enrollment, 150 (83.3%) were established on risdiplam for >6 months (mean [SD]: 22.6 [8.2] months). There were 104 individuals (67.1%) who previously received nusinersen (SPINRAZA®) and 22 (14.6%) who were treated with onasemnogene abeparvovec (ZOLGENSMA®).

SUMMARY/CONCLUSION: We will provide data on risdiplam's real-world use, safety, and effectiveness in a broad population of individuals with SMA.

Disclosures:

Imran Tanvir - is an employee of Genentech Inc. and shareholder of F. Hoffmann-La Roche.

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Sheila Shapouri - is an employee of Genentech Inc. and shareholder of F. Hoffmann-La Roche.

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POST INFLAMMATORY SENSORY GANGLIONOPATHY IN ASSOICATION WITH COVID VACCINATION

ChaVonne Tatum (DeKalb, IL), Arjun Seth (Chicago, IL)

INTRODUCTION/BACKGROUND: Sensory ganglionopathies are typically related to a post-infectious, nutritional, paraneoplastic, or autoimmune cause. COVID vaccinations have been linked to new onset autoimmune phenomenon. Here we report a rare case of sensory ganglionopathy associated with COVID vaccination treated with intravenous immunoglobulin (IVIg).

CASE REPORT: A 40-year-old woman with asthma received COVID vaccinations in March 2021. Approximately 2 weeks after her second dose, she developed ascending numbness in her limbs with associated gait instability and falls over several months. Exam showed diminished sensation to all modalities distally with areflexia, sensory ataxia, and normal strength. EMG/NCS showed a severe sensory axonal neuropathy. MRI C-spine showed a longitudinally extensive T2 signal hyperintensity involving the dorsal columns. Labs showed serum protein electrophoresis /immunofixation electrophoresis negative, HIV non-reactive, erythrocyte sedimentation rate 15, -reactive protein < 10, Vitamin B12 1190, TSH 6.75, paraneoplastic panel negative, Vitamin B6 8.9, antinuclear antibody negative, HbA1C 4.9%. cerebrospinal fluid showed white blood cells < 1, red blood cells 1, glucose 72, protein 48, negative oligoclonal bands. She was treated with prednisone with no improvement, later started and continued IVIg with improvement in gait, initially ambulating with cane to ambulating independently. Her neurologic exam at follow-up over1 year remained stable. IVIg was weaned and stopped. Repeat NCS has shown reduced but improved left upper limb sensory responses.

SUMMARY/CONCLUSION: We report a rare case of a post inflammatory sensory ganglionopathy in association with COVID vaccination. In patients with gait or functional impairment, physicians can consider treatment with IVIg with eventual wean of medication once exam and EDX studies remain stable.

ASYMMETRIC SENSORY MOTOR DEMYELINATING NEUROPATHY SECONDARY TO NOVEL GJB1 MUTATION

ChaVonne Tatum (Chicago, IL), Arjun Seth (Chicago, IL), Glenn Harris (Chicago, IL)

INTRODUCTION/BACKGROUND: Genetic neuropathies typically present with specific characteristics on nerve conduction studies, such as uniform demyelination in Charcot Marie Tooth disease 1A. We report a novel genetic mutation in GJB1 which showed an asymmetric demyelinating neuropathy on nerve conduction studies.

CASE REPORT: A 30-year-old African American male presents with 15 years of gait instability and falls initially beginning with difficulty with balance and moving his feet. His exam showed pes cavus, hammer toes, ankle contractures, atrophy, and weakness of his intrinsic hand muscles and distal > proximal weakness. Sensory exam showed decreased sensation to all modalities in a length dependent manner. His mother and maternal grandfather had similar symptoms and were wheelchair bound by their 50s. Neither had genetic testing and both are deceased. NCSs showed a length dependent sensory motor demyelinating > axonal neuropathy with asymmetric median and ulnar sensory responses and non-uniform slowed conduction velocities. Cerebrospinal fluid studies showed white blood cell 2, red blood cell < 1, protein 20, glucose 63. Labs showed: HbA1C 5.7%, SPEP/IFE normal, Vitamin B12 432, antinuclear antibody negative, erythrocyte sedimentation rate5, ganglioside antibody negative, HIV negative, Lyme negative. Invitae Comprehensive Neuropathies Panel showed a hemizygous variant of unknown significance in the GJB1 gene (c.231G > T (p. Trp77Cys)), W77C.

SUMMARY/CONCLUSION: Genetic neuropathies typically present with symmetric demyelination on EDX testing. The W77C mutation in GJB1 has been described as causing non-functional channels in xenopus oocytes but has not been previously noted in humans. This case represents as atypical finding of asymmetric demyelination associated with a previously undescribed mutation in GJB1.

INTRAVENOUS IMMUNOGLOBULIN THERAPY FOR POST-COVID-19 POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME

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INTRODUCTION: Post-COVID-19 POTS has been reported in about 30% of adults following acute COVID infection. Although the pathophysiology remains unknown, immune dysregulation may play a role based on the presence of non-specific immune markers seen in patients with post-COVID-19 autonomic dysfunction and anecdotal reports of a favorable response to intravenous immunoglobulin (IVIg).

OBJECTIVE: To characterize the clinical features of post-COVID-19 postural orthostatic tachycardia syndrome (POTS) and response to IVIg.

METHODS: This was a retrospective review of eight patients with post COVID-19 POTS that were treated with IVIg. Data collected included clinical symptoms, autonomic testing, autoantibody serology and qualitative response to treatment.

RESULTS: This study included eight patients with POTS confirmed by tilt table testing who received IVIg. Median age was 38 years, and all patients were female. The most commonly reported symptoms included dizziness, palpitations, neuropathic pain and gastrointestinal disturbances. Four out of five patients demonstrated abnormal results on quantitative sudomotor axon reflex testing or skin biopsy, supporting the diagnosis of neurogenic POTS. All patients received 2gm/kg/month of IVIg for minimum of 3 months in weekly or monthly doses. At 3 months, significant improvement was seen in six out of eight patients characterized by reduced orthostatic intolerance and less neuropathic pain. Of those that responded to IVIg, four were seropositive for neural autoantibodies.

SUMMARY/CONCLUSION: IVIg appeared beneficial in the symptomatic treatment of POTS and associated neuropathic pain. Although larger studies are needed, the presence of neural autoantibodies suggests an immune-mediated mechanism in some cases of post-COVID-19 POTS and may be predictive of responsiveness to IVIg.

Disclosures:

Jinny Tavee - is a consultant for CSL Behring.

SOCIAL DETERMINANTS OF HEALTH ARE ASSOCIATED WITH DELAYED DIAGNOSIS IN MYASTHENIA GRAVIS

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INTRODUCTION: Early diagnosis of generalized myasthenia gravis (gMG) may help alleviate symptoms and improve function.

OBJECTIVE: To determine if social determinants of health (SDoH) were associated with delayed diagnosis.

METHODS: Using IQVIA LAAD insurance claims, a retrospective observational cohort study was conducted among 3,873 adults diagnosed with MG between 9/1/18 and 8/31/20. Eligible individuals had 12+ months of claims history prior to index MG diagnosis. Delayed diagnosis was defined as >90 days from presentation (claim for MG-associated symptom (diplopia, ptosis, dysphagia, etc.) or diagnostic procedure (ophthalmology exam, brain MRI, swallow study, etc.) to index. SDoH measures included Socially Determined community risk measures (high vs. low) of housing, food, economic, transportation, health literacy, social connectedness, and digital landscape.

RESULTS: Delayed diagnosis was present in 1,837 (46.1%) individuals. Most common presenting symptoms were muscle weakness (27.6%), ptosis (15.8%), dysphagia (15.5%), and diplopia (15.4%). Most common diagnostic procedures were ophthalmology exam (26.3%) and brain MRI (20.7%). Individuals with delayed diagnosis were more likely female, of older age, and to have higher medical and psychiatric comorbidity burden. High-risk economic, digital landscape, and social connectedness ZIP codes were associated with elevated (but non-significant) odds for delayed diagnosis. Individuals in communities with high-risk housing (odds ratio (OR) 1.22) and poor health literacy (OR 1.21) had meaningful elevated odds. After adjustment for demographics, insurance, and comorbidities, housing risk remained a meaningful factor (nominal $p<0.05$).

SUMMARY/CONCLUSION: Social determinants risk contributes to diagnosis delays and should be addressed to optimize care for individuals with potential MG. Sponsor: UCB Pharma

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Joshua N. Liberman - is an employee of Health Analytics, LLC.
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EVIDENCE OF MISDIAGNOSIS IN ADMINISTRATIVE CLAIMS DATA FOR INDIVIDUALS WITH MYASTHENIA GRAVIS

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INTRODUCTION: Establishing a diagnosis of myasthenia gravis (MG), a rare neuromuscular disorder, can be complicated by variation in symptom presentation.

OBJECTIVE: To determine if social determinants of health (SDoH) are associated with misdiagnosis in MG.

METHODS: Using IQVIA LAAD insurance claims, a retrospective observational cohort study was conducted among 3,873 adults diagnosed with MG between 9/1/18 and 8/31/20. Eligible individuals had 12+ months of claims prior to and following index MG diagnosis. Possible misdiagnosis was defined by select conditions with one or more claims prior to index and no claims following index. Conditions included stroke, COPD, chronic fatigue syndrome, MS, thyroid eye disease, Hashimoto's thyroiditis, malignant thymus neoplasm, Guillain-Barré syndrome, Graves' disease, systemic lupus erythematosus, ALS, and myositis. SDoH measures included Socially Determined community risk measures.

RESULTS: 425 (11.0%) individuals had evidence of misdiagnosis. The most common condition was stroke (5.5%), followed by chronic obstructive pulmonary disease (4.5%), chronic fatigue (2.2%), Graves' disease (1.5%), multiple sclerosis (1.4%), and Guillain-Barré syndrome (1.1%). Misdiagnosed individuals had meaningfully higher medical and psychiatric comorbidity burden including congestive heart failure (20.5% vs. 11.5%), anxiety (25.9% vs. 15.5%), and major depressive disorder (26.1% vs. 15.7%) (all nominal $p<0.05$). Misdiagnosed individuals were more likely to be diagnosed in an inpatient facility (37.4% vs. 25.3%). Six high-risk SDoH measures had an elevated unadjusted odds ratio (OR) for misdiagnosis, with the highest OR for social connectedness (OR 1.40) and housing risk (OR 1.24). Social connectedness risk remained meaningful after adjustment for demographics and comorbidities.

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Judith Thompson - is an employee of UCB Pharma.
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TARSAL TUNNEL SECONDARY TO AN ANKLE CYST DIAGNOSED BY ULTRASOUND: A CASE REPORT

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INTRODUCTION/BACKGROUND: Tarsal tunnel syndrome (TTS) is characterized by compression of the tibial nerve resulting in pain and numbness localized mainly in the plantar foot. Tibial entrapment neuropathy is infrequent in pediatric patients. Many etiologies, both intrinsic and extrinsic, have been implicated in TTS in patients, including pes planus deformity, inflammatory conditions, and ganglion cysts. This case report focuses on a rare incident of TTS secondary to a ganglion cyst in a pediatric patient, diagnosed and confirmed with EDX testing and neuromuscular ultrasound (NMUS).

CASE REPORT: A 12-year-old child with 2 years of ankle and foot pain presented with acutely worsening pain over 6 months. Initially, symptoms occurred with physical activity and were attributed to poorly fitting shoes. Symptoms then developed at rest, with associated sharp, shooting pain and numbness into the toes. Subsequently, the patient followed with orthopedic surgery, where initial MRI imaging revealed a posterior tibialis tendinopathy. Conservative measures with physical therapy, rest, and immobilization with a walking boot were unsuccessful. Examination revealed neutral foot alignment, tenderness along the medial calcaneus and posterior medial malleolus. Special testing revealed a positive Tinel's test with radiation noted to the toes. EDX was performed, demonstrating no response to the lateral plantar nerve with slowing of the medial plantar nerve, consistent with TTS. NMUS was performed and revealed a 5x5x11mm ganglion cyst compressing the underlying nerve.

SUMMARY/CONCLUSION: TTS is a rare diagnosis in the pediatric population. NMUS is a cost-effective, safe adjuvant to EDX testing in evaluating for extrinsic causes of mononeuropathy, such as ganglion cysts.

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TO ASSESS THE EFFICACY AND REPRODUCIBILITY OF A DEEP LEARNING ALGORITHM IN THE SEGMENTATION OF THE MEDIAN NERVE ON ULTRASOUND IMAGES

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INTRODUCTION: Advances in ultrasound imaging have improved our capacity to study peripheral nerve infrastructures and pathological states. The next step in improving the reliability of nerve identification is to use deep learning algorithms to automate the process. Deep learning algorithms can be an ideal platform to perform automated peripheral nerve analysis.

OBJECTIVE: Evaluating deep learning efficacy in segmenting the median nerve at the wrist and forearm from B-mode ultrasound images.

METHODS: We obtained 500 images of the median nerve at the wrist and 500 at the forearm from 21 healthy volunteers. The nerve was manually outlined by a neurologist. Each batch was randomly divided into a training set/testing set ratio of 4:1. The U-Net model was trained on the training set. Model performance on the testing set was evaluated using the mean Intersection-over-Union (IoU) and Dice scores. Agreement between the cross-sectional area measurements obtained from U-Net and a neurologist was assessed using paired t-test and intraclass correlation coefficient (ICC2).

RESULTS: Mean IoU ± standard deviation (SD) and Dice score (±SD) of the forearm segmentation results were 0.84(±0.06) and 0.92(±0.04) respectively. Those of the wrist were 0.82(±0.09) and 0.90(±0.06) respectively. The estimated ICC2 agreements were excellent (0.91) at the forearm, and moderate (0.67) at the wrist. The paired t-test showed systematic bias at the forearm (mean=5.81 for neurologist, mean=5.68 for U-Net, $p = 0.04$) and no systematic bias at the wrist ($p = 0.42$).

SUMMARY/CONCLUSION: Our study showed that deep learning can identify the median nerve with high certainty.

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NERVE ULTRASOUND IN THE DIAGNOSIS OF ULNAR NEUROPATHY AT THE ELBOW DUE TO HANSEN'S DISEASE - CASE REPORT

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INTRODUCTION/BACKGROUND: Advancements in ultrasound (US) technology has allowed clinicians to obtain high resolution images of peripheral nerves and to investigate the infrastructures of different nerve pathological states at bedside. Hansen's disease is a rare medical phenomenon in the United States that presents with multifocal peripheral neuropathies. Nerve US can allow us to visualize the pathological state of this disease.

CASE REPORT: A 68-year-old man with Hansen's disease, presents with numbness in the fourth and fifth digits in both hands without any weakness and distal leg sensory loss. A focused neurological exam showed diminished sensation to light touch and cold temperature in the medial side of both hands. EMG/NCS showed bilateral ulnar sensorimotor neuropathy at the level of the elbows, with a conduction block on the right side. Nerve US showed significant enlargement of the ulnar nerves at (Right: 19.29 mm2; Left: 17.6 mm2, Upper-Limit-Of-Normal [ULN]: 8.8 mm2) and above (Right: 24.74 mm2; Left: 24.5 mm2, ULN: 9.3 mm2) the elbows. There were also enlarged fascicles and increased nerve vascularity at those levels. The tibial nerve at the medial malleolus and fibular nerve at the fibular neck were also markedly enlarged, though EDX studies were normal. The median nerves were normal on US and EDX studies.

SUMMARY/CONCLUSION: The use of US helped us visualize the pathological changes of Hansen's disease on the ulnar nerves by assessing nerve size and vascularity. The results coincide with the EMG/NCS and clinical findings, further confirming an ulnar neuropathy. This highlights the effectiveness of diagnostic US in assessing atypical peripheral neuropathies.

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TRANSIENT LEUKOENCEPHALOPATHY ASSOCIATED WITH GJB1 GENE X-LINKED CHARCOT-MARIE-TOOTH DISEASE: CASE REPORT

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INTRODUCTION: Charcot-Marie-Tooth disease (CMT) is an inherited neurological disorder characterized by progressive distal muscle weakness, pes cavus, and loss of deep tendon reflexes. CMTX1, an x-linked subtype caused by mutations in the GJB1 gene, characterized by a mixed demyelinating and axonal neuropathy. Accounts for 10-15% of CMT cases, also presents with transient central nervous system (CNS) manifestations, extending the phenotype beyond peripheral neuropathy. This case report describes a patient with CMTX1 who presented with transient CNS dysfunction, highlighting the diagnostic challenges and importance of genetic testing.

CASE REPORT: A 19-year-old male presented with sudden onset of right upper extremity weakness extending to the lower extremity and speech disturbance lasting 3 hours with complete recovery. Despite a normal physical examination, brain MRI showed hyperintense lesions on T2 and FLAIR, distributed in both semi-oval centers, with diffusion restriction on DWI, which disappeared spontaneously on a follow-up MRI three months later. Neurophysiologic studies revealed sensory and motor axonal polyneuropathy. Genetic analysis identified the hemizygous likely pathogenic variant GJB1: c.72G>C (p.Trp24Cys), confirming the diagnosis of reversible transient leukoencephalopathy associated CTX1.

CONCLUSION: This case highlights the phenotypic variability and potential for transient CNS symptoms in CMTX1, challenging the conventional view of CMT as a purely peripheral disorder. It emphasizes the need for a comprehensive evaluation, including genetic testing, in patients with inherited neuropathies, especially when presenting with atypical symptoms. Recognizing the full spectrum of CMTX1 manifestation can avoid misdiagnosis and guide appropriate treatment, highlighting the critical role of genetics in the diagnosis and understanding of inherited neuropathies.

EMPASIPRUBART (ARGX-117) IN MULTIFOCAL MOTOR NEUROPATHY: BASELINE CHARACTERISTICS AND MMN CONFIRMATION COMMITTEE OUTCOME OF THE PHASE 2 ARDA STUDY COHORT 1

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INTRODUCTION: Multifocal motor neuropathy (MMN) is a rare immune-mediated neuropathy characterized electrophysiologically by motor nerve conduction block, clinically by progressive asymmetric limb weakness and spared sensation, and pathologically by antibody-mediated complement activation. Intravenous immunoglobulin (IVIg) is the only proven efficacious therapy. Empasiprubart blocks activation of classical and lectin complement pathways via C2 binding. ARDA (NCT05225675) is a phase 2, multicenter, randomized, placebo-controlled, double-blinded, parallel-group study that assesses the safety, efficacy, and tolerability of empasiprubart in adults with MMN. An MMN confirmation committee (MCC) evaluated the presence of MMN and assessed IVIg dependency during screening of ARDA participants.

OBJECTIVE: To present updated baseline characteristics, demographics, and MCC outcomes of participants in ARDA cohort 1.

METHODS: ARDA enrolled 54 participants with probable or definite MMN (2010 European Federation of Neurological Societies/Peripheral Nerve Society guidelines). All had proven IVIg dependency and were on stable IVIg regimen leading to randomization. MMN diagnosis and IVIg dependency were confirmed by the MCC which was composed of an international panel of four neurologists experienced in the diagnosis and treatment of MMN.

RESULTS: Among 27 participants treated in cohort 1, 74.1% had definite MMN and 25.9% had probable MMN. MCC screening found that 55.6% of participants were IVIg dependent, while 44.4% were uncertain. The median age was 49 years, 40.7% were female, and 88.9% were Whit e. The median time from diagnosis to study randomization was 8.6 years. Further results will be presented at the meeting.

SUMMARY/CONCLUSION: This ongoing ARDA study will inform the utility and safety of empasiprubart in patients with MMN.

Disclosures:

Eduardo Nobile-Orazio - consultant fees from argenx, CSL Behring,Dianthus, Janssen, Kedrion, LFB, Roche, Sanofi, Takeda.

Emma Persson - is an employee of argenx.

Iris Van Hoomissen - is an employee of argenx.

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Miodrag Vujcic - is an employee of argenx.

Olivier Van de Steen - is an employee of argenx.

Jeffrey A. Allen - consultant fees for Akcea therapeutics, Alexion, Alnylam, Annexon, argenx SE, CSL Behring, Grifols, Immuovant, Immupharma, Johnson & Johnson, Pfizer, Sanofi, and Takeda.

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Sharam Attarian - consultant fees from Alexion, argenx, Biogen, Janssen, LFB, Pfizer, Sanofi, UCB.

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Chafic Karam - consultant for Acceleron, Alpine, Alexion, Alnylam, Annexon, argenx, Astra Zeneca, Corino, Biogen, CSL Behring, Genentech, Ionis, Neuroderm, Novo Nordisk, Pfizer, Sanofi, UCB, Takeda, and Zai lab.

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THE BURDEN PEOPLE SUFFERING FROM CIDP EXPERIENCE IN TERMS OF UTILITIES: COMPARISON WITH THE GENERAL POPULATION

Febe Brackx (Brussels, Belgium), Geoffrey Istas (Ghent, Belgium), Benjamin Van Hoorick (Ghent, Belgium), Trevor Mole (Ghent, Belgium), Petra Koopmans (Ghent, Belgium), Clémence Arvin-Bérod (Ghent, Belgium), Sarah Dewilde (Brussels, Belgium)

INTRODUCTION: Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare autoimmune disorder characterized by distal/proximal weakness and/or sensory deficits.

OBJECTIVE: The objective of this analysis is to compare utility values between ADHERE CIDP patients and the general population, and their association with disease severity.

METHODS: ADHERE is the largest CIDP trial conducted in which efficacy of efgartigimod was demonstrated. In the open-label stage A of this trial, all patients (n=322) received efgartigimod for up to 12 weeks or until evidence of clinical improvement (ECI). The Inflammatory Neuropathy Cause and Treatment (INCAT) score was used as one of the efficacy scales measuring the degree of disability in patients ranging from 0 (no disability) to 10 (severely disabled). EQ-5D-5L utility values at the last assessment of stage A were compared to the general population for responders (ECI) and non-responders (no ECI) separately. POPUP is a multinational digital observation study among 9000 general population participants to estimate health-related quality-of-life population norms, including the EQ-5D-5L.

RESULTS: The mean utility score is 0.339 (SD=0.327) for non-responders, 0.601 (SD=0.248) for responders, and 0.799 (SD=0.213) for the general population. CIDP patients report more problems than the general population on all items of the EQ-5D-5L, apart from anxiety and depression. Furthermore, it was found that a higher INCAT score corresponds to lower utility values (0.675, 0.518 and 0.259 and -0.061 for INCAT score <=3, 4-5, 6-7 and >7 respectively).

SUMMARY/CONCLUSION: The utility values of ADHERE CIDP patients are lower than the general population and higher disease severity is associated with lower utility values.

Disclosures:

Febe Brackx - received honoraria for the analysis of the data and reporting.

Geoffrey Istas - is an employee of argenx, the sponsor of the ADHERE study.

Benjamin Van Hoorick - is an employee of argenx, the sponsor of the ADHERE study.

Trevor Mole - is an employee of argenx, the sponsor of the ADHERE study.

Petra Koopmans - is an employee of argenx, the sponsor of the ADHERE study.

Clémence Arvin-Bérod - is an employee of argenx, the sponsor of the ADHERE study.

Sarah Dewilde - received honoraria for the analysis of the data and reporting.

HETEROGENEITY OF EQ-5D-5L UTILITIES AMONG PEOPLE SUFFERING FROM CIDP

Sarah Dewilde (Brussels, Belgium), Geoffrey Istas (Ghent, Belgium), Benjamin Van Hoorick (Ghent, Belgium), Trevor Mole (Ghent, Belgium), Petra Koopmans (Ghent, Belgium), Clémence Arvin-Bérod (Ghent, Belgium), Febe Brackx (Brussels, Belgium)

INTRODUCTION: Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare autoimmune disorder characterized by distal/proximal weakness and/or sensory deficits.

OBJECTIVE: The objective of this analysis was to compare utility values in ADHERE patient subgroups.

METHODS: ADHERE is the largest CIDP trial conducted in which efficacy of efgartigimod was demonstrated. In the open-label stage A of this trial, all patients (n=322) received efgartigimod for up to 12 weeks. Using analysis of variance (ANOVA), we tested for difference in EQ-5D-5L utility values at the end of stage A between subgroups.

RESULTS: Symptom severity measured with the Inflammatory Neuropathy Cause and Treatment (INCAT) score had a significant impact ($p<0.0001$) on utility values, with higher symptom severity being associated with lower utility values (0.675, 0.518, 0.259 and -0.061 for INCAT scores <=3, 4-5, 6-7 and >7 respectively). No significant difference was found for subgroups defined by age category (p=0.164, 0.607 for 18-20 years, 0.560 for 30-39 years, 0.549 for 40-49 years, 0.565 for 50-59 years, 0.456 for 60-69 years and 0.567 for 70+ years); sex (p=0.908, 0.540 male, 0.536 female); disease duration (p=0.346, 0.559 for diagnosis <=1 year ago, 0.550 for 1-4 years ago, 0.536 for 4-10 years ago, 0.454 for >10 years ago); disease evolution (p=0.057, 0.506 progressive, 0.572 relapsing); treatment history (p=0.500, 0.530 treatment-experienced, 0.556 treatment-naïve); CIDP type (p=0.959, 0.539 atypical, 0.537 typical); and CIDP disease activity status (CDAS) level at screening (p=0.598, 0.686 level 2, 0.543 level 3, 0.555 level 4, 0.527 level 5).

SUMMARY/CONCLUSION: We observed a significant effect of CIDP symptom severity on utility values.

Disclosures:

Sarah Dewilde - received honoraria for the analysis of the data and reporting.

Geoffrey Istas - is an employee of argenx, the sponsor of the ADHERE study.

Benjamin Van Hoorick - is an employee of argenx, the sponsor of the ADHERE study.

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Clémence Arvin-Bérod - is an employee of argenx, the sponsor of the ADHERE study.

Febe Brackx - received honoraria for the analysis of the data and reporting.

COLCHICINE-INDUCED TUBULAR AGGREGATE MYOPATHY MIMICKING DISTAL MYOPATHY: A CASE REPORT

Laura Vargas (Greenville, SC), Eduardo Cortez-Garcia (Taylors, SC), Cynthia De la Rosa Zapata (Greer, SC)

INTRODUCTION/BACKGROUND: To highlight a unique pattern of colchicine-induced tubular aggregate myopathy (TAM) mimicking a distal myopathy.

Colchicine is a medication commonly used for gout; there are many reported cases of colchicine leading to toxic myopathy. Risk factors include decreased renal function and age. Toxic myopathies anecdotally present as proximal symmetrical weakness. Identifying alternative clinical presentations may be corroborated with muscle biopsy and EMG.

CASE REPORT: 79-year-old male with chronic kidney disease, heart transplant on cyclosporine and azathioprine, presented with a 2-week history of subacute severe extremity weakness. Examination revealed asymmetric, distal-predominant, upper extremity weakness and proximal lower extremity weakness. Reflexes were diminished in the upper extremities and areflexic in the lower extremities. Clinical myotonia was absent. Myotonic dystrophy versus inclusion body myositis vs atypical immune mediated myopathy was considered. Work up revealed creatine kinase of 1,599 IU/L. EMG revealed a severe, asymmetric, irritable myopathy involving myotonic discharges. A distal axonal sensorimotor neuropathy in the lower extremities was also detected. Myositis panel negative. Left quadriceps muscle biopsy revealed a tubular aggregate myopathy. It was discovered that the patient had started colchicine a few weeks prior to onset of symptoms and was discontinued. One month follow up revealed only moderate weakness to hip flexor muscles.

SUMMARY/CONCLUSION: Our case report elucidates a unique pattern of TAM mimicking a distal myopathy. Distal myopathy patterns are typically seen in myotonic dystrophy type 1 and inclusion body myositis. Detection of this phenotypic pattern should raise concern for TAM and toxic exposure to colchicine should be investigated.

DNTH103, A POTENTIALLY SAFER AND MORE CONVENIENT NOVEL THERAPY FOR GENERALISED MYASTHENIA GRAVIS

John Vissing (Copenhagen, Denmark), Stojan Peric (Belgrade, Serbia), Lisa Lewis (Worcester, NY), Jeffrey Stavenhagen (New York, NY), Sankalp Gokhale (New York, NY)

INTRODUCTION: Complement inhibition is an effective treatment pathway in generalized myasthenia gravis (gMG). DNTH103 is a fully human, potent, monoclonal antibody with a long half-life. It selectively binds to active human C1s to block only the classical complement pathway (CP) and maintain complement-mediated bacterial killing. DNTH103 is in phase 2 for gMG (2024 phase 2 planned for multifocal motor neuropathy and chronic inflammatory demyelinating polyneuropathy).

OBJECTIVE: Three preclinical studies aimed to evaluate the efficacy or safety of DNTH103.

METHODS: 1: DNTH103 functional activity was characterized with Human-on-a-Chip Neuromuscular Junction (NMJ) System using healthy induced pluripotent stem cells -derived motoneurons, skeletal muscle myotubes and sera from three healthy and three acetylcholine receptor-positive (AChR+) gMG patients. Fatigue index was calculated using continuous electrical stimulation of neuromuscular junctions with or without DNTH103 or anti-C5 antibody. 2: complement assays using DNTH103 and anti-C5 antibody evaluated inhibition of lectin and alternative pathways. 3: serum bactericidal assays with DNTH103, anti-C5 antibody, or control were conducted with 80% normal human sera and anti-capsular antibodies mimicking vaccination against Neisseria meningitidis.

RESULTS: DNTH103 at 0.1 and 1μM reduced muscle fatigue index in AChR+ gMG samples by 24.8% and 27.8% respectively; similar results were observed with anti-C5. DNTH103 did not inhibit the lectin or alternative pathways nor impede bacterial killing (similar to untreated control); anti-C5 inhibited all pathways and blocked bacterial killing by complement.

CONCLUSION: Efficacy of DNTH103 in improving neurotransmission and muscle contraction and selective inhibition of CP provides an attractive development candidate for gMG – potentially reducing risks of severe infection seen with current gMG therapies.

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Stojan Peric - consultancy fees from Dianthus Therapeutics, Inc.
Lisa Lewis - consultancy fees from Dianthus Therapeutics, Inc.
Jeffrey Stavenhagen - is an employee of Dianthus Therapeutics.
Sankalp Gokhale - is an employee of Dianthus Therapeutics.

COVID-19 VACCINATION RESPONSE IN PARTICIPANTS RECEIVING EFGARTIGIMOD IV OR EFGARTIGIMOD PH20 SC IN ADAPT+ OR ADAPT-SC+

Tuan Vu (Tampa, FL), Francesco Saccà (Naples, Italy), James F. Howard Jr (Chapel Hill, NC), John W. Sleasman (Durham, NC), Fien Gistelinck (Ghent, Belgium), Paul Duncombe (Ghent, Belgium), Benjamin Van Hoorick (Ghent, Belgium), Sophie Steeland (Ghent, Belgium), Renato Mantegazza (Milan, Italy), Jan L. De Bleecker (Ghent, Belgium), Antoine Azar (Baltimore, MD), Kevin Winthrop (Portland, OR)

INTRODUCTION: Patients with generalized myasthenia gravis (gMG) experience a greater risk of adverse outcomes from respiratory infections, including COVID-19. Some immunosuppressive therapies used in gMG management may increase risk of infection and impair vaccine responses.

OBJECTIVE: To investigate the effect of treatment with efgartigimod administered intravenously (IV) or subcutaneously (SC, coformulated with recombinant human hyaluronidase PH20)], a human immunoglobulin G1 (IgG1) antibody Fc-fragment that reduces total and pathogenic IgG levels through neonatal Fc receptor blockade, on humoral immune responses to COVID-19 vaccination in participants with gMG.

METHODS: In ADAPT+ (completed) and ADAPT-SC+ (ongoing open-label extension), efgartigimod IV (10 mg/kg) or efgartigimod PH20 SC (1000 mg) were administered in cycles of four once-weekly infusions/injections. Among other COVID-19 receptor binding domain-specific IgGs, SARS-CoV-2-IgG-RBD responses were assessed, nominally, at prevaccination, ≥4 weeks after vaccination, and subsequently at 1 week after the fourth efgartigimod PH20 SC injection (when total IgG levels were maximally reduced). One sample was collected if postvaccination time points coincided with each other.

RESULTS: Eighteen participants in ADAPT-SC+ received a COVID-19 vaccine during or after a cycle. For 78% (n=14/18) of participants, this was their second or third vaccine dose. A 35.9-fold increase in SARS-CoV-2-IgG-RBD levels occurred from prevaccination to ≥4 weeks postvaccination. Similarly, from prevaccination to 1 week after the fourth efgartigimod PH20 SC injection, a 33.8-fold increase was seen. Similar results were observed with efgartigimod IV during ADAPT+.

SUMMARY/CONCLUSION: Consistent with efgartigimod IV results, participants receiving efgartigimod PH20 SC were able to mount antigen-specific IgG responses to COVID-19 immunization.

Disclosures:

Tuan Vu - has served as a speaker and consultant for argenx and participated in trials sponsored by argenx; served as a speaker for Alexion, CSL Behring, and Allergan/AbbVie; performed consulting work related to MG for Alexion/AstraZeneca and UCB; participated in trials in MG sponsored by Alexion/AstraZeneca, argenx, UCB, Horizon, Johnson & Johnson, Dianthus, Remegen, Regeneron, Immunovant, Cartesian, and Sanofi.

Jan L. De Bleecker - has served as a consultant for argenx, Alexion Pharmaceuticals, Inc, CSL, UCB Pharma, Alnylam Pharmaceuticals Inc, Janssen, and Sanofi Genzyme.

Antoine Azar - has received research support from X4 and Grifols and is a consultant for Grifols, Takeda, Pfizer, Janssen, and argenx.

Kevin Winthrop - has received research support from Bristol Myers Squibb and Pfizer and consulting honoraria from Pfizer, AbbVie, UCB, Eli Lilly, Galapagos, GSK, Roche, Gilead, Bristol Myers Squibb, Regeneron, Sanofi, AstraZeneca, and Novartis.

Francesco Saccà - received speaker honoraria from Alexion Pharmaceuticals, Inc, Biogen, Mylan, Novartis, Roche, Sanofi, and Teva; received honoraria from Alexion Pharmaceuticals, Inc, Almirall, argenx, Avexis, Biogen, Forward Pharma, Lexeo Therapeutics, Merk, Novartis, Pomona, Roche, Sanofi, and Takeda for consulting services; and served as PI in clinical trials supported by Alexion Pharmaceuticals, Inc, argenx, Novartis, Prilenia, and Sanofi.

James F. Howard Jr - has received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, and UCB Pharma; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc (now Amgen), Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, UCB Pharma, and Zai Labs; non-financial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Pharma and Zai Labs.

John W. Sleasman - receives research and salary support from the National Institutes of Health, Cellective, Enzyvant, and the Jeffrey Modell Foundation and is a consultant for argenx.

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Paul Duncombe - is an employee of argenx.

Benjamin Van Hoorick - is an employee of argenx.

Sophie Steeland - is an employee of argenx.

Renato Mantegazza - has received consulting fees/honoraria or support for meeting participation from Alexion Pharmaceuticals, argenx, Ra Pharmaceuticals, Biomarin, Catalyst, UCB, TEVA, Merck, Roche, and Biogen.

A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY WITH AN OPEN-LABEL EXTENSION PERIOD TO EVALUATE THE EFFICACY AND SAFETY OF TELITACICEPT IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS

Tuan Vu (Lutz, FL), Xiaoming Cui (Beijing, China), Jianmin Fang (Beijing, China), Qing Zuraw (Philadelphia, PA)

OBJECTIVE: Telitacicept is a fully human TACI-Fc fusion protein that targets B-lymphocyte stimulator (BLyS) and a proliferating-inducing ligand (APRIL), neutralizing their interactions with receptors on B cells, thereby inhibiting B-cell proliferation and maturation. This suppression at the proximal portion of the immune response may alleviate symptoms of autoimmune diseases such as generalized myasthenia gravis (gMG). Data from a phase 2 study (NCT04302103) of telitacicept showed efficacy and safety in adults with acetylcholine receptor (AChR) autoantibody positive gMG. Here we present the study design of our pivotal phase 3, randomized, double-blind, placebo-controlled study with an open-label extension (OLE) in adult patients with gMG.

METHODS: The study will enroll 180 adult patients, with AChR or muscle specific tyrosine kinase (MuSK) autoantibody positive gMG and inadequate response to stable standard-of-care therapies. Key eligibility criteria include confirmed diagnosis of gMG, Myasthenia Gravis Foundation of America (MGFA) Class II-IV severity, Myasthenia Gravis-Activities of Daily Living (MG-ADL) score ≥ 6 and Quantitative MG (QMG) score ≥ 11 at screening and baseline. The study will consist of a screening period of ≤4 weeks, a 24-week double-blind placebo-controlled phase, 1:1 randomization to either placebo or telitacicept subcutaneously every week, and an open label extension (OLE) of 48 weeks. The primary outcome is the mean change from baseline in MG-ADL score at week 24.

RESULTS: Study enrollment begins in Q2 2024.

SUMMARY/CONCLUSION: The study will assess the efficacy, safety, and pharmacokinetics/ pharmacodynamics of telitacicept in adult patients with gMG.

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Tuan Vu - related to MG: Research or grant support from Alexion/AstraZeneca Rare Disease, argenx, Cartesians, Dianthus, Amgen, Regeneron, UCB, Johnson & Johnson, and Immunovant; consultant and/or serving on speaker bureau for Alexion/AstraZeneca Rare Disease, argenx, CSL Behring, ImmunAbs, and Dianthus.

Xiaoming Cui - is an employee of RemeGen Co., Ltd. and owns company stock.

Jianmin Fang - is an employee of RemeGen, Ltd. and owns company stock.

Qing Zuraw - is an employee of RemeGen Biosciences and owns company stock.

ROZANOLIXIZUMAB IN PATIENTS AGED ≥65 YEARS WITH GENERALIZED MYASTHENIA GRAVIS: A POST HOC ANALYSIS OF THE PHASE 3 MYCARING STUDY

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INTRODUCTION: Patients with generalized myasthenia gravis (gMG) aged ≥65 years are often underrepresented in clinical studies.

OBJECTIVE: Evaluate rozanolixizumab in patients with gMG aged ≥65 years.

METHODS: In the Phase 3 MycarinG (NCT03971422) study, adults with acetylcholine receptor or muscle-specific tyrosine kinase autoantibody-positive gMG were randomized 1:1:1 to weekly subcutaneous placebo, rozanolixizumab 7mg/kg, or rozanolixizumab 10mg/kg for 6 weeks. Primary endpoint: change from baseline (CFB) to Day 43 in Myasthenia Activities of Daily Living (MG-ADL) score. Baseline characteristics and incidence of treatment-emergent adverse events (TEAEs) were analyzed by age (<65 and ≥65 years) post hoc.

RESULTS: Overall, 200 patients received placebo (<65 years: n=51; ≥65 years: n=16) or rozanolixizumab (n=100; n=33). Baseline characteristics were broadly similar between subgroups. Concomitant medications were used by 98.0% (n=148/151) of patients aged <65 years and all patients aged ≥65 years. Comorbidities, including cardiac and vascular disorders, were generally more common in the older subgroup than the younger subgroup. Mean standard deviation (SD) change from baseline (CFB) today 43 in MG-ADL scores for placebo- and rozanolixizumab-treated patients aged <65 years: −1.1 (2.7) and −3.7 (3.2), respectively; ≥65 years: 0.7 (2.8) and −2.1 (4.0). TEAEs occurred in 60.8% (n=31/51) and 85.0% (n=85/100) of placebo- and rozanolixizumab-treated patients aged <65 years, respectively, and 87.5% (n=14/16) and 72.7% (n=24/33) of patients aged ≥65 years. Headache, the most common TEAE, was more common in the younger subgroup (placebo: 21.6% [n=11/51]; rozanolixizumab: 49.0% [n=49/100]) than the older subgroup (12.5% [n=2/16]; 18.2% [n=6/33]).

SUMMARY/CONCLUSION: Rozanolixizumab was well tolerated and efficacious in patients with gMG aged ≥65 years.
Funding: UCB Pharma.

Disclosures:

Tuan Vu - is the USF Site Principal Investigator for MG clinical trials sponsored by Alexion Pharmaceuticals, Amgen, argenx, Cartesian Therapeutics, Dianthus, Immunovant, Johnson and Johnson, UCB Pharma, Regeneron Pharmaceuticals, RemeGen and has served as a speaker for Alexion Pharmaceuticals, Allergan/AbbVie, argenx and CSL Behring. He performed consulting work for Alexion Pharmaceuticals, argenx, Dianthus, RemeGen, ImmunAbs and UCB Pharma. Funding UCB Pharma

Ali A. Habib - has received research support from Alexion Pharmaceuticals, argenx, Cabaletta Bio, Genentech/Roche, Immunovant, Regeneron Pharmaceuticals, UCB Pharma and Viela Bio (now Amgen). He has received honoraria from Alexion Pharmaceuticals, Alpine Immune Sciences, argenx, Genentech/Roche, Immunovant, Inhibrx, Regeneron Pharmaceuticals, NMD Pharma and UCB Pharma.

Robert M. Pascuzzi - is Professor Emeritus of Neurology at Indiana University and receives compensation for his professional work from Indiana University Health. He has no financial relationship with any pharmaceutical company and receives no compensation from any pharmaceutical company (present or past). Robert M. Pascuzzi speaks at educational seminars on a broad variety of general neurology topics for primary care physicians through the organization Medical Education Resources (an educational organisation with no links or ties to any pharmaceutical or healthcare business company). Therefore, Robert M. Pascuzzi has no conflicts of interest related to this research, manuscript, presentation or publication.

Fiona Grimson - is an employee and shareholder of UCB Pharma.

Irene Pulido-Valdeolivas - is an employee and shareholder of UCB Pharma.

Thaïs Tarancón - is an employee and shareholder of UCB Pharma.

Vera Bril - is a consultant for Akcea, Alexion Pharmaceuticals, Alnylam, argenx, CSL, Grifols, Ionis, Immunovant, Janssen Pharmaceuticals, Momenta (now Johnson and Johnson), Novo Nordisk, Octapharma, Pfizer, Powell Mansfield, Roche, Sanofi, Takeda and UCB Pharma. She has received research support from Akcea, Alexion Pharmaceuticals, argenx, CSL, Grifols, Immunovant, Ionis, Momenta (now Johnson and Johnson), Octapharma, Takeda, UCB Pharma and Viela Bio (now Amgen).

EFFICACY AND SAFETY OF NIPOCALIMAB IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: TOPLINE RESULTS FROM THE DOUBLE-BLIND, PLACEBO-CONTROLLED, RANDOMIZED PHASE 3 VIVACITY-MG3 STUDY

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INTRODUCTION: Monoclonal antibodies or fragments targeting neonatal Fc receptors (FcRn) have been approved for reducing general myasthenia gravis (gMG) manifestations; however, persisting safety concerns and flexible dosing schedules that require patients to deteriorate before re-dosing, create uncertainty. Nipocalimab, an FcRn blocker that is molecularly unique from marketed anti-FcRns and has predictable dosing, has the potential to deeply lower IgG, and provide sustained disease control.

OBJECTIVE: To assess the efficacy and safety of nipocalimab in patients with gMG.

METHODS: Seropositive (anti-AChR+/MuSK+/LRP4+) and seronegative patients with gMG (MGFA Class II-IV) inadequately controlled on standard of care (SOC) therapy were enrolled in a 24-week double-blind placebo-controlled study. Randomization was 1:1 (nipocalimab + SOC, or placebo + SOC]. The primary endpoint was mean change in MG-activities of daily living (ADL) score from baseline over weeks 22, 23 and 24 in seropositive patients. Secondary endpoints included change in qualitative (QMG) score.

RESULTS: Of 199 patients enrolled, 153 were seropositive. Baseline demographics were balanced (77 nipocalimab, 76 placebo). Nipocalimab showed statistically significant improvement in clinical efficacy with mean change in MG-ADL score of -4.70 (standard error [SE] 0.329) from baseline over weeks 22-24 on nipocalimab vs. -3.25 (SE 0.335) on placebo (difference of LS means -1.45; p=0.002). Statistically significant improvement was seen in mean change in QMG score of -4.86 (SE 0.504) from baseline over weeks 22-24 on nipocalimab vs. -2.05 (SE 0.499) on placebo (difference of LS means -2.81, p<0.001). Nipocalimab was well-tolerated with incidence of adverse events comparable to placebo.

SUMMARY/CONCLUSION: Nipocalimab treatment demonstrated sustained efficacy and safety in this trial of adult patients with seropositive gMG.

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Teresa Sevilla - received honoraria for attendance at advisory boards from Argenx, UCB, Momenta (J&J), Alnylam and Pfizer.

Sarah Hoffmann - speakers´ honoraria: Alexion, argenx, Grifols, Roche, UCB; honoraria/attendance at advisory boards: Alexion, argenx, Roche; member of the medical advisory board: the German Myasthenia Society, DMG.

Eriene Youssef - is an employee of Janssen Pharmaceuticals; may hold stock or stock options in Johnson & Johnson.

Panna Sanga - is an employee of Janssen Pharmaceuticals; may hold stock or stock options in Johnson & Johnson.

Keith Karcher - is an employee of Janssen Pharmaceuticals; may hold stock or stock options in Johnson & Johnson.

Yaowei Zhu - is an employee of Janssen Pharmaceuticals; may hold stock or stock options in Johnson & Johnson.

Carlo Antozzi - funding travel, meeting attendance & advisory board participation: Alexion, argenx, Momenta, Sanofi, UCB.

Leona Ling - is an employee of Janssen Pharmaceuticals; may hold stock or stock options in Johnson & Johnson.

Hong Sun - is an employee of Janssen Pharmaceuticals; may hold stock or stock options in Johnson & Johnson.

Sindhu Ramchandren - is an employee of Janssen Pharmaceuticals; may hold stock or stock options in Johnson & Johnson.

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CASE REPORT- ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA)-ASSOCIATED VASCULITIS (AAV) PRESENTING WITH CONCURRENT NEUROMYOPATHY

Han Wang (Mankato, MN), Yu-Ting Chen (Omaha, NE)

INTRODUCTION: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) induces inflammation of small to medium vessels, predominantly affecting the respiratory tract and kidneys. Neurological involvement often manifests as peripheral neuropathy, while muscular involvement is a rare clinical presentation.

OBJECTIVE: We report a case of AAV presenting with unusual concurrent length-dependent axonal polyneuropathy and myositis along with literature review.

CASE REPORT: A woman in her 70s presented with numbness, pain, and weakness. She first noticed numbness, pain, and weakness in her feet. Symptoms progressed to her thighs over several days, and she became non-ambulatory. She later developed numbness, pain, and weakness in her hands, alongside achy pain in both of her thighs and upper arms. Physical examination showed diffuse areflexia, symmetric distal more than proximal weakness as well as glove-stocking distribution sensory loss. Lab was significant for elevated creatine kinase (CK) of 1024 IU/L, aldolase, creatinine, and positive anti-myeloperoxidase (MPO) antibodies.
Renal biopsy showed necrotizing arteritis consistent with AAV. The EDX testing confirmed severe length-dependent sensorimotor axonal polyneuropathy with superimposed non-irritable myopathy. Treatment with intravenous immunoglobulin and steroids facilitated a gradual improvement in both strength and sensation.

RESULTS: To our knowledge, this is the first reported AAV case presenting with concurrent myositis and polyneuropathy. There were only eight AAV cases presenting with myopathy reported. Most cases had normal creatine kinase (except one). MRI universally showed muscle edema. Seven patients underwent muscle biopsy. Vascular pathology was identified in all, including fibrinoid necrosis in four. Myofiber pathology was uncommon, and only two had necrotic fibers. None presented with coexisting neuropathy.

SUMMARY/CONCLUSION: AAV could present with neuromyopathy.

COPPER DEFICIENCY INDUCED MYELONEUROPATHY WITH COEXISTING VITAMIN B6 AND B12 DEFICIENCY

Han Wang (Mankato, MN)

INTRODUCTION: Copper deficiency is a rare etiology of myeloneuropathy that should be considered in patients with risk factors or when patients do not show expected improvement after treatment for other malnutrition.

OBJECTIVE: Here we presented a case of myeloneuropathy with concomitant copper, vitamin B6 and vitamin B12 deficiency.

METHODS: The patient is a 71-year-old man with a history of gastric and bowel surgery for an ulcer, as well as chronic alcohol use. He was never instructed to take supplements after surgery. He presented with progressive ascending weakness and numbness over several months, leading to a transition from independence to wheelchair bound. Upon examination he had glove-stocking sensory loss, diffuse hyporeflexia, and mild weakness in all four extremities. He was found to have a vitamin B12 level of 201 and was started on a supplement. He also took zinc, thiamine, and iron on his own. His symptoms continued to worsen despite treatment. Additional evaluations revealed extremely low copper (<10) and low pyridoxal 5-phosphate (3). MRI cervical and thoracic spine showed non-enhancing hyperintensity in the posterior column. Lumbar puncture was unremarkable. He was given oral and IV copper with gradual improvement in strength.

RESULTS: To our knowledge, this is the first reported copper deficiency myeloneuropathy case presenting with coexisting vitamin B6 and B12 deficiencies. Coexisting vitamin B12 and copper deficiencies have been reported. This case highlighted the importance of considering copper deficiency in patients with risk factors, or when they do not improve after treating for known deficiencies.

SUMMARY/CONCLUSION: Copper deficiency can coexist with vitamin B6 and B12 deficiencies and contributes to myeloneuropathy.

EFGARTIGIMOD SUCCESSFUL TREATMENT IN A CASE OF ANTI-AMPAR LIMBIC ENCEPHALITIS ASSOCIATED WITH THYMOMATOUS MYASTHENIA GRAVIS

Lin Wang (Beijing, China), Changzheng Sui (Beijing, China), Wenliang Feng (Beijing, China)

INTRODUCTION/BACKGROUND: Few thymomatous MG has been reported in patients with anti-AMPAR, and treatment needs to be explored. Efgartigimod, the first FcRn antagonist, showed promising results in IgG mediated neurological autoimmune disorders. We report one case on treatment with efgartigimod in one such patient.

CASE REPORT: A 40-year-old male underwent thymoma resection in June 2023. One month later, he experienced symptoms of ocular MG. Then the patient developed a fever two months after thymectomy. The disease progressed so rapidly that the patient became unresponsive and exhibited abnormal mental and aggressive behavior. His brain MRI was normal and showed no new infarct foci. The serum antibody tests showed positive AChR IgG and AMPAR-Ab (titer 1:320), while cerebral spinal fluid antibody tests showed positive AMPAR-Ab (titer 1:100). The symptoms did not improve after intravenous immunoglobulin (IVIg), IVMP and IA. The patient was unable to cooperate with commanded movements and occurred involuntary movements because of the disease progression and infection. An urgent trachea intubation was performed. Then he received efgartigimod 10mg/kg IV weekly for four doses. Prior to this, the patient had been in the ICU receiving anti-infective and anti-epileptic treatments. The patient was discharged after three doses of efgartigimod. His involuntary movement was less than before. The sputum was significantly reduced. The patient could cooperate with eye movement, nodding, limb movement and indicate the answer to the orientation and calculation. The titer of serum AMPAR antibodies decreased from 1:320 to 1:30.

SUMMARY/CONCLUSION: This is a case of AMPAR antibody encephalitis associated with thymomatous AChR antibody positive MG treated with efgartigimod. Patient showed a positive response to efgartigimod.

CONCOMITANT INTRAVENOUS IMMUNOGLOBULIN OR PLASMA EXCHANGE HAS NO EFFECT ON COMPLEMENT INHIBITION BY ZILUCOPLAN

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INTRODUCTION: Macrocyclic peptide complement component 5 inhibitor, zilucoplan, significantly improved myasthenia gravis (MG)-specific outcomes in the Phase 3 RAISE study (NCT04115293). An open-label extension, RAISE-XT (NCT04225871), is ongoing.

OBJECTIVE: Evaluate the impact of rescue therapy (intravenous immunoglobulin [IVIg] or plasma exchange [PLEX]) on zilucoplan concentration and complement inhibition in RAISE and RAISE-XT.

METHODS: In RAISE, adults with acetylcholine receptor autoantibody-positive generalized MG were randomized 1:1 to daily subcutaneous zilucoplan 0.3mg/kg or placebo for 12 weeks. Patients completing qualifying double-blind studies (NCT03315130/NCT04115293) could enter RAISE-XT to receive zilucoplan 0.3mg/kg daily. RAISE-XT primary outcome: incidence of treatment-emergent adverse events (TEAEs). Zilucoplan plasma concentration was measured pre- and post-administration on the day of rescue therapy by liquid chromatography-tandem mass spectrometry. Complement activity was measured by sheep red blood cell lysis assay, with post-measurement taken ≤1 day after rescue.

RESULTS: In patients with ≥1 week of zilucoplan 0.3mg/kg exposure during RAISE and RAISE-XT (N=200), 21 (10.5%) received IVIg and 10 (5.0%) received PLEX. Where available, zilucoplan steady-state concentrations were comparable between patients with and without rescue therapy. Mean (standard deviation) complement inhibition remained complete (>95%) pre- and post-rescue: 97.1% (0.80) and 97.4% (0.63) for IVIg (10 events with data), respectively. Pre- and post-rescue complement inhibition was 96.3% and 95.9% for PLEX (1 event with data), respectively. TEAEs occurred in 188 (94.0%) patients (data cutoff: September 08, 2022).

SUMMARY/CONCLUSION: Complete complement inhibition was maintained with rescue therapy during zilucoplan treatment, confirming that zilucoplan can be used concomitantly with IVIg and PLEX without the need for supplemental dosing.

Disclosures:

Michael D. Weiss - has received honoraria for serving on scientific advisory boards for Alexion Pharmaceuticals, Immunovant, Ra Pharmaceuticals (now UCB Pharma), argenx, Biogen, Mitsubishi Tanabe Pharma and Amylyx, consulting honoraria from Cytokinetics and CSL Behring, and speaker honoraria from Soleo Health. He also serves as a special government employee for the Food and Drug Administration.

Anna Nordmark - is a contractor for UCB Pharma.

Natasa Savic - is an employee and shareholder of UCB Pharma.

James F. Howard Jr. - has received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention (Atlanta, GA, USA), the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health (including the National Institute of Neurological Disorders and Stroke and the National Institute of Arthritis and Musculoskeletal and Skin Diseases), PCORI and UCB Pharma; honoraria from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-La Roche, Medscape CME, Merck EMD Serono, NMD Pharma, Novartis, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, UCB Pharma, Regeneron Pharmaceuticals, Sanofi US, Horizon Therapeutics (now Amgen) and Zai Labs; non-financial support from Alexion AstraZeneca Rare Disease, argenx, UCB Pharma and Toleranzia AB.

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Tuan Vu - is the USF Site Principal Investigator for MG clinical trials sponsored by Alexion Pharmaceuticals, Amgen, argenx, Cartesian Therapeutics, Dianthus, Immunovant, Johnson and Johnson, UCB Pharma, Regeneron Pharmaceuticals, RemeGen and has served as a speaker for Alexion Pharmaceuticals, Allergan/AbbVie, argenx and CSL Behring. He performed consulting work for Alexion Pharmaceuticals, argenx, Dianthus, RemeGen, ImmunAbs and UCB Pharma.

Babak Boroojerdi - is an employee and shareholder of UCB Pharma.

René Bouw - is an employee and shareholder of UCB Pharma.

Fiona Grimson - Fiona Grimson is an employee and shareholder of UCB Pharma.

STEROID USE, TOXICITY, AND MONITORING IN PATIENTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY: A SURVEY OF NEUROLOGISTS IN THE UNITED STATES

Gil Wolfe (Buffalo, NY), Neelam Goyal (Palo Alto, CA), Deborah Gelinas (Hingham, MA), Tom Hughes (Boston, MA), Vijayaraghava Rao (Hingham, MA), Paul Nisbet (Mt Pleasant, SC), John Stone (Boston, MA), Pushpa Narayanaswami (Boston, MA)

INTRODUCTION: European Academy of Neurology (EAN)/Peripheral Nerve Society (PNS) 2021 guideline for chronic inflammatory demyelinating polyneuropathy (CIDP) states, “Because of abundant clinical practice experience, corticosteroid (CS) treatment can be used as first-line treatment” and that nonsteroidal immunosuppressants (NSISTs) may be considered, as CS-sparing agents.

OBJECTIVE: We surveyed board-certified United States-based neurologists to assess awareness and monitoring of CS toxicity.

METHODS: Cross-sectional online survey was completed by neurologists (n=99) managing ≥3 patients with CIDP/year (≥10 mg CS for ≥1 month).

RESULTS: Neurologists reported ~58% of patients were treated with CSs and 44% with NSISTs. For long-term treatment (≥6 months), 43% of neurologists considered CS doses ≤10 mg/day (prednisone equivalent) well tolerated; an additional 32% consider 20-40 mg/day well tolerated. Half their patients are able to taper to <10 mg/day in <6 months. Only 55% of neurologists feel very/extremely familiar with CS toxicities; they identified increased appetite/weight gain (68%), mood/behavioral change (56%), insulin resistance (53%), decreased bone density (47%), and immunosuppression (37%) as the most-common adverse effects with long-term CS use. Top psychological/behavioral changes named as indicating CS toxicity were mood swings, irritability, mania, and sleep disorders. One-third of neurologists reported relying solely on experience/training in balancing CS effectiveness and toxicity; two-thirds reported using guideline(s). The majority (85%) said a tool to systematically monitor CS toxicity, if available, would be valuable to their practice.

SUMMARY/CONCLUSION: Although two-thirds of respondents reported following guideline(s) to manage CSs, EAN/PNS guideline states that the best CS regimen for CIDP is unknown. These findings substantiate the ongoing need for guidance on managing CSs and monitoring toxicity in patients with CIDP.

Disclosures:

Gil Wolfe - is a consultant/advisor for Alexion, argenx, BPL, Cartesian, Grifols, Janssen, Takeda, UCB, and receives or has received research support from Alexion, argenx, Immunovant, Roche, UCB, and the Myasthenia Gravis Foundation of America.

Neelam Goyal - is a consultant/advisor for argenx, Alexion, UCB, Janssen, Amgen, and Lycia Therapeutics and receives or has received grant support from argenx.

Deborah Gelinas - is an employee of argenx.

Tom Hughes - is an employee of argenx.

Vijayaraghava Rao - is an employee of argenx.

Paul Nisbet - is an employee of One Research, LLC, which was paid by argenx to conduct the survey and analyze the data.

John Stone - has served as a consultant to argenx on glucocorticoid toxicity and is the chair of the Scientific Advisory Board at Steritas.

Pushpa Narayanaswami - is a consultant/advisor for argenx, Alexion, UCB, Janssen, Dianthus, GSK, and Novartis; has served on a data safety monitoring board for Sanofi; and receives or has received research support from PCORI, Alexion, Janssen, Dianthus, and UCB, and receives royalties from Springer Nature.

CLINICAL OUTCOMES, DISEASE COURSE, AND QUALITY OF LIFE IN PATIENTS WITH MULTIFOCAL MOTOR NEUROPATHY: IMMERSION, STUDY IN PROGRESS

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INTRODUCTION: Multifocal motor neuropathy (MMN) is a rare, peripheral, immune-mediated, chronic neuropathy resulting from motor nerve conduction block and complement activation, leading to axonal degeneration and progressive, disabling asymmetric limb weakness with absence of sensory loss. Data on patient experience and clinical management of MMN are limited to small cohorts and retrospective analyses.

OBJECTIVE: To further understand MMN diagnosis, disease course, and management and to characterize the healthcare resource use of patients with MMN.

METHODS: iMMersioN (NCT05988073), a global, prospective, longitudinal study will enroll approximately 150 participants. No investigational medicinal product will be administered. Participants will be observed as they receive standard of care treatments. Site visits will coincide with regular MMN treatment visits and will occur approximately every 3 months, with participants being followed for up to 24 months. In certain countries, optional blood samples may be collected from participants.

RESULTS: The objectives of the iMMersioN study are: to characterize MMN participant profiles, assess disease management and disease course, including outcomes measures such as MMN-Rasch-built Overall Disability Score (MMN-RODS), modified MRC-10 (MMRC-10), and adjusted Inflammatory Neuropathy Cause and Treatment (INCAT), estimate the economic burden and impact of MMN on quality of life, and collect data on relevant disease biomarkers such as autoantibody titers against gangliosides, components of the complement cascade, and a marker of neurological degeneration. The first participant was enrolled on November 29, 2023.

SUMMARY/CONCLUSION: iMMersioN is an ongoing global, prospective, longitudinal study to examine clinical outcomes, disease course, resource utilization, and health-related quality of life in adult patients with MMN.

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Marqus Hamwright - is an employee of argenx.

Olivier Van de Steen - is an employee of argenx.

Clémence Arvin-Bérod - is an employee of argenx.

Jeffrey Allen - is a consultant honoraria for Akcea Therapeutics, Alexion, Alnylam, Annexon, argenx SE, CSL Behring, Grifols, Immuovant, ImmuPharma, Johnson & Johnson, Pfizer, Takeda.

Jamie Wood - is a shareholder for argenx.

Luis Querol - research grants: CIBERER, Fundació La Marató, GBS-CIDP Foundation International, Grifols, Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), and UCB.Speaker or expert testimony honoraria: Annexon, Alnylam, argenx, Avilar Therapeutics, Biogen, CSL Behring, Dianthus, Janssen, LFB, Lundbeck, Merck, Novartis, Octapharma, Roche, Sanofi, and UCB.Steering Committee member: Sanofi.Principal Investigator: UCB.

Inge Van de Walle - is an employee of argenx.

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AN ATYPICAL CASE OF CIDP WITH NEUROFASCIN 155 ANTIBODY AND POLYCYTHEMIA VERA MIMICKING POEMS SYNDROME

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INTRODUCTION: Chronic inflammatory demyelinating polyneuropathy (CIDP) with neurofascin antibodies is atypical demyelinating polyneuropathy. POEMS syndrome may present with polyneuropathy initially, similar to CIDP.

OBJECTIVE: We report an atypical case of CIDP with neurofascin 155 antibody and polycythymia vera mimicking POEMS syndrome.

METHODS: We present a 43-year-old man complaining of paresthesia in lower extremities for the past 8 months. Paresthesia progressed over 5 months to his hands and the EMG was consistent with CIDP. Lab tests showed positive neurofascin 155 antibody and IgG Kappa band. He had rapid decline within 1 month from independent ambulation to wheelchair bound. Paresthesia progressed to chest level after rituximab. MRI of full spine showed enlarged cauda equina with contrast enhancement. His serum free Kappa significantly increased (64.62 mg/dL) with polycythemia and thrombocytosis. PET scan showed hepatomegaly and splenomegaly. Endocrinology tests were normal. No skin changes were noted. Vascular endothelial growth factor (VEGF) level was more than 4000. Bone marrow biopsy reported polycythemia vera without abnormal plasma cell clone.

RESULTS: His clinical presentation fits the diagnostic criteria of POEMS syndrome (polyneuropathy, M protein, elevated VEGF, organomegaly, thrombocytosis). However, his PET scan did not show any sclerotic, necrotic bone lesions, or lymphadenopathy. Bone marrow did not reveal abnormal plasma cell clone. The elevated VEGF, organomegaly and thrombocytosis are related to the polycythemia vera. He received plasmapheresis and improved to independent ambulation.

SUMMARY/CONCLUSION: Our case had atypical CIDP with neurofascin 155 antibody, gammopathy, elevated VEGF, unsatisfactory response to rituximab, mimicking POEMS syndrome. Systemic review with broader differential diagnosis will be helpful to achieve the right diagnosis.

PREDICTION OF SURVIVAL OUTCOMES FOR PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS UTILIZING MACHINE LEARNING

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INTRODUCTION: ALS is a heterogeneous disorder for which survival prediction has been challenging. The European Network to Cure ALS (ENCALS) utilized the Royston-Parmar (RP) model to predict survival from symptom onset, using data from the diagnosis day. However, data from diagnosis days may not be available. Hence, a model which predicts survival outcome from any clinical visit is helpful to physicians and patients for individualized therapy.

OBJECTIVE: To use machine learning (ML) to predict 12-month survival for patients with ALS based on clinical observations in individual visits during the disease.

METHODS: We utilized demographic, clinical, and laboratory parameters from 11,024 patient samples in the PRO-ACT database to develop and validate both an ML Extreme Gradient Boosting (XGBoost) and RP model to predict 12-month survival from any clinical visit. Top predictive features for survival were identified using XGBoost. Refined XGBoost and RP models were trained utilizing top five features.

RESULTS: XGBoost demonstrated superior performance with an AUROC of 0.819 ± 0.011 for 12-month forecasts, exceeding the RP's 0.798 ± 0.021. Top survival predictors identified by XGBoost included albumin level, onset location, ALSFRS-R slope, bicarbonate level, and basophil count. A refined XGBoost model using the top features still performed robustly, with an area under the curve-receiver operating characteristic of 0.762 ± 0.012, compared to the refined RP model's 0.731 ± 0.009.

SUMMARY/CONCLUSION: We developed a ML model that can accurately predict 12-month survival outcome from any clinical visit. Future studies would involve validating the model in more clinic patient cohorts. Key predictors identified by our ML model provide targets for further research.

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PATIENT PREFERENCES FOR GENERALIZED MYASTHENIA GRAVIS TREATMENT PROFILES: RESULTS OF A WEB-BASED SURVEY

Karen S. Yee (Boston, MA), Christine Poulos (Research Triangle Park, NC), Cooper Bussberg (Research Triangle Park, NC), Kelley Myers (Research Triangle Park, NC)

INTRODUCTION: Generalized myasthenia gravis (gMG) is a rare, chronic autoimmune disorder. Therapeutic approaches differ among available treatments for anti-acetylcholine receptor antibody positive (AChR+) gMG, but patient treatment preference data remain limited.

OBJECTIVE: To understand treatment preferences of patients with AChR+ gMG and estimate the relative importance of preferred treatment attributes.

METHODS: US adults with a self-reported physician diagnosis of AChR+ gMG completed a web-based survey. Two object-case, best-worst scaling exercises were analyzed. The first exercise assessed preferences across different treatment profiles (similar to ravulizumab, eculizumab, efgartigimod intravenous and subcutaneous, or zilucoplan). The second exercise obtained preferences for attributes used to define the treatment profiles (mode and dosing administration followed by consistent disease control and meningococcal vaccination requirements). The most important gMG treatment attribute was identified.

RESULTS: Of 153 respondents, mean age was 49 years, 77% female, 84% White, 54% with college degree or higher, 41% employed, and 27% had been diagnosed for <3 years. Mean MG-Activities of Daily Living score was 8.0 (min-max: 0-17). Respondents preferred the ravulizumab-like profile vs all other profile-based scenarios: 35% vs 10%-22% when considering mode and dosing administration, 44% vs 3%-31% with addition of consistent disease control, and 39% vs 5%-29% when considering all four attributes. Consistent disease control was selected as the most important attribute when choosing a treatment (82%), followed by mode (10%) and dosing administration (6%) and meningococcal vaccination requirements (3%).

SUMMARY/CONCLUSION: Patients with gMG preferred treatments with less frequent dosing schedules and consistent disease control; consistent disease control was the most important attribute when choosing a therapy.

Disclosures:

Karen S. Yee - is an employee of Alexion, AstraZeneca Rare Disease, and holds stock options in AstraZeneca.

Christine Poulos - is an employee of RTI Health Solutions, which received funding to conduct this research.

Cooper Bussberg - is an employee of RTI Health Solutions, which received funding to conduct this research.

Kelley Myers - is an employee of RTI Health Solutions, which received funding to conduct this research.

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FAMILY WITH A VCP MUTATION: VARIABLE PHENOTYPICAL PRESENTATIONS LINKED BY ABNORMAL RNA METABOLISM

Jessica Yi (Philadelphia, PA), Goran Rakocevic (Philadelphia, PA)

INTRODUCTION: Valosin-containing protein (VCP) mutations cause abnormal RNA metabolism, leading to disturbed protein degradation and deposition of ubiquitinated inclusions in muscle and brain. This results in a multi-system proteinopathy with a spectrum of phenotypes including hereditary inclusion body myopathy (hIBM, in 90% of patients), frontotemporal dementia (FTD, in 30%), Paget's disease (in 40-50%), and amyotrophic lateral sclerosis (in 10%). Rarer phenotypes mimic other inherited neuropathies and muscular dystrophies. Over 50 different pathogenic VCP mutations have been identified.

OBJECTIVE: Describe genotype-phenotype variation in the neurologic manifestations seen in five family members with the same VCP gene mutation.

METHODS: The index patient with hIBM was characterized clinically and genetically, along with his older brother with IBMPFD (hIBM with Paget's and FTD) and younger sister with FTD. Their deceased father and paternal uncle had myopathy and Paget's. Videos of index patient will be supplemented.

CASE REPORT: Index patient was initially suspected of sporadic IBM and was subsequently found to have a heterozygous mutation at codon 97 of the VCP gene, resulting in exchange of glycine for glutamic acid (c.G290A, p.G97E). His brother and sister have the same mutation. His deceased father and uncle did not have genetic testing.

CONCLUSION: This report emphasizes the importance of recognizing a heterogeneous pattern of neurologic manifestations within the same or subsequent generations. The genetic basis of neurologic diseases is becoming increasingly important as targeted gene therapies are developed. Heterogeneous clinical presentations due to numerous pathogenic mutations may pose a challenge in developing effective therapies for VCP disease.

IN VIVO DETECTION OF NEUROFASCIN (NF)155 ANTIBODIES IN A PATIENT WITH PROGRESSIVE CIDP

David Younger (New York, NY), Kathrin Doppler (Würzburg, Germany), Claudia Sommer (Würzburg, Germany)

INTRODUCTION/BACKGROUND: Autoantibodies to neurofascin (NF) are detected in a very small proportion of patients with autoimmune neuropathy, but may nevertheless be pathogenic in these cases.

CASE REPORT: A 38-year-old woman developed severe weakness in the legs in the summer of 2023 that progressed to paralysis by the fall 2023 despite treatment with parenteral corticosteroids, plasma exchange, and rituximab; nor did she tolerate intravenous immunoglobulin (IVIg) therapy. Serial EDX studies showed prolongation of distal motor latencies, segmental motor nerve conduction velocity, slowing, and F-wave prolongations followed by decline or absence of compound muscle action potentials. Concentric needle EMG showed profuse active distal denervation without volitional motor unit action potentials. Anti-NF155 autoantibodies were detected by enzyme-linked immunosorbent assay (ELISA) and confirmed using binding assays with NF155 transfected human embryonic kidney (HEK) 293 cells. Blood studies revealed NF155 IgG4, elevated speckled ANA titers, with 5% lymphocytes, markedly reduced circulating lymphocytes, and an IgG-kappa spike by serum immunofixation. Binding assays with the patient's serum on murine teased fibers showed distinct binding to paranodes.

SUMMARY/CONCLUSION: Anti-NF155 autoantibodies were detected by ELISA, cell-based assays, and binding assays on murine teased fibers. The present clinical, EDX, and experimental findings are consistent with other investigations indicating the potential enhancement and prolongation of ongoing neuritis by NF-reactive autoantibodies. However, antibodies to NF alone may not be pathogenic, requiring instead the target to be accessible in association with a pronounced immune cell response that disrupts the blood-nerve barrier, providing access to the autoantibody targets.

SAFETY AND EFFICACY OF TOFACITINIB IN PATIENTS WITH REFRACTORY MYASTHENIA GRAVIS: A PILOT STUDY

Rui Zhao (Shanghai, China), Chong Yan (Shanghai, China), Sushan Luo (Shanghai, China), Chongbo Zhao (Shanghai, China)

INTRODUCTION: Myasthenia gravis (MG) is one of the most common autoimmune neuromuscular disorders. About 10% MG patients still are refractory and there still is an unmet need for effective, well tolerated, and convenient treatment options for these patients.

OBJECTIVE: Our research group conducted a small sample study to evaluate the safety and effectiveness of tofacitinib in treating patients with refractory MG.

METHODS: This registered open-label, single-arm pilot study was conducted from June 2020 through December 2023 (NCT04431895). Refractory gMG patients received tofacitinib (5mg, twice a day) as the only immunosuppressant in combination with corticosteroids. Clinical scales, including QMG score, MG-ADL, MG-QoL15, and MGC were assessed prospectively from the baseline to 24 weeks after Tofacitinib initiation. The phosphorylation level of STAT3 in peripheral blood CD4+T cells for MG patients were detected by multi-color flow cytometry.

RESULTS: We enrolled 19 refractory gMG cases. By week 24 after tofacitinib administration, a significant reduction was observed in MG-ADL (2.4 vs 6.0 at baseline; $p = 0.0002$) and QMG (8.8 vs 15.0 at baseline; $p = 0.001$), respectively. Corticosteroids doses were significantly reduced from 21.32 mg to 13.68 mg ($p = 0.001$). Tofacitinib induced the elevation of triglycerides in some patients. Phosphorylation flow cytometry revealed that tofacitinib inhibits the phosphorylation levels of STAT3 protein in Th17.1 cells in MG who received tofacitinib.

SUMMARY/CONCLUSION: The study provided preliminary evidence of the safety and efficacy profile of tofacitinib in treating patients with refractory gMG. The therapeutic effect of tofacitinib was probably associated with the inhibition of pro-inflammatory Th17.1 cells.

CASE REPORT: EFGARTIGIMOD PLUS RITUXIMAB IMPROVES MUSK AUTOANTIBODY POSITIVE MYASTHENIA GRAVIS PRESENTING AS DYSPNEA

Yiming Zheng (Peking, China), Feng Gao (Peking, China)

INTRODUCTION/BACKGROUND: Predominant respiratory muscle weakness presenting as dyspnea, caused by muscle-specific tyrosine kinase (MuSK) autoantibody-positive myasthenia gravis (MG), is very rare and makes the diagnosis challenging. MuSK autoantibody positive MG patients may need more aggressive maintenance immunosuppression earlier on to maintain remission, often with rituximab. The neonatal Fc receptor antagonist efgartigimod, which can rapidly reduce autoantibodies and is already approved for acetylcholine receptor-positive MG, may also be suitable for MuSK autoantibody-positive MG. We report a case of MuSK autoantibody positive MG presenting as dyspnea and successfully treated with efgartigimod plus rituximab.

CASE REPORT: A 44-year-old female, in excellent health and taking no medications, presented with a 5-year history of progressive exertional dyspnea. Except for occasional hoarseness and diplopia, she did not exhibit dysphagia or limb muscle weakness. Neurological examination also revealed ophthalmoplegia, facial and neck flexor muscle weakness. Diaphragmatic ultrasound showed abnormal diaphragm function. Positive MuSK autoantibodies and evidence of neuromuscular junction transmission defect on repetitive nerve stimulation, confirmed the diagnosis of MuSK autoantibody positive MG. She experienced no improvement with pyridostigmine or neostigmine. However, she dramatically and rapidly improved with efgartigimod plus rituximab therapy.

SUMMARY/CONCLUSION: This case highlights the need to consider MuSK autoantibody positive MG as well as other neuromuscular disorders when evaluating patients presenting as exertional dyspnea. Our findings of fast and excellent response to efgartigimod and combined with rituximab as a long-term maintenance therapy, may provide a new treatment strategy for MuSK autoantibody positive MG.

PLASMA BIOMARKER-BASED ENDOTYPES OF MYASTHENIA GRAVIS AND ASSOCIATION WITH CLINICAL SUBTYPES AND THERAPEUTIC RESPONSE

Huahua Zhong (Shanghai, China), Ran Chen (Shanghai, China), Jie Song (Shanghai, China), Sushan Luo (Shanghai, China), Chongbo Zhao (Shanghai, China)

INTRODUCTION: Although hypercytokinemia has been documented in the peripheral blood of myasthenia gravis (MG) patients, the use of peripheral immune biomarkers to investigate MG endotypes and their correlation with subtypes has been rarely explored.

OBJECTIVE: To investigate the peripheral cytokine endotype-phenotype relationships in MG.

METHODS: A total of 22 cytokines, including APRIL, BAFF, IL-6, IL-8, IL-10, IL-17, IL-19, IL-23, CXCL2, CXCL5, CXCL4, CCL3, C2, C5a, C9, IL-4, IL-2, IL-18, TNF-alpha, IFN-alpha, IFN-beta, IFN-gamma, were quantified by Luminex Discovery Assay from peripheral plasma derived from 219 MG patients with consecutive clinical data and 40 healthy controls (HCs).

RESULTS: Acetylcholine receptor antibody positive (AChR+) MG showed peripheral dominance of hypercytokinemia in comparison to muscle-specific receptor tyrosine kinase antibody positive (MuSK+) and seronegative MG patients, as well as healthy controls. A significant elevation was observed in IL-23 for AChR+ MG (P = 2.4e-02) and IFN-alpha in seronegative MG (P=4.0e-03), respectively, while low APRIL (P=2.5e-03) and BAFF (P=2.1e-05) were preferentially identified in MuSK+MG. IL-17 exhibited the most relevant associations with MG clinical scores (P<5.0e-03). Elevated IL-4 was correlated with a better outcome at 6 months and 12 months after immunotherapies. Baseline CXCL5 was a predictor for patients who had good response to first-line therapies (P=3.3e-04), while IL-10 predicted a necessitation of escalated immune therapies (P=7.8e-03).

SUMMARY/CONCLUSION: Plasma biomarker-based endotypes had correlations with the clinical subtypes. Baseline CXCL5 and IL-10 might predict the therapeutic response in MG patients.

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RESPONSE TO SINGLE LOW-DOSE RITUXIMAB CAN PREDICT A BETTER OUTCOME OF MULTI-CYCLE TREATMENT IN REFRACTORY MYASTHENIA GRAVIS: A SINGLE-CENTER STUDY

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INTRODUCTION: The relationship between the response to the first rituximab treatment and the efficacy of subsequent multi-cycle low-dose rituximab treatment remains unclear.

OBJECTIVE: This study aims to evaluate the relationship between the response to single rituximab and multi-cycle treatment outcomes in myasthenia gravis (MG).

METHODS: This retrospective cohort study with prospectively collected data involved 47 refractory patients who received 500/600 mg rituximab every 6 months in Huashan Hospital. We divided the patients into a response group (n=30) and a non-response group (n=17) based on a decrease of >=3 points from baseline in quantitative MG (QMG) score 6 months after the first cycle rituximab treatment. We compared the change of QMG and Activities of Daily Living (ADL) scores and the time to reaching minimal symptom expression between the two groups.

RESULTS: Six months after the fourth rituximab treatment, the QMG score was lower in the response group (-6.07; p=0.005;95%CI, -10.26 to -1.88) compared with that in the non-response group; the equivalent mean changes from baseline were -9.95(95%CI, -11.78 to -8.12) and -0.45(95%CI, -3.38 to 2.49), respectively. ADL score was lower in the response group (-2.84; p=0.006;95%CI, -4.83 to -0.852) compared with that in the non-response group; the equivalent mean changes from baseline were -5.40(95%CI, -6.74 to -4.05) and -1.99(95%CI, -4.18 to 0.21), respectively. The median time to minimal symptom expression was shorter in the response group (6.5 months versus not available; hazard ration:15.83; 95% confidence interval,3.53-70.91; $p < 0.001$ after adjustment).

SUMMARY/CONCLUSION: The response to single low-dose rituximab can predict a better outcome of multi-cycle treatment in refractory MG.

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A PREDICTIVE NOMOGRAM FOR SHORT-TERM OUTCOMES OF MYASTHENIA GRAVIS PATIENTS TREATED WITH LOW-DOSE RITUXIMAB

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INTRODUCTION: Up to now, predictors for treatment response to rituximab in myasthenia gravis (MG) have not been investigated. Since there is wide heterogenicity in the treatment efficacy among different patients, it is essential to identify predictors related to treatment response in MG.

OBJECTIVE: This study aims to establish and validate a predictive nomogram for the short-term clinical outcomes of MG patients treated with low-dose rituximab.

METHODS: We retrospectively reviewed 108 patients who received rituximab of 600 mg every 6 months in Huashan Hospital and Tangdu Hospital. Of them, 76 patients from Huashan Hospital were included in the derivation cohort to develop the predictive nomogram, which was externally validated using 32 patients from Tangdu Hospital. The clinical response is defined as a >=3 points decrease in quantitative MG score within 6 months. Both clinical and genetic characteristics were included to screen predictors via multivariate logistic regression. Discrimination and calibration were measured by the area under the receiver operating characteristic curve (AUC-ROC) and Hosmer-Lemeshow test, respectively.

RESULTS: Disease duration (odds ration [OR]=0.987, p=0.032), positive anti-muscle specific tyrosine kinase antibodies (OR=19.8, p=0.007), and genotypes in FCGR2A rs1801274 (AG: OR=0.131, p=0.024; GG: OR=0.037, p=0.010) were independently associated with clinical response of post-rituximab patients. The nomogram identified MG patients with clinical response with an area under the curve-receiver operating characteristic (AUC-ROC) (95% confidence interval) of 0.875(0.798-0.952) in the derivation cohort and 0.741(0.501-0.982) in the validation cohort. Hosmer-Lemeshow test showed a good calibration (derivation: chi-square=3.181, p=0.923; validation: chi-square=8.098, p=0.424).

SUMMARY/CONCLUSION: The nomogram achieved an optimal prediction of short-term outcomes in patients treated with low-dose rituximab.

CREATION OF PATIENT-CENTERED EDUCATIONAL VIDEOS FOR GLUCOCORTICOID TREATMENT COUNSELLING

Annie Zhu (Toronto, Canada), Charles Kassardjian (Toronto, Canada)

INTRODUCTION: Glucocorticoids are often first-line therapy for many neuromuscular disorders. While clinicians counsel patients about potential glucocorticoid complications, research has demonstrated that there are discrepancies in the information retained by patients, and discussions may not address side effects that patients prioritize most.

OBJECTIVE: To understand patient perspectives about adverse effects of glucocorticoids and use this data to inform the creation of an educational video for treatment counselling.

METHODS: Qualitative surveys were distributed to consecutive patients taking glucocorticoids at the St. Michael's Hospital Neuromuscular Clinic. Descriptive analysis was performed to assess patient perspectives and recollection of counselling. These results will inform the development of an educational video, which will then be evaluated through further patient surveys.

RESULTS: Patients (n=13) reported the following side effects as most important to quality of life: risk of infection, weight gain, osteoporosis, and metabolic disorders (e.g. diabetes). While side effects were generally concordant with the ones discussed during counselling, 61% of patients reported being counselled on less than half of the listed adverse effects of glucocorticoids. We are using these data to create an informational video, which will be presented at the time of the conference, and then evaluate the video as a tool to improve counselling effectiveness.

SUMMARY/CONCLUSION: We report on the glucocorticoid side effects most important to neuromuscular patients and note that patient recollection of counseling is not always concordant with the discussion recorded by the physician. We hope that an educational video (presented at the conference) will help to address this gap.

SCIENTIFIC SESSION OF THE MYASTHENIA GRAVIS FOUNDATION OF AMERICA, INC. (MGFA)

https://myasthenia.org/2024-MGFA-Scientific-Session-Poster-List-and-Numbers

UNIQUE CASE OF POST-COVID19 MYASTHENIA GRAVIS WITH SPONTANEOUS RESOLUTION

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INTRODUCTION: COVID-19 is recognized for its diverse neurological manifestations. Among these, several cases of Myasthenia Gravis emerging after COVID-19 have been reported. Described cases indicate that patients required treatments with steroids and other forms of immunotherapy. Our case is unique in that patient improved without immunotherapy.

OBJECTIVE: We present a rare case of self-resolved seropositive Myasthenia Gravis (MG) following COVID-19 recovery, exploring the link between COVID-19 and immune response. Some cases might be self resolved without aggressive immunotherapy.

METHODS: Case report.

RESULTS: We present a case of a 36-year-old woman who developed self-resolving MG after recovering from COVID-19. Following COVID-19 diagnosis, she underwent MAB treatment due to being considered a high risk patient. She never received steroids. Two weeks later, she began experiencing left eye ptosis, arm weakness and jaw fatigue. Lab tests revealed elevated acetylcholine receptor (AChR) binding, blocking and modulating antibodies. She was started on pyridostigmine that improved symptoms. Patient had complex past medical history- stage IV-B neuroendocrine carcinoma, originating from the lung with widespread metastases. She was s/p left pneumonectomy, followed by lanreotide treatment. No disease modifying therapy was initiated in light of improving symptoms from pyridostigmine alone. Patient was closely monitored. She remained stable for months, gradually pyridostigmine was tapered. AChR antibodies remained positive, however clinically all MG symptoms disappeared and to this date she remains asymptomatic.

SUMMARY/CONCLUSION: This case demonstrates a link between COVID-19, MAB therapy, and MG suggestive of transient immune dysregulation syndrome following acute infection that can self-improve with time and not all cases might be needing immunotherapy.

CLINICAL EYELID MYOTONIA IN MYASTHENIA GRAVIS

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INTRODUCTION: Myotonia occurs as a sustained skeletal muscle contraction and results in the inability to relax. While typically associated with hereditary myotonic conditions, it is scarcely reported in association with myasthenia gravis. Here, we describe two patients with acetylcholine-receptor antibody (AChR-Ab) seropositive myasthenia gravis and eyelid myotonia at symptom onset.

RESULTS: 76- [P1] and 79-year-old [P2] unrelated male patients presented with bilateral fatigable ptosis. Both had difficulty opening their eyes for 10-15 seconds after forced and reflexive closure. Both had absent percussion myotonia. P2 had a brother with myasthenia gravis while P1 had no family history of neuromuscular disorders. Labs revealed AChR-Ab seropositivity for both patients. P2 underwent facial EMG which revealed myopathic units and active denervation without appreciable myotonic discharges in the right orbicularis oculi, orbicularis oris, and frontalis muscles. P2 has hypothyroidism; however, neither had thymomas present on chest CT. Both were trialed on pyridostigmine, prednisone, and mycophenolate without significant improvement of eyelid myotonia. In addition, P2 trialed efgartigimod without improvement.

SUMMARY/CONCLUSION: Although clinical and/or electrical myotonia in limb musculature has been reported in myasthenia gravis, myasthenia-associated eyelid myotonia is an extraordinarily rare phenomenon that is seldom reported in the literature. Interestingly, all prior cases have not demonstrated electrical eyelid myotonia. While associated with myasthenia gravis, our patients' eyelid myotonia has been largely refractory to typical myasthenic treatments. Clinicians should be cognizant of this rare, yet possible, myotonic association in myasthenia gravis.

ASSESSING THE SUITABILITY OF THE NEURO-QOL FATIGUE TO EVALUATE FATIGUE IN PATIENTS LIVING WITH MYASTHENIA GRAVIS

Sheryl Pease (Whitmore Lake, MI), Kayla Scippa (Raritan, NJ)

INTRODUCTION: Generalized myasthenia gravis (gMG) is a rare, chronic, autoantibody-mediated neuromuscular disease characterized by fatigable muscle weakness. The objectives of this research were to identify an appropriate patient-reported outcome (PRO) measure to assess fatigue in patients living with gMG and to conduct patient interviews to evaluate the content validity of the measure.

OBJECTIVE: To identify an appropriate patient-reported outcome (PRO) measure to assess fatigue in MG patients.

METHODS: A literature review identified the Neuro-QoL Fatigue as a suitable candidate PRO to assess fatigue in gMG. Twenty-three interviews were conducted with adults living with gMG. All participants were recruited from the United States via research partners following IRB approval. Each interview explored the symptoms and impacts of gMG on participants' daily lives. The final 8 interviews included cognitive debriefing of the Neuro-QoL Fatigue to determine its appropriateness for use in gMG.

RESULTS: All participants reported experiencing fatigue as part of their experience with gMG and that fatigue impacted their ability to participate and carry out daily activities. Among those asked to provide bothersome ratings, 80% (n=12 of 15) reported that fatigue was their most bothersome symptom. The debriefing exercise demonstrated that nearly all participants interpreted the Neuro-QoL Fatigue instructions, items, and recall period as intended.

SUMMARY/CONCLUSION: Fatigue is a bothersome symptom of gMG that limits patients' abilities to participate in daily life. The interview insights support the content validity of the Neuro-QoL Fatigue in gMG patients. Future research will focus on evaluating the psychometric properties of the Neuro-QoL Fatigue in the gMG patient population.

Disclosures:

Sheryl Pease – Employee of Johnson & Johnson.

Kayla Scippa – Employee of Johnson & Johnson.

THERAPEUTIC PLASMA EXCHANGE IN ACHR-AB POSITIVE GENERALIZED MYASTHENIA GRAVIS: A REAL WORLD STUDY ABOUT ITS EARLY RESPONSE

Jiaxin Chen (Washington, DC), Huiyu Feng (Guangzhou, China)

INTRODUCTION: Since there is no clear priority or selection principle in the guidelines for myasthenia crisis, therapeutic plasma exchange (TPE) and intravenous immunoglobulin are often administered randomly. However, it should be more prudent in taking TPE due to its higher cost and risk.

OBJECTIVE: Studying the early response factors of TPE is crucial for managing myasthenia crisis and can improve medical and economic benefits.

METHODS: Patients classified as having "impending myasthenia crisis" or experiencing a myasthenia crisis and treated by TPE were included. The primary endpoint was the response after TPE. Univariate logistic regression analysis and repeated measurement were performed to analyze factors related to TPE efficacy.

RESULTS: A total of 30 patients who were treated with TPE as their fast-acting treatments were enrolled. After TPE, those whose QMGs and/or MGCs decreased by ≥ 5 points or ≥ 30% of the baseline were judged as "response group", accounting for 66.67% (20/30). Respiratory symptoms had a response rate of 72.00% (18/25), showing the most remarkable improvement. Thymoma (100.00% vs 50.00%, P=0.002) and a high concentration of AChR-Ab (37.37 nmol/L vs 25.4 nmol/L, P=0.039) were common in the early response group. Repeated measures showed significant changes in AChR-Ab and CD19+ B cells before and after TPE. After treatment, the CD19+ B cells tended to decrease in the response group.

SUMMARY/CONCLUSION: For AChR-Ab positive generalized MG, TPE can quickly improve respiratory symptoms. Thymoma and a high concentration of AChR-Ab before TPE predict an early better response. Additionally, TPE may work by decreasing AChR-Ab levels and inducing immune regulation.

ONE PATIENT WITH THREE ANTIBODY-CONFIRMED NEUROLOGICAL AUTOIMMUNE SYNDROMES: A CASE REPORT

Lauren Nguyen (Honolulu, HI), Frishan Paulo (Honolulu, HI), Jordan Peterson (Honolulu, HI), J. Douglas Miles (Honolulu, HI)

INTRODUCTION: The occurrence of multiple autoimmune neurological disorders in one patient is rare. Here, we report the case of a woman who has clinical features of myasthenia gravis (MG), neuromyelitis optica (NMO), and anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis, and antibody titers consistent with all three conditions.

RESULTS: A 37-year old woman with a history of myasthenia gravis (MG) presented with a left cerebellar stroke. While the symptoms of her stroke improved, she began complaining of central vision loss in her right eye ten days later. Magnetic resonance imaging (MRI) revealed new right optic nerve enhancement, and further MRIs of the cervical and thoracic spine showed continuous central cord demyelination. Suspicion for a primary demyelinating syndrome was high, and an NMO antibody titer was positive. Two years later, she began to experience behavioral changes, neglecting her usual household responsibilities and being less responsive. She was mute and not following commands. NMDAR encephalitis was suspected, and an extensive work-up revealed positive NMDAR antibodies as well as serum NMO-IgG antibodies > 160 U/mL. A diagnosis of anti-NMDAR encephalitis was made. She was treated with plasma exchange, which resulted in significant near-resolution of her encephalopathy.

SUMMARY/CONCLUSION: Over the course of 12 years, this patient developed clinical manifestations of three rare neurological autoimmune disorders. Clinicians should be vigilant about overlapping neurological syndromes to avoid delays in the diagnosis and treatment in order to prevent poor clinical outcomes.

PLASMA BIOMARKER-BASED ENDOTYPING REVEALS DISTINCT INFLAMMATORY PATTERNS IN MYASTHENIA GRAVIS SUBTYPES

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INTRODUCTION: Myasthenia gravis (MG) is an antibody-mediated autoimmune disorder directed against the post-synaptic neuromuscular junctions of skeletal muscle, resulting in fluctuating weakness of ocular, limb, bulbar and even respiratory muscles.

OBJECTIVE: Plasma biomarkers have the potential for endotype identification and prediction of therapeutic response.

METHODS: Using a national neuromuscular center-based cohort, plasma from 219 patients with MG and 40 healthy controls (HCs) were analysed for 22 cytokines/chemokines/complements using the magnetic Luminex assay. MG-relevant scores were retrospectively assessed and their correlations with plasma inflammatory patterns were analyzed. The response of immunotherapies was longitudinally collected in anti-acetylcholine receptor (AChR) antibody-positive MG.

RESULTS: Hypercytokinemia was featured in plasma derived from MG compared with HCs. The inflammatory endotypes of MG can be characterized by either pan-elevated Th1/Th2/Th17/Treg/Neutrophil/B cell associated responses or complement pathway dominance. Distinct immune endotypes were revealed among AChR-MG, muscle-specific kinase (MuSK)-MG and seronegative MG (SNMG). Baseline plasma IFN-α (13.5 ± 7.1, $P < 0.01$), IL-23 (487.3 ± 296.4, $P< 0.1$), IL-2 (10.5 ± 7.6, $P < 0.01$), CXCL2 (1104.2 ± 621.0, $P < 0.05$), CXCL4 ($6.2e05 \pm 2.5e05$, $P < 0.01$) and CXCL5 (2117.9 ± 1382.0,$P < 0.01$)were closely associated with the response to initial corticosteroid therapies.

SUMMARY/CONCLUSION: Plasma biomarker-based endotypes differed among MG antibody groups and were closely related to the therapeutic response to the immunotherapies.

CLINICAL OUTCOME IN IMPENDING MYASTHENIC CRISIS: A PROSPECTIVE COHORT STUDY

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INTRODUCTION: Impending Myasthenic Crisis (MC) was defined as a rapid worsening in myasthenia gravis (MG) which can progress to respiratory failure in days to weeks. Fast-acting rescue therapies are recommended to treat patients with MC. However, the effectiveness of preventing the transition from impending to manifest MC remained unknown and there is a lack of evidence from prospective cohort studies.

OBJECTIVE: To explore the efficacy of timely rescue therapies in transformation from impending crisis to manifest crisis.

METHODS: This multicenter cohort enrolled impending MC from 6 University hospitals who were given timely rescue therapies with either IVIg or therapeutic plasma exchange (TPE) within 48 hours of admission. The primary outcome was defined as the transformation to manifest MC.

RESULTS: Among gMG patients with the chief complaint of dyspnea admitted from April 2021 to February 2024, 21.8% (37/170) with hypoxemia and/or hypercapnia in blood gas analysis but still satisfied by oxygen inhalation were included as the impending crisis cohort. With rescue therapies, the transformation rate from impending to manifest MC was 24.32% (9/37), including 8 with non-invasive ventilation and 1 with mechanical ventilation (MV). As compared with those who developed MC, a significantly shorter hospital stay was observed in those who did not (P=0.004). A shorter disease duration from onset to this admission was observed in impending crisis who did not transform (P=0.003) and a lower QoL-15 score at baseline (P= 0.006).

SUMMARY/CONCLUSION: With the timely intervention of fast-acting therapies, patients at impending MC state can effectively be prevented from transforming into MC.

PRECLINICAL PHARMACOLOGY OF S-1117, A NOVEL ENGINEERED FC-FUSED IGG CLEAVING ENZYME, FOR CHRONIC TREATMENT OF AUTOANTIBODY-MEDIATED DISEASES INCLUDING MYASTHENIA GRAVIS

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OBJECTIVE: To assess the PK, PD and preclinical efficacy of an engineered pan-IgG protease.

INTRODUCTION: Pathogenic autoantibodies are key effectors of inflammation, promoting immune cell responses that cause tissue damage in autoantibody-mediated diseases such as myasthenia gravis (MG). Antibody degradation using an IgG protease represents a new therapeutic opportunity.

S-1117, a novel Fc-fused pan-IgG protease, was engineered for chronic administration using a proprietary machine learning enabled platform to augment manufacturability while maintaining potency and reduce immunogenicity. S-1117 addresses multiple mechanisms of autoimmunity by cleaving plasma IgG and BCR on memory B cells while reducing IgG effector functions and IC-mediated cell activation.

METHODS: Plasma IgG, BCR, and IC cleavage assays were performed in vitro. A murine PK/PD model evaluated S-1117 function in vivo.

RESULTS: S-1117 cleaves soluble IgG and BCR on memory B cells derived from healthy individuals and MG patients with comparable potency. S-1117 directly eliminates IgG effector functions including ADCC, CDC, and IC-mediated immune cell activation in vitro.

A single dose of S-1117 induced a rapid (<24 hours), deep (>90%), and sustained reduction of human IgG administered to mice. Human PK/PD QSP modeling indicates that infrequent chronic low doses will achieve titratable IgG reductions of 90% or greater as clinically indicated.

SUMMARY/CONCLUSION: S-1117 is a novel engineered pan-IgG protease that demonstrates rapid and sustained reduction of human IgG levels and effector function. Advantages of enzymatic

degradation and sustained PK enable a convenient treatment regimen. Since S-1117 addresses multiple pathogenic mechanisms as a single drug, it has potential to achieve superior clinical outcomes in MG.

Disclosures:

Julia Manasson – Received personal compensation for serving as an employee of Seismic Therapeutic. Has stock in Seismic Therapeutic.

Yi Xing – Received personal compensation for serving as an employee of Seismic Therapeutic. Has stock in Seismic Therapeutic.

Heather Vital - Received personal compensation for serving as an employee of Seismic Therapeutic. Has stock in Seismic Therapeutic, Relay Therapeutics.

Nathan Higginson-Scott - Received personal compensation for serving as an employee of Seismic Therapeutic. Has stock in Seismic Therapeutic.

John S. Sundy - Received personal compensation for serving as an employee of Seismic Therapeutic. Has received personal compensation for serving as a Consultant for Tome Biosciences, Rome Therapeutics, Upstream Bio, Imhotex. Has received personal compensation for serving as an officer or member of the Board of Directors for Sanofi S.A. and Neutrolis, Inc. Has stock in Gilead Sciences, Seismic Therapeutic, Rome Therapeutics, Upstream Bio, Neutrolis.

Kevin L. Otipoby - Received personal compensation for serving as an employee of Seismic Therapeutic. Has stock in Seismic Therapeutic. Has received personal compensation for serving as member of the Scientific Advisory Board for Eurofins Scientific. Has received personal compensation for serving as a consultant for Lucy Therapeutics and LogicBio Therapeutics.

Ivan Mascanfroni - Received personal compensation for serving as an employee of Seismic Therapeutic. Has stock in Seismic Therapeutic.

Alex Pellerin - Received personal compensation for serving as an employee of Seismic Therapeutic. Has stock in Seismic Therapeutic. An immediate family member has stock in Biogen.

Liliana Sanmarco - Received personal compensation for serving as an employee of Seismic Therapeutic. Has stock in Seismic Therapeutic.

Jordan Anderson - Received personal compensation for serving as an employee of Seismic Therapeutic. Has stock in Seismic Therapeutic.

Nathan Rollins - Received personal compensation for serving as an employee of Seismic Therapeutic. Has stock in Seismic Therapeutic.

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Agustin Plasencia - Received personal compensation for serving as an employee of Seismic Therapeutic. Has stock in Seismic Therapeutic.

Andita Newton - Received personal compensation for serving as an employee of Seismic Therapeutic. Has stock in Seismic Therapeutic.

Ryan Peckner - Received personal compensation for serving as an employee of Seismic Therapeutic. Has stock in Seismic Therapeutic.

MISMATCH BETWEEN NEUROMUSCULAR SPECIALISTS AND MYASTHENIA GRAVIS PATIENTS IN THE US MEDICARE POPULATION

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Introduction: There is a mismatch between clinical need and access to neurologists across the US. Myasthenia gravis (MG) incidence and prevalence are increasing, particularly in US patients older than 65 years. Clinical need and access to neuromuscular physicians across the US have not been systematically studied.

OBJECTIVES: Compare prevalent number of MG patients over age 65 years to number of board-certified neuromuscular physicians (BCNMP) by state, census divisions and regions.

METHODS: Utilizing Medicare Fee-For-Service Parts A/B coverage non-HMO claims data, MG cases were ascertained using a validated algorithm.

Number of BCNMP per state was determined using verifyCERT, through American Board of Psychiatry and Neurology and American Board of Physical Medicine and Rehabilitation resources. Physicians with unexpired certifications were included.

MG prevalence, BCNMP, and ratios of cases per BCNMP were calculated by state, census division and region for 2012-13 and 2018-19. Ratios between periods were tested using Poisson regression.

RESULTS: BCNMP increased from 585 in 2012-13 to 806 in 2018-19. Six states had no BCNMP at both timepoints. National ratio of MG cases per BCNMP improved from 49.5 in 2012-13 to 44.3 in 2018-19. In 2018-19 regional ratios varied from 29.8 (Northeast) to 63.7 (South). South divisions and region had largest ratios at both timepoints. Ratios improved in all regions ($p<0.001$), by the largest margin in Northeast. Ratio worsened in East Central South division, up 8.9 cases per physician ($p<0.001$).

CONCLUSIONS: While the number of BCNMP has increased nationally, supply and demand are not evenly distributed. US ratio of MG cases per BCNMP is variable.

Disclosures:

Yuebing Li - Received honorariums from Alexion, argenx, Catalyst, Immunovant and UCB Pharma. Received research funding from Argenx.

Nicholas Silvestri - Consultant/advisor: argenx, Alexion, Amgen, Janssen, Immunovant, UCB. Speaker for argenx, Immunovant, Takeda, UCB.

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LAMBERT-EATON MYASTHETIC SYNDROME MAY NOT BE COINCIDENTAL IN PROSTATE CANCER

Iris Li (Waltham, MA), Stephannie Ford (Chelmsford, MA), Min Zhu (Chelmsford, MA)

INTRODUCTION: Lambert Eaton myasthenic syndrome has been well documented in patients with small cell lung cancer, but rare and considered coincidental in prostate cancer.

OBJECTIVE: We are curious if Lambert-Eaton myasthenia has solid link to prostate cancer. Better understanding of their relationship will help early diagnosis and improved prognosis.

METHODS: Here we report a patient with Lambert-Eaton myasthenia and other paraneoplastic syndrome symptoms, who was diagnosed with prostate adenocarcinoma. We performed literature review on Lambert-Eaton myasthenia and prostate cancer.

RESULTS: This case is an elderly gentleman in his 90s, who presented with 2-3 years of episodic slurred speech, generalized weakness and gait difficulty. His brain imaging and cerebral vascular studies were unremarkable. His continuous EEG interestingly captured epileptic discharges during his events. Initial workup for myasthenia was negative. He later tested positive for voltage gated calcium channel antibody. He was found to have prostate adenocarcinoma of acinar type based on biopsy. No other primary malignancy was found. His symptoms improved with treatment of prostate cancer, antiepileptics, and amifampridine. Through literature review we found multiple cases of Lambert-Eaton myasthenia reported in patients with prostate cancer since 1989.

SUMMARY/CONCLUSION: This case is unique in raising awareness that Lambert Eaton myasthenic syndrome may coexist with other neurological features of paraneoplastic syndrome, and its occurrence in patients with prostate cancer, especially the adenocarcinoma type, may not be a coincidence.

A STUDY OF THE COMMON FACTORS THAT INFLUENCE FATIGUE IN MYASTHENIA GRAVIS

Christopher Evans (Fairfax, VA), Deep Patel (Cleveland, OH), Emma Parolisi (Richmond, VA), Xinli Du (Glen Allen, VA), Qihua Fan (Richmond, VA), Neel Dixit (Richmond, VA), A. Gordon Smith (Richmond, VA), Zachary Ward (Winston Salem, NC), Shanshan Chen (Richmond, VA), Kelly Gwathmey (Charlottesville, VA)

INTRODUCTION: Myasthenia gravis (MG) is an autoimmune disorder causing fatigable muscle weakness. Fatigue as a symptom is driven by the central or peripheral nervous systems ("central fatigue" and "peripheral fatigue") and influenced by many factors.

OBJECTIVE: To characterize fatigue in MG patients at a single center and identify non-myasthenic contributors.

METHODS: MG patients with symptomatic fatigue were enrolled. Baseline demographic information and disease characteristics were obtained. Fatigue was evaluated with the Neuro-Quality of Life (QOL) Fatigue and Fatigue Severity Scale (FSS), sleepiness with the Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS), depression and anxiety with the Neuro-QOL Depression and Anxiety scales. Laboratory testing evaluated metabolic causes: hemoglobin/hematocrit, B12/methylmalonic acid, vitamin D, and TSH. Spearman correlations and multiple linear regression models were used to assess associations between fatigue, sleep quality, and metabolic causes.

RESULTS: 46 participants enrolled, 73.9% female, 80.4% AChR+. PSQI, MG-QOL15r, and MG-ADL scores were significantly associated with Neuro-QOL Fatigue and FSS marginally using Spearman correlation and conditionally after adjusting for symptom distribution in multiple regression models. Vitamin D and B12 levels were negatively associated with Neuro-QOL Fatigue score (Spearman's rho = -0.3, p=0.046 and -0.25, p=0.10 respectively). After adjusting for age, symptom types and MG-QOL15r, PSQI was no longer significantly associated with Neuro-QOL Fatigue scale but B12 was significantly associated with fatigue (p=0.037) in the multiple regression model.

SUMMARY/CONCLUSION: Sleepiness, poor QOL, MG disease severity, vitamin D and B12 deficiency are associated with worse fatigue in MG. These variables should be assessed in patients with clinically significant symptomatic fatigue.

Disclosures:

A.Gordon Smith - Consultant for: Alexion, argenx, Eidos, Lilly. UCB, Kriya, Arcellx, Lexicon, Seismic.

Qihua Fan - Speaker and consultant for Alnylam, Consultant for argenx.

Kelly Gwathmey - Consultant for: argenx, UCB, Alexion, Amgen, Speaker for argenx.

IMAGING PATTERNS IN CONGENITAL MYASTHENIC SYNDROME (CMS) - INSIGHTS FROM MRI

Prashanth Poulose (Bangalore, India), Atchayaram Nalini (Bangalore, India), Seena Vengalil (Bangalore, India), Deepak Menon (Bangalore, India), Saraswati Nashi (Bangalore, India), Ankit Arora (Bangalore, India), Mariamma Philip (Bangalore, India)

INTRODUCTION: Muscle imaging can be a valuable adjunct in the comprehensive evaluation of CMS, but its utility remains less well characterized.

OBJECTIVE: To examine MR imaging profile of muscle involvement across various CMS

METHODS: 18 genetically proven CMS patients from NIMHANS with muscle MRI of lower limbs were included in this retrospective descriptive study. Fatty infiltration graded by T1w (Mercuri score) & oedema STIR (Stramare scale)

RESULTS: 18 patients (M:F- 12:6) with mean age of 23.3±15.5 yrs were classified as pre-synaptic (n=1,SYT2), synaptic(n=1 ,Col Q), post - synaptic(n=11)CHRNE(n=4) ,AGRN (2) ,CHRNA1 (2),DOK 7 (2),SCN4A (1) and glycosylation defects(n=5) GFPT-1(4) ,DPAGT-1(1).The mean T1w score in post synaptic group at mid- thigh was 0.84 (Range:0 to 5), mid-calf 1.22 (0-5). Mean T1w score among glycosylation defect at mid-thigh=0.25 (range 0-2) and mid-calf 0.2 (0-1) . Mean STIR score among post synaptic at mid -thigh was 0.26 (0-3), mid-calf=0.64 (0-3) and glycosylation defect mid-thigh=0.11(0-2), mid-calf=0.08 (0-1).Higher grades of fatty infiltration in mid-thigh(2) and mid-calf (1.8) were noted in Dok-7, CHRNA-1, mid-thigh (2) in SYT-2, pelvic (1.5) and mid-calf (1.75) in AGRN. STIR hyperintensities were maximum in CHRNA-1 in pelvis (2), anterior mid-thigh (2.5) and all calf compartments (1.5) followed by CHRNE.

SUMMARY/CONCLUSION: There was overall predilection for higher fatty infiltration in the pelvic muscles, anterior mid-thigh and posterior mid-calves across subgroups. Higher muscle oedema grades were noted in anterior mid-thigh, anterior and posterior mid-calves. Across groups showed non-selective pattern of fatty infiltration. GFPT-1 and DPAGT-1 showed less fatty infiltration than post synaptic.

TRANSCRIPTOME-WIDE AND STRATIFIED GENOMIC STRUCTURAL EQUATION MODELING IDENTIFY NEUROBIOLOGICAL PATHWAYS SHARED ACROSS MYASTHENIA GRAVIS AND NEUROPSYCHIATRIC DISORDERS

Mayra Aldecoa (Montreal, Canada), Miranda Medeiros (Montreal, Canada), Patrick Dion (Montreal, Canada), Dan Spiegelman (Montreal, Canada), Guy Rouleau (Montreal, Canada)

INTRODUCTION: Myasthenia gravis (MG), an autoimmune neuromuscular disorder, has been associated with neuropsychiatric symptoms and movement disorders, suggesting potential shared neurobiological pathways.

OBJECTIVE: To examine if there are genetic commonalities between MG and depression, fibromyalgia, restless leg syndrome and anxiety and if these relations depend on the age of onset of the MG disease.

METHODS: We used the publicly available summary statistics from genome-wide association studies (GWAS) of MG early onset, late onset and the neuropsychiatric comorbidities to calculate the genetic correlation between phenotypes and collapse them using GenomicSEM.

We studied the effects of tissue-specific gene expression using FUSION based on Genotype-Tissue Expression Program (GTEx) v84, incorporating brain, skeletal muscle and tibial nerve transcriptomic data correlating them with the latent variable to determine which genes are commonly expressed across the disorders.

RESULTS: Using the Common Factor Model we revealed a latent variable that explains the relation between the other disorders. For that model, the relations showed a negative standardized coefficient for most of the traits except for restless leg syndrome.

In the User model we found 2 latent variables that correlated positively and between each other.

In the transcriptomic analysis, we found many genes expressed that are involved in all the traits.

SUMMARY/CONCLUSION: Our findings offer valuable insights into the underlying mechanisms of the comorbidities in MG and may inform the development of targeted therapeutic interventions for individuals with overlapping neuropsychiatric and autoimmune disorders. Our limitations stemmed primarily from the scarcity of available data and potential improvements in model fitting.

DEVELOPMENT OF A MYASTHENIA GRAVIS PATIENT JOURNEY MAP AS A TOOL TO IDENTIFY CHALLENGES AND UNMET NEEDS IN THE PATIENT COMMUNITY

James F. Howard, Jr. (Chapel Hill, NC), Margaret Arbogast (New York, NY), Lorah Perlee (Tarrytown, NY), Ching Lum (Tarrytown, NY), Christopher Hartford (Tarrytown, NY), Rodrigo Pavani (Tarrytown, NY), Rosemarie Sellati (Tarrytown, NY)

INTRODUCTION: Myasthenia gravis (MG) is a rare, autoimmune disorder of the neuromuscular junction characterized by muscle weakness that can cause sleep disturbances, pain, and exertional fatigability. MG includes a spectrum of symptoms, ranging from double vision and fatigue to difficulty breathing. Despite effective treatments, patients live with high disease burden, indicating an unmet need in care.

OBJECTIVE: Refine the MG patient journey map (PJM) with patient advocate council (PAC); identify challenges and unmet need at various disease stages; and gain patient perspectives on treatments.

METHODS: An initial PJM was created by querying data from 18 patient and professional MG organizations, and auditing content from 74 MG resources. Next, experiences of patients with MG were obtained through patient (n=5) and caregiver (n=1) interviews. Lastly, a PAC was convened to validate the PJM, identifying gaps and opportunities to improve MG care.

RESULTS: The refined PJM, validated by PAC, identified challenges and limitations that impacted stakeholders across the patient-provider continuum, resulting in suboptimal care. The need for educational materials for patients and professionals was highlighted. Early symptom dismissal, lack of MG awareness, and difficulty in accessing diagnostic tests delayed diagnosis. Challenges in relationships and family dynamics due to symptoms like incontinence and sexual dysfunction underscored the need to address psychological and psychosocial burdens, and the value of developing caregiver support mechanisms. MG has significant socio-economic impact due to healthcare costs and lost work productivity.

SUMMARY/CONCLUSION: This research generated a comprehensive MG PJM from the patient perspective and identified opportunities to improve their care.

Disclosures:

James F. Howard, Jr. - Received research funding (paid to institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, Ra Pharmaceuticals/UCB Bioscience, and Takeda Pharmaceuticals; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc (now Amgen), Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Ra Pharmaceuticals/UCB Bioscience, Regeneron Pharmaceuticals, Sanofi US, and Zai Labs; non-financial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Bioscience and Zai Labs.

Margaret Arbogast - Received professional service fees (paid to VOZ Advisors, Inc.) from Regeneron Pharmaceuticals, Inc.

Lorah Perlee - Regeneron Pharmaceuticals, Inc. employee/stockholder.

Ching Lum - Regeneron Pharmaceuticals, Inc. employee/stockholder.

Christopher Hartford - Regeneron Pharmaceuticals, Inc. employee/stockholder.

Rodrigo Pavani - Regeneron Pharmaceuticals, Inc. employee/stockholder.

Rosemarie Sellati - Regeneron Pharmaceuticals, Inc. employee/stockholder

POZELIMAB AND CEMDISIRAN COMBINATION THERAPY IN PATIENTS WITH MYASTHENIA GRAVIS: PHASE 3 NIMBLE TRIAL DESIGN

Saiju Jacob (Birmingham, United Kingdom), Umesh Chaudhari (Tarrytown, NY), Kosalai Mohan (Tarrytown, NY), Lorah Perlee (Tarrytown, NY), Rodrigo Pavani (Tarrytown, NY), Ching Lum (Belle Mead, NJ), James F. Howard, Jr. (Chapel Hill, NC)

INTRODUCTION: Generalized myasthenia gravis (gMG) is a rare autoimmune disease of the neuromuscular junction driven by acetylcholine receptor (AChR) antibodies. IgG1 AchR (and less commonly anti-lipoprotein receptor-related protein 4, LRP4) antibodies are likely responsible for neuromuscular junction damage via terminal complement activation, in most patients with gMG. Pozelimab and cemdisiran are investigational agents for gMG that inhibit the terminal complement pathway. Cemdisiran is an N-acetylgalactosamine-conjugated small interfering RNA that suppresses liver production of C5, while pozelimab is a monoclonal antibody inhibitor to C5.

OBJECTIVE: We describe the design of the ongoing phase 3 NIMBLE trial (NCT05070858), which aims to evaluate the efficacy and safety of pozelimab plus cemdisiran combination in patients with symptomatic gMG.

METHODS: This is a multinational, randomized, double-blind, placebo-controlled trial in patients with clinically confirmed gMG (seropositive for anti-AChR or anti-LRP4 antibodies). The study includes: 5-week screening period; 24-week double-blind placebo-controlled treatment period; 28-week double-blind extension treatment period, 68-week open-label long-term treatment period; and a 52-week post-treatment follow-up period. On Day 1, patients will be randomized to one of four treatment arms. This study will enroll approximately 235 patients. The primary endpoint is the change in myasthenia gravis-activities of daily living total score from baseline to week 24.

RESULTS: The first patient was enrolled on December 14, 2021.

SUMMARY/CONCLUSION: This ongoing study (open for recruitment) is designed to evaluate the effect of pozelimab plus cemdisiran combination on safety and MG efficacy measures, such as daily functioning and other quality of life measures, in patients with symptomatic gMG.

Disclosures:

Saiju Jacob - Served as an international advisory board member for Alexion, Alnylam, argenx, Immunovant, Regeneron, and UCB; is currently an expert panel member of the Myasthenia Gravis Consortium for argenx; and has received speaker fees from Eisai Pharmaceuticals and Terumo BCT.

Umesh Chaudhari - Employee of and stockholder in Regeneron Pharmaceuticals, Inc.

Kosalai Mohan - Employee of and stockholder in Regeneron Pharmaceuticals, Inc.

Lorah Perlee - Employee of and stockholder in Regeneron Pharmaceuticals, Inc.

Rodrigo Pavani - Employee of and stockholder in Regeneron Pharmaceuticals, Inc.

Ching Lum - Employee of and stockholder in Regeneron Pharmaceuticals, Inc.

James F. Howard, Jr. - Received research funding (paid to institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, Ra Pharmaceuticals/UCB Bioscience, and Takeda Pharmaceuticals; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc (now Amgen), Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Ra Pharmaceuticals/UCB Bioscience, Regeneron Pharmaceuticals, Sanofi US, and Zai Labs; non-financial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Bioscience and Zai Labs.

EFGARTIGIMOD ALFA-FCAB USE IN A PREGNANT WOMAN WITH GENERALIZED MYASTHENIA GRAVIS: A CASE REPORT

Ryan Verity (Saskatoon, Canada), Pushpa Narayanaswami (Boston, MA)

INTRODUCTION: Efgartigimod alfa-fcab is a neonatal Fc receptor (FcRn) antagonist that reduces circulating immunoglobulin G (IgG) levels. It is approved for acetylcholine receptor antibody positive (AChR-Ab +) generalized myasthenia gravis (gMG). Its safety in pregnancy and lactation are unknown. This information is important given the role of the placental FcRn receptor in passive transfer of IgG to the fetus.

OBJECTIVE: To describe the use of efgartigimod in a pregnant woman with AChR-Ab+ gMG.

METHODS: Case report

RESULTS: A 30-year-old female with AChR-Ab+ gMG (MG-ADL 11) was treated with pyridostigmine, prednisone and azathioprine with good improvement (MG-ADL 0), until prednisone was weaned (MG ADL 4). She was started on intravenous efgartigimod with rapid resolution of symptoms. Three months later, she became pregnant. Efgartigimod was continued through the first 2 trimesters. Total IgG levels were 45% -78% of baseline during treatment. Antibody titres to immunizations remained positive except for one equivocal rubella IgG titre. Efgartigimod was stopped in the third trimester. Eight weeks later, she developed mild bulbar and generalized weakness (MG-ADL 2). She was treated with pyridostigmine, and prednisone was increased. She received 3 plasma exchanges in anticipation of labor induction at 38 weeks. She delivered a healthy baby boy, via vaginal delivery. There were no signs of neonatal MG. She was restarted on efgartigimod one month after delivery.

SUMMARY/CONCLUSION: Intravenous efgartigimod in the first two trimesters of pregnancy did not affect response to immunizations. MG symptoms recurred with discontinuation of efgartigimod, requiring additional management. Labor and delivery were normal, with no evidence for neonatal MG.

Disclosures:

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COMPARATIVE EFFICACY OF TREATMENT MODALITIES IN MYASTHENIA GRAVIS

Manvi Punukollu (Augusta, GA)

INTRODUCTION: Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disorder characterized by muscle weakness and fatigue. Various treatment modalities are available, but their comparative efficacy remains unclear.

OBJECTIVE: This systematic review and meta-analysis aimed to compare the effectiveness of different treatment modalities in MG patients.

METHODS: A systematic literature search was conducted in PubMed using the terms "myasthenia gravis" and "treatment". Inclusion criteria comprised randomized controlled trials, cohort studies, and case-control studies assessing treatment efficacy in MG. Data extraction and quality assessment were performed, and a comparative meta-analysis was conducted.

RESULTS: These studies evaluated treatments such as acetylcholinesterase inhibitors, immunosuppressants, and thymectomy. Meta-analysis revealed differences in treatment efficacy, with certain interventions demonstrating superior outcomes in terms of clinical improvement, remission rates, and adverse events.

SUMMARY/CONCLUSION: This systematic review provides valuable insights into the comparative effectiveness of treatment modalities in MG patients. The findings emphasize the importance of tailored treatment approaches based on individual patient characteristics and disease severity. Clinicians can utilize this evidence to make informed treatment decisions, ultimately optimizing outcomes for MG patients. Further research is needed to address remaining uncertainties and refine treatment strategies for this complex autoimmune disorder.

CHARACTERISTICS AND TREATMENT PATTERNS OF A UNITED STATES GENERALIZED MYASTHENIA GRAVIS POPULATION: INTERIM ANALYSIS OF REAL-WORLD DATA

Lesley-Ann Miller-Wilson (New York, NY), Joe Conyers (Bollington, United Kingdom), Shiva Lauretta Birija (Bollington, United Kingdom), Ciara Ringland (Bollington, United Kingdom), Gregor Gibson (Bollington, United Kingdom), Niall Hatchell (Bollington, United Kingdom), Yuriy Edwards (New York, NY)

INTRODUCTION: Generalized myasthenia gravis (gMG) is a chronic autoimmune neuromuscular disease characterized by muscle weakness and fatigue. New therapies aim to reduce symptoms and disease burden.

OBJECTIVE: To explore current real-world disease burden and treatment patterns in gMG.

METHODS: Cross-sectional survey data collected from US neurologists between February and April 2024 were drawn from the Adelphi MG II Disease Specific Programme™. Sociodemographic, clinical, and treatment characteristics are reported here.

RESULTS: This interim analysis includes data from 36 physicians describing 197 patients with gMG. Patients were primarily male (52%) and Caucasian/White (78%), with a mean (SD) age of 56.9 (14.9) years. Mean (SD) time since diagnosis was 4.7 (6.5) years, and 62% of patients were MGFA class II. The most frequently reported symptoms included ptosis (76%), diplopia (63%), dysphagia (46%), difficulty chewing (41%) and dysarthria (39%). Concomitant conditions were reported in 76% of patients; of those, 35% had hypertension. Nearly half (44%) of patients were misdiagnosed prior to their gMG diagnosis. Regarding treatment, patients had received a mean (SD) of 1.9 (0.9) regimens. Among patients receiving maintenance treatment (81%), 85%, 37%, 36%, and 31% were receiving acetylcholinesterase inhibitors, corticosteroids, non-steroidal immunosuppressants, and biologics, respectively. Side effects across all treatments were common (53%), particularly weight gain and fatigue (each 10%). Quality of life was reported as fair/poor for 31% of patients. Data collection is ongoing.

SUMMARY/CONCLUSION: More than 75% of patients with gMG are symptomatic, and existing biologics are not widely utilized, highlighting the need for novel therapeutics that address symptomatic burden.

Disclosures:

Lesley-Ann Miller-Wilson - is an employee of Immunovant, Inc.

Joe Conyers - is an employee of Adelphi Real World.

Shiva Lauretta Birija - is an employee of Adelphi Real World.

Ciara Ringland - is an employee of Adelphi Real World.

Gregor Gibson - is an employee of Adelphi Real World.

Niall Hatchell - is an employee of Adelphi Real World.

Yuriy Edwards - is an employee of Immunovant, Inc.

REAL-WORLD EXPERIENCE WITH INDIVIDUALIZED DOSING OF EFGARTIGIMOD IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS

Nicholas Silvestri (Amherst, NY)

INTRODUCTION: Efgartigimod, a human immunoglobulin G1 (IgG) antibody Fc-fragment, reduces IgG levels through neonatal Fc receptor (FcRn) blockade. This retrospective, single-center clinical case series describes the experience of individualized efgartigimod dosing for patients with anti-acetylcholine receptor antibody positive (AChR-Ab +) generalized myasthenia gravis (gMG) who lack adequate symptom control while receiving oral medications and/or intravenous (IV) immunoglobulin.

OBJECTIVE: To describe our approach to efgartigimod dosing in patients with AChR-Ab+ gMG.

METHODS: Efgartigimod (10 mg/kg IV) was administered using a specific dosing approach. Fixed intervals were used for the first 3 cycles (4 once-weekly infusions followed by a 4-week period prior to initiation of next cycle). Beginning with the fourth cycle, individual clinical evaluation of patients was utilized to determine time between cycles and when to initiate subsequent treatment cycles; if patients responded well, time between cycles was gradually increased.

RESULTS: Twenty patients were included in the analysis and received a mean (SD) of 4.4 (1.5) cycles of efgartigimod. Clinically meaningful improvement in Myasthenia Gravis Activities of Daily Living (MG-ADL) total score from baseline to post-efgartigimod treatment was observed in all 20 patients, with a mean (SD) improvement of 5.9 (2.5) points. Minimal symptom expression (MG-ADL 0-1), was achieved by 35% (n=7/20) of patients. Daily mean (SD) prednisone dose decreased from baseline (21.4 [20.6] mg/kg) to post-efgartigimod treatment (2.9 [5.1] mg/kg). Efgartigimod was generally well tolerated.

SUMMARY/CONCLUSION: Substantial improvements in MG-ADL scores were observed with individualized dosing and cadence of efgartigimod treatment in these patients with AChR-Ab+ gMG. Additionally, dose of concomitant corticosteroids was reduced.

Disclosures:

Nicholas Silvestri - served as a consultant and speaker for argenx, Alexion, and UCB; consultant for Immunovant and Janssen; speaker for Takeda; and participated in advisory boards for argenx, Alexion, UCB, Immunovant, Amgen, and Roche.

QUANTITATING FACTORS INFLUENCING THE MYASTHENIA GRAVIS TELEHEALTH EXAMINATION

Henry Kaminski (Washington, DC), Quentin Lesport (La Rochelle, France), Helen Girma (Washington, DC), Gülşen Öztosun (Washington, DC), Marc Garbey (Washington, DC)

INTRODUCTION: Telemedicine offers an opportunity for video-recording of examinations followed by quantitative analysis of all aspects of the patient-examiner interaction. Currently, telemedicine examinations are adapted from standard clinical visits, but their benefits and deficiencies have not been rigorously assessed.

METHODS: We utilized a bank of videos obtained from 54 subjects with myasthenia gravis (MG), each undergoing two telemedicine examinations by neuromuscular experts. These examinations included the MG Core Examination (MG-CE) and the MG Activities of Daily Living (MG-ADL). We applied a spectrum of artificial intelligence algorithms, including computer vision, speech analysis, and natural language processing, to generate quantitative metrics from the digital records.

RESULTS: We successfully developed technology to assess video examinations. While overall MG-CE examination scores were consistent across examiners, individual metrics exhibited significant variability, with up to a 25% variation in scoring within the MG-CE's range. Compliance with MG-ADL instructions varied widely across examiners.

DISCUSSION: Our digital analysis of neuromuscular examinations identified variations in outcome measures based on examiner instructions, video recording limitations, and patient disease severity. Notably, we observed a high standard deviation in scores for patients with low disease severity. This finding aligns with other studies indicating that clinical outcome measures often struggle to accurately reflect the disease burden in patients with mild MG.

The work was supported by the MGNet, a member of the Rare Disease Clinical Research Network Consortium (NIH U54 NS115054)

Disclosures:

Henry Kaminski - is a consultant for Roche, Takeda, Cabaletta Bio, UCB Pharmaceuticals, Canopy Immunotherapeutics, EMD Serono, Ono Pharmaceuticals, ECoR1, Gilde Healthcare, and Admirix, Inc. Argenix provides an unrestricted educational grant to George Washington University. He is an unpaid consultant for Care Constitution. Dr. Kaminski has equity interest in Mimivax, LLC.

Marc Garbey - is CEO of Care Constitution, a company designed to develop AI tools for the neurological examination.

CAN NON-THYMOMATOUS LATE-ONSET MYASTHENIA GRAVIS BENEFIT FROM THYMECTOMY? A SYSTEMATIC REVIEW AND META-ANALYSIS

Jiaxin Chen (Washington, DC), Ahmed Abdaltawab (Washington, DC), Huiyu Feng (Washington, DC), Chunhua Su (Washington, DC), Henry Kaminski (Washington, DC)

INTRODUCTION: Thymectomy, as an effective treatment for early-onset and thymoma-associated MG, whether it is of any benefit in non-thymomatous late-onset MG (NT-LOMG) has been questioned for years and no conclusion has been drawn. Given the increasing incidence of the NT-LOMG, the question of whether thymectomy is therapeutic in these patients is important to address.

OBJECTIVE: To estimate the efficacy of thymectomy in NT-LOMG, and identify the characteristics of the response group.

METHODS: Four electronic databases were searched to identify studies until May 20, 2024. Both thymectomized and medical NT-LOMG patients were reported in six eligible studies and enrolled in the meta-analysis. Another 14 studies with only a the surgical group were included as well. The primary outcome was the response (remission or minimal manifestations) of NT-LOMG.

RESULTS: In NT-LOMG, response in thymectomized group was higher than that in medical group [OR=1.42 (0.86-2.35), P=0.169], but not significantly. Subgroup analysis showed when age of MG onset ≥45 or age of thymectomy ≥50 years old, thymectomy appeared better than medical therapy alone [OR=1.92 (1.06-3.48), P=0.031]. For all 20 studies, the response to thymectomy in NT-LOMG was 34% (24-44%). Higher response appeared for patients with AChR-Ab positive [40% (21-61%), P=0.02], and preoperative duration within 3 years [39% (16-65%), P＜0.001]. Other factors, including presence of titin antibodies, MG severity and thymic pathology were discussed in studies and may relate to the response.

SUMMARY/CONCLUSION: NT-LOMG patients may benefit from thymectomy. AChR-Ab positive and MG duration within 3 years could be helpful for surgical decision-making. A randomized controlled study is needed.

CYCLIC AND EVERY-OTHER-WEEK DOSING OF INTRAVENOUS EFGARTIGIMOD FOR GENERALIZED MYASTHENIA GRAVIS: PART A OF ADAPT NXT

Kelly Gwathmey (Charlottesville, VA), Ali Habib (Irvine, CA), Kristl Claeys (Leuven, Belgium), Vera Bril (Toronto, Canada), Yessar Hussain (Austin, TX), Gregory Sahagian (Carlsbad, CA), Elena Cortés-Vicente (Barcela, Spain), Eddie Brauer (Boston, MA), Deborah Gelinas (Durham, NC), Anne Sumbul (Ghent , Belgium), Rosa Jimenez (Ghent, Belgium), Daniela Hristova (Ghent, Belgium), Delphine Masschaele (Ghent, Belgium), Renato Mantegazza (Milan, Italy), Andreas Meisel (Berlin, Germany), Shahram Attarian (Marseille, France)

INTRODUCTION: Individualized cyclic dosing of efgartigimod, a human immunoglobulin G1 Fc-fragment that blocks the neonatal Fc receptor, was well tolerated and efficacious in the ADAPT/ADAPT+ phase 3 trials in generalized myasthenia gravis (gMG).

OBJECTIVE: The phase 3b ADAPT NXT study (NCT04980495) investigated the efficacy, safety, and tolerability of efgartigimod administered either every other week (Q2W) or in fixed cycle dosing regimens.

METHODS: Adult participants with anti-acetylcholine receptor antibody positive gMG were randomized 3:1 to Q2W or cyclic (4 once-weekly infusions, 4 weeks between cycles) dosing of 10 mg/kg efgartigimod for a 21-week period.

RESULTS: Sixty-nine participants were treated (cyclic, n=17; Q2W, n=52). Least squares mean (95% CI) of the change from baseline in Myasthenia Gravis Activities of Daily Living (MG-ADL) total score from Week 1-21 (primary endpoint) was -5.1 (-6.5 to -3.8) in the cyclic arm and -4.6 (-5.4 to -3.8) in the Q2W arm; changes remained similar through week 21. Clinically meaningful improvements in mean (SE) MG-ADL total scores were observed as early as week 1 (-2.0 [0.4], both arms) and were maintained over time. Achievement of minimal symptom expression (MG-ADL score 0-1) was observed in 47.1% (n=8/17) and 44.2% (n=23/52) of participants in the cyclic and Q2W arms, respectively. Efgartigimod was well tolerated; COVID-19, upper respiratory tract infection, and headache were the most common treatment-emergent adverse events.

SUMMARY/CONCLUSION: The results of ADAPT NXT build upon previous studies and provide additional efgartigimod dosing approaches (fixed cycles and Q2W) to maintain clinical efficacy in participants with gMG.

Disclosures:

Kelly Gwathmey – has received consulting/speaking honoraria from Alexion and consulting honoraria from UCB and argenx.

Anne Sumbul - is an employee of argenx.

Rosa Jimenez - is an employee of argenx.

Daniela Hristova - is an employee of argenx.

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EPIDEMIOLOGICAL STUDY OF MYASTHENIA GRAVIS IN ELDERLY US POPULATION: A LONGITUDINAL ANALYSIS OF THE MEDICARE CLAIMS DATABASE FROM 2006-2019

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INTRODUCTION: Epidemiological studies suggest increasing incidence and prevalence of myasthenia gravis (MG) among the elderly population outside the United States (US).

OBJECTIVE: We aimed to provide an estimation of MG incidence and prevalence and their trend among the Medicare Fee-For-Service (FFS)-covered elderly US population.

METHODS: We performed a retrospective longitudinal study using Medicare claims data (2006 - 2019). Study-eligible beneficiaries were age ≥65 years, had at least one month of FFS Parts A/B coverage, and were without any health maintenance organization insurance coverage. Study-eligible beneficiaries were aggregated into 2-year periods from 2006-2007 through 2018-2019. MG cases were ascertained using a validated algorithm of two MG claims within each 2-year period, from two outpatient office visits or a combination of one inpatient admission and one outpatient office visit, separated by ≥28 days.

RESULTS: The period prevalence of MG increased from 81 to 119 per 100,000 FFS A/B population from 2006-2007 to 2018-2019 ($p<0.001$). Increasing trends of prevalence were observed in all sex, age, race/ethnic, and census region subgroups. MG incidence increased from 12.2 to 13.3 per 100,000 PY from 2008-2009 to 2018-2019 ($p<0.05$). Increasing incidence trends were significant in the following subgroups: both males and females; all age groups except 75 to 79 years; White non-Hispanic race; Northeast, Midwest, and South census regions. All-cause mortality among MG beneficiaries was stable from 2006-2007 to 2018-2019.

SUMMARY/CONCLUSION: Increasing trends in MG prevalence and incidence in the elderly US population, with variation in rates of certain subgroups, are confirmed in this 14-year period.

Disclosures:

Yuebing Li - served as a consultant for Advisory Board Meeting by Alexion, argenx, Catalyst, Immunovant, and UCB Pharma and received grant support from argenx.

Ikjae Lee - received research funding from the National Institute of Health, American Academy of Neurology, and American Brain Foundation that are unrelated to the current manuscript. I. Lee has served on the advisory board for Amylyx, Alexion, MedLink, Medscape and Regeneron and on the Data Safety Monitoring Board for Regeneron.

Jesse Schold - received funding from the National Institutes of Health, Department of Defense, Kidney Transplant Collaborative, and has served on the advisory board for Novartis, Sanofi, Veloxis and eGenesis.

Nicholas Silvestri - served on the advisory board for argenx, Alexion, Immunovant, Janssen, UCB, and Takeda, and on the Data Safety Monitoring Board for Regeneron.

Michael Hehir – serves on the advisory board for argenx, Alexion, Janssen, UCB, and Immunovant. (2016 MGFA and ABF Clinician-Scientist Development Award in Myasthenia Gravis and Related Disorders of the Neuromuscular Junction).

SERONEGATIVE MYASTHENIA GRAVIS IN CHILDREN WITH AUTOINFLAMMATORY SYNDROMES

Alexander Fay (San Francisco, CA)

INTRODUCTION: Myasthenia gravis (MG) is associated with antibodies that target the neuromuscular junction, but in spite of advances in the sensitivity of antibody tests and identification of antibodies beyond the acetylcholine receptor, about 15 % of children are still classified as seronegative. Electrodiagnostic testing is often poorly tolerated in children, making diagnosis challenging when antibodies are negative. Reaching a diagnosis of MG is critical in these cases to appropriately treat a child's symptoms.

OBJECTIVE: This study aims to retrospectively characterize a cohort of children with seronegative MG, compared to those with seropositive disease.

METHODS: We analyzed patients' symptoms, co-existing diagnoses, exam findings, results of antibody and electrodiagnostic testing, and response to treatments among a cohort of 36 children with myasthenia gravis over 7 years, and compared seronegative to seropositive patients.

RESULTS: We identified seronegative patients with autoinflammatory syndromes (AIS), pain-associated MG, and ocular MG. Several children in the seronegative, AIS group required ICU care and plasma exchange, underscoring the severity of seronegative MG. Furthermore, some seronegative children without characteristic 10 % decremental response on repetitive nerve stimulation showed robust response to immunotherapies, including steroids, IVIg, plasma exchange and rituximab. We additionally report treatment responses to antibody therapies not widely reported in children, including eculizumab, efgartigimod, daratumumab and obinutuzumab.

SUMMARY/CONCLUSION: Children with seronegative MG may manifest with severe disease, and sometimes do not have characteristic findings on repetitive nerve stimulation, making diagnosis more challenging. Those with AIS may have refractory disease that is responsive to monoclonal antibody therapies not widely reported in the pediatric MG population.

ANTI-BCMA CAR T-CELL THERAPY IN PATIENTS WITH REFRACTORY MYASTHENIA GRAVIS

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INTRODUCTION: Autoreactive B cells with autoantibody formation play a key role in the pathogenesis of Myasthenia gravis (MG). Eque-cel is a fully human B-cell maturation antigen (BCMA) targeted chimeric antigen receptor (CAR) T cell therapy.

OBJECTIVE: To evaluate the safety and efficacy of Eque-cel in patients with refractory MG.

METHODS: Two refractory MG patients received 1.0×106 total CAR T cells/kg after lymphodepletion therapy. Both patients received pyridostigmine without any other concomitant treatment post Eque-cel infusion.

RESULTS: Case 1: A 33-year-old woman with typical AChR-IgG and Titin-IgG seropositive generalized MG. Following treatment with Eque-cel, she experienced transient grade 1 cytokine release syndrome (CRS). Functional disability measurement scores demonstrated significant reduction from baseline by 1 year, with maintenance at the 24-month follow up visit. Clinical remission was paralleled by serologic remission with the rapid decrease of anti-AChR and anti-Titin antibodies. She delivered a healthy baby boy safely by 20-month post-treatment. Case 2: A 60-year-old woman with MuSK-IgG4 seropositive, showing pharyngeal, and tongue weakness, with poor scores (QMG 18, MG-ADL 11). She had a 20-year-long history of MG. No CRS or neurologic toxic effects was observed post infusion. The patient markedly improved in physical function by 6-month (QMG 2, MG-ADL 0) and recovered to normal by 21-month post-treatment. Serum MuSK-IgG was gradually decreased, and maintained negative beyond 18 months. Longitudinal single-cell analysis highlights distinct characteristics of CAR-T cells in MG and reconstitution of B-cell lineages.

SUMMARY/CONCLUSION: CAR-BCMA T cells are well tolerated and highly effective in treating refractory MG.

VISUALIZATION AND CHARACTERIZATION OF COMPLEMENT ACTIVATION IN ACETYLCHOLINE RECEPTOR ANTIBODY SEROPOSITIVE MYASTHENIA GRAVIS

Anna Punga (Uppsala, Sweden), Yu-Fang Huang (Uppsala, Sweden), Kerstin Sandholm (Kalmar, Sweden), Barbro Persson (Uppsala, Sweden), Bo Nilsson (Uppsala, Sweden)

INTRODUCTION: Complement inhibitors are a beneficial treatment for refractory generalized myasthenia gravis (gMG) with antibodies against the acetylcholine receptor (AChR). Nevertheless, there are no available blood biomarkers to monitor the treatment effect, and visualization of the AChR antibody-induced membrane attack complex (MAC) at the human muscle membrane is lacking.

OBJECTIVE: This study analyzed complement activation products and six native complement components in AChR antibody seropositive gMG patients and healthy controls (HC) and used in vitro muscle cell modeling to visualize MAC and AChR loss from AChR antibody-mediated attack.

METHODS: We assessed complement components and activation product levels using ELISA and magnetic bead-based sandwich assays in plasma and sera from 23 MG patients and matched HC with ROC curve analysis. Complement levels were correlated with MG Composite (MGC) scores, and gMG pathogenesis was studied in human muscle cells using sera from nine gMG patients and three HC.

RESULTS: MG patients had significantly higher plasma levels of C5 ($p=0.0003$), C3a, and sC5b-9 ($p<0.0001$) than HCs, with ROC analysis showing clear separation for C3a (AUC=0.9720) and sC5b-9 (AUC=0.8917). MG patients also had higher plasma Factor I (FI; $p=0.0002$) and lower properdin levels ($p<0.0001$), with MGC scores moderately correlating with plasma Factor B, FI, C5, properdin, and serum FI. MG patient sera triggered MAC deposition on human muscle membranes and reduced AChRs.

SUMMARY/CONCLUSION: Plasma C3a and sC5b-9 are promising blood biomarkers for complement activation in MG. The in vitro study allowed visualization of MAC deposition after applying AChR antibody seropositive MG patient sera on human muscle cells.

Disclosures:

Anna Punga - 2024 MGFA High Impact Pilot Project Grant Award Recipient.

FAST-ACTING TREATMENT OF MYASTHENIC CRISIS WITH EFGARTIGIMOD FROM THE PERSPECTIVE OF THE NEONATAL INTENSIVE CARE UNIT

Haiyan wang (Guangzhou, China), Fangyi Shi (Guangzhou, China), Huiyu Feng (Guangzhou, China)

INTRODUCTION: Myasthenic crisis (MC) refers to rapid deterioration of myasthenia gravis (MG), affecting lung muscles and causing breathing difficulties. Currently, efgartigimod has shown good therapeutic effects in patients with generalized myasthenia gravis (GMG).

OBJECTIVE: This retrospective real-world study explored the effectiveness of efgartigimod in patients with MC.

METHODS: Reviewing the clinical data of five patients with MC who received efgartigimod at the First Affiliated Hospital of Sun Yat-sen University, all of these patients were admitted from September 2023 to December 2023.

RESULTS: Each patient received 20mg/kg of efgartigimod on the first and fifth day. After discharge, all patients showed a clinically meaningful decrease in MG-ADL score (a decrease of ≥2 points) and an improvement in their lung function. Additionally, all patients had a decrease in IgG levels (58.59±18.48 % after one cycle of efgartigimod). We also explored the ICU stay and mechanical ventilation (MV) duration for these five patients, and found no significant improvement compared to a large sample data. In terms of safety, four patients experienced adverse events (AEs), all of which were mild. At the last follow-up, four patients achieved the minimal symptom expression (MSE) status (an MG-ADL score of 0 or 1） after 6.25±3.30 weeks. Only one patient experienced a worsening of symptoms in the second week after discharge, but she also achieved the MSE status after receiving a second cycle of efgartigimod treatment.

SUMMARY/CONCLUSION: Given the conclusion that intravenous efgartigimod is a non-invasive fast-acting treatment with fewer AEs, this provides NICU workers with another option for managing patients with MC.

EVIDENCE GAP ANALYSIS OF THE BURDEN OF DISEASE AND TREATMENT OF MYASTHENIA GRAVIS

Kati Copley-Merriman (Ann Arbor, MI), Lesley-Ann Miller-Wilson (New York, NY), Jessica Costello (Manchester, United Kingdom), Jennifer Schwinn (New York, NY), Yuriy Edwards (New York, NY)

INTRODUCTION: Myasthenia gravis (MG) is a chronic autoimmune neurological disorder characterized by fatigable muscle weakness resulting from defective transmission at the neuromuscular junction.

OBJECTIVE: To assess current evidence related to burden of disease (BOD) in MG and identify evidence gaps in the scientific literature.

METHODS: A targeted review of scientific literature published between May 4, 2013 and May 4, 2023 identified articles describing epidemiologic, clinical, humanistic, and economic BOD and treatment patterns of MG. Supplemental online searches were conducted for information on health technology assessments, ongoing clinical trials, and primary sources for review articles identified in the literature search.

RESULTS: A total of 251 unique records describing MG BOD were identified. Symptoms and comorbidities of MG are well studied, but differences by autoantibody subtype, age of onset, and geography are not reported adequately. The humanistic burden of MG has also been widely studied using various quality-of-life instruments, although further studies capturing differences across patient subgroups are needed. The economic burden is substantial, with associated direct costs of $28,780/year in the US, and up to $164,730 in costs per hospitalization. Besides traditional non-specific immunosuppressive agents, recently available biologics (eg, eculizumab, ravulizumab, efgartigimod, rozanolixizumab, zilucoplan) are increasingly used in MG to target specific components of the immune pathway. Therefore, treatment pattern studies are needed to assess the real-world effectiveness of emerging therapies.

SUMMARY/CONCLUSION: We identified several gaps in the literature, including the need for comprehensive studies to advance our understanding of the overall BOD and evolving treatment pathways in MG.

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Kati Copley-Merriman - is an employee of RTI Health Solutions.

Lesley-Ann Miller-Wilson - is an employee of Immunovant, Inc.

Jessica Costello - is an employee of RTI Health Solutions.

Jennifer Schwinn - is an employee of Immunovant, Inc.

Yuriy Edwards - is an employee of Immunovant, Inc.

SHORT-TERM CHANGES IN SERUM MIRNA LEVELS AND PATIENT-REPORTED OUTCOMES IN MYASTHENIA GRAVIS

Anna Punga (Uppsala, Sweden), Yu-Fang Huang (Uppsala, Sweden), Amol Bhandage (Uppsala, Sweden), Lisa Diaz-Pintado Adestrom (Uppsala, Sweden)

INTRODUCTION: The circulating microRNAs (miRNAs) miR-150-5p, miR-30e-5p, and miR-21-5p are potential biomarkers for Myasthenia Gravis (MG), but their short-term variations and associations with patient-reported outcomes are not well understood.

OBJECTIVE: To assess the short-term fluctuations in miRNA levels and patient-reported outcome measures in MG.

METHODS: This prospective cohort study included 39 MG patients who attended regular follow-ups and maintained stable medications at the Neurology outpatient clinic at Uppsala University Hospital. Over a month, patients had weekly visits for blood sample collection and assessment of MG activities of daily living (MG-ADL), MG quality-of-life-15 (MG-QoL15), and Fatigue Severity Score (FSS). Serum levels of miR-150-5p, miR-30e-5p, and miR-21-5p were measured using quantitative real-time PCR.

RESULTS: Intra-individual levels of miR-30e-5p and miR-150-5p were stable, whereas miR-21-5p levels were significantly reduced between week 1 to week 2 ($p=0.0024$) and between week 2 to week 3 ($p<0.0001$). There were intra-individual differences over a short time in MG-ADL in female patients, with higher scores ($p=0.0281$) and a significant reduction from the 1st to the 2nd weeks ($p=0.0281$), whereas MG-QoL15 and FSS scores were stable.

SUMMARY/CONCLUSION: The suggested MG blood biomarkers miR-30e-5p and miR-150-5p were more stable than miR-21-5p over a short time, indicating their short-term stability. Prospective multi-center studies with longer follow-up periods and matched controls are needed to validate these miRNAs as biomarkers in MG.

Disclosures:

Anna Punga - 2024 MGFA High Impact Pilot Project Grant Award Recipient.

POST-HOC ANALYSIS OF CLINICALLY RELEVANT ANTI-VACCINE ANTIBODIES IN PARTICIPANTS TREATED WITH NIPOCALIMAB

Faye Yu (Cambridge, MA), Eugene Myshkin (Cambridge, MA), Carolina Bobadilla Mendez (Spring House, PA), Marta Cossu (Leiden, Netherlands), Kaiyin Fei (Spring House, PA), Qingmin Wang (Spring House, PA), Matthew J. Loza (Spring House, PA), Dessislava Dimitrova (Spring House, PA), Sheng Gao (Spring House, PA)

INTRODUCTION: Nipocalimab is a fully human, high-affinity, aglycosylated, effectorless IgG1 monoclonal antibody designed to selectively block FcRn, thereby lowering IgG levels. In the IRIS-RA study (NCT04991753), participants with rheumatoid arthritis received nipocalimab 15 mg/kg or placebo intravenously every 2 weeks for 10 weeks.

OBJECTIVE: To assess the impact of nipocalimab on pre-existing clinically relevant anti-vaccine antibodies and on the humoral response to SARS-CoV-2 challenge in IRIS-RA participants.

METHODS: Serum IgG antibody levels against tetanus toxoid (TT) and varicella zoster virus (VZV) were measured at baseline and post-treatment in available biomarker samples (nipocalimab: n=33; placebo: n=20). In participants with documented SARS-CoV-2 vaccination or infection during the study, antibodies against different epitopes of SARS-CoV-2 were measured.

RESULTS: Nipocalimab reduced pre-existing anti-TT and anti-VZV antibodies by 65% and 61% at Week 12, similar to total IgG reduction (observed median pre-dose/minimal reduction: 62%) and consistent with nipocalimab's mechanism of action. Anti-TT and anti-VZV antibody levels returned to baseline by Week 18, 8 weeks post-last dose. The majority of participants treated with nipocalimab who were immune to TT and VZV at baseline maintained protective antibody levels during and post-treatment. Participants receiving SARS-CoV-2 vaccination during nipocalimab treatment (n=3) elicited a humoral response for anti-spike antibodies, while participants with SARS-CoV-2 infection during nipocalimab treatment (n=4) had increased levels of anti-spike and anti-nucleocapsid antibodies.

SUMMARY/CONCLUSION: Findings suggest that the majority of nipocalimab-treated patients remained protected for TT and VZV, that nipocalimab did not impact humoral responses to SARS-CoV-2 infection/vaccination, and that nipocalimab-treated

patients may be able to follow recommended vaccination schedules as appropriate.

Disclosures:

Faye Yu – Employee of Janssen Research & Development and may hold stock in Johnson & Johnson.

Eugene Myshkin - Employee of Janssen Research & Development and may hold stock in Johnson & Johnson.

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EXTRAOCULAR MUSCLE VOLUME ON TIME-OF-FLIGHT MAGNETIC RESONANCE ANGIOGRAPHY IN PATIENTS WITH MYASTHENIA GRAVIS

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INTRODUCTION: Despite being a prominent feature of myasthenia gravis (MG), extraocular muscle (EOM) has received little attention in clinical research.

OBJECTIVE: The aim of this study was to examine EOM volume in patients with MG and controls using time-of-flight magnetic resonance angiography (TOF-MRA).

METHODS: EOM volumes (overall and individual rectus muscles) were calculated using TOF-MRA images and compared between MG patients (including subgroups) and controls. The correlation between EOM volume and disease duration was examined. Predictive equations for the selected parameters were developed using multiple linear regression analysis.

RESULTS: EOM volume was lower in MG patients than controls, especially in MG patients with ophthalmoparesis (MG-O). MG-O exhibited a significant negative correlation between EOM volume and disease duration. Multiple linear regression showed that disease duration and EOM status (ophthalmoparesis or not) account for 48.4% of EOM volume.

SUMMARY/CONCLUSION: Patients with MG show atrophy of the EOMs, especially those with ophthalmoparesis and long disease duration.

CONVENTIONAL DENDRITIC CELLS ARE MORE ACTIVATED IN THE HYPERPLASTIC THYMUS OF MYASTHENIA GRAVIS PATIENTS

Pei Chen (Guangzhou, China), Jiaxin Chen (Washington, DC), Hao Huang (Nanning, China), Weibin Liu (Guangzhou, China)

INTRODUCTION: Dendritic cells (DCs) are crucial to form ectopic germinal centers (GCs) in the hyperplastic thymus (HT), which are typically found in anti-acetylcholine receptor autoantibody-positive myasthenia gravis (MG) patients. However, the characteristics of such DCs in the HT and their roles in thymic hyperplasia formation remain unclear.

OBJECTIVE: To describe the characteristics of DCs in thymic hyperplasia.

METHODS: We collected thymic tissue from MG patients and patients who underwent cardiac surgery. The tissues were cut into sections for immunohistochemistry and immunofluorescence or digested into a single cell suspension for flow cytometry.

RESULTS: In addition to formation of ectopic GCs, we found that the proportion of the medulla in the thymic parenchyma was higher than that in the cortex (areacortex/areamedulla, 1.279 vs. 0.6576) in the HT of MG patients. The density of conventional dendritic cells (cDCs) in the HT was 131±64.36 per mm2, whereas in normal thymic tissue, the density was 59.17±22.54 per mm2. The more abundant cDCs expressed co-stimulatory molecules (CD80 and CD86) strongly. Moreover, the more abundant subset was mainly CD141+ DCs (cDC1s), accounting for an increase from 15% to 29%. However, these increased cDC1s appeared to be unrelated to Hassall's bodies and ectopic GCs.

SUMMARY/CONCLUSION: Thymic hyperplasia in MG patients is manifested as an increase in the proportion of the thymic medulla accompanied by increases in the density and functional activation as well as changes in the subset composition of cDCs.

A RANDOMIZED, OPEN-LABEL STUDY ON THE EFFECT OF NIPOCALIMAB ON VACCINE RESPONSES IN HEALTHY PARTICIPANTS

Marta Cossu (Leiden, Netherlands), Carolina Bobadilla Mendez (Spring House, PA), Amanda Jackson (La Jolla, CA), Eugene Myshkin (Cambridge, MA), Grace Liu (Raritan, NJ), Edwin Lam (Spring House, PA), Ulf H. Beier (Spring House, PA), Kathleen Weisel (Spring House, PA), Brittney Scott (Spring House, PA), Jocelyn H. Leu (Spring House, PA), Sheng Gao (Spring House, PA), Dessislava Dimitrova (Spring House, PA)

INTRODUCTION: Nipocalimab is a human IgG1 monoclonal antibody targeting FcRn that selectively reduces IgG levels without impacting antigen presentation, T- and B-cell functions.

OBJECTIVE: To investigate the effect of nipocalimab on IgG response to T-cell-dependent/independent vaccines (tetanus, diphtheria, pertussis vaccine [Tdap]; pneumococcal polysaccharide vaccine [PPSV®23], respectively) in healthy participants.

METHODS: This open-label, parallel, interventional study randomized participants 1:1 to receive intravenous 30mg/kg nipocalimab at Week (Wk) 0 and15mg/kg at Wk2 and Wk4 (active) or no drug (control). On Day 3, participants received Tdap and PPSV®23 vaccinations and were followed through Wk16. The primary endpoint was the percentage of participants with a positive anti-tetanus IgG response (2-fold increase from baseline) at Wk4.

RESULTS: Twenty-nine participants completed the study and were included in this analysis (active, n=15; control, n=14). The percentage of participants with a positive anti-tetanus IgG response was comparable between groups at Wk2 and Wk16, but lower in the nipocalimab versus control group at Wk4 (3/15 [20%] vs 7/14 [50%]; P=0.089). All participants maintained anti-tetanus IgG above the protective threshold (0.16IU/mL) through Wk16. While anti-pneumococcal-capsular-polysaccharide (PCP) IgG levels were lower during nipocalimab treatment, the percent increase from baseline at Wk2 and Wk16 was comparable between groups. Post-vaccination, anti-PCP IgG remained above 50mg/L and showed a 2-fold increase from baseline throughout the study in both groups. Nipocalimab co-administration with Tdap and PPSV®23 was safe and well-tolerated.

SUMMARY/CONCLUSION: These findings suggest that nipocalimab does not impact the development of an adequate IgG response to T-cell-dependent/independent vaccines and that

nipocalimab-treated patients can follow recommended vaccination schedules.

Disclosures:

Marta Cossu - Employee of Janssen Research & Development and may hold stock in Johnson & Johnson.

Jocelyn H. Leu - Employee of Janssen Research & Development and may hold stock in Johnson & Johnson.

Sheng Gao - Employee of Janssen Research & Development and may hold stock in Johnson & Johnson.

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Kathleen Weisel - Employee of Janssen Research & Development and may hold stock in Johnson & Johnson.

Brittney Scott - Employee of Janssen Research & Development and may hold stock in Johnson & Johnson.

TOWARDS A GENOME-WIDE ASSOCIATION FOR MUSK MYASTHENIA GRAVIS

Henry Kaminski (Washington, DC), Anosha Khan (Washington, DC), Gülşen Öztosun (Washington, DC), Preethy Feit (Washington, DC), MGNet Investigators (Washington, DC)

INTRODUCTION: Acetylcholine receptor (AChR) antibody-positive myasthenia gravis has been the subject of several genome-wide association studies (GWAS), which have successfully identified single nucleotide polymorphisms that are associated with MG and have stratified risk factors by patient age.

OBJECTIVE: The rare disease clinical research network dedicated to myasthenia gravis, MGNet, has established the MuSK 1000 study (musk1000.smhs.gwu.edu) to collect 1000 saliva samples from MuSK myasthenia patients appropriate for DNA analysis for a GWAS to be performed by the intramural branch of the National Institutes of Neurological Disorders and Stroke.

METHODS: The Administrative Core of MGNet based at George Washington University is casting a broad outreach program through the MG Foundation of America, other MG patient advocacy groups, social media, and academic medical centers to reach this small group of patients in the United States.

RESULTS: The presentation will summarize recruitment numbers, provide basic demographics of the recruited subjects, and an analysis of the most successful recruitment approaches.

SUMMARY/CONCLUSION: When successful, the GWAS will provide insights into genetic risk factors for MuSK MG and provide the world’s largest registry of patients with MuSK MG.

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Henry Kaminski - Consultant for Roche, Takeda, Cabaletta Bio, UCB Pharmaceuticals, Canopy Immunotherapeutics, EMD Serono, Ono Pharmaceuticals, ECoR1, Gilde Healthcare, and Admirix, Inc. Argenix provides an unrestricted educational grant to George Washington University; unpaid consultant for Care Constitution; has equity interest in Mimivax, LLC.

STEROID USE, TOXICITY, AND MONITORING IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: A SURVEY OF NEUROLOGISTS IN THE UNITED STATES

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INTRODUCTION: The 2020 international consensus guidance recommends corticosteroids (CSs) as standard immunosuppressive therapy for generalized myasthenia gravis (gMG); however, patients treated with CSs should be monitored for CS toxicity/adverse effects.

OBJECTIVE: We surveyed board-certified US-based neurologists to assess awareness and monitoring of CS toxicity.

METHODS: Cross-sectional online survey was completed by neurologists (n=101) managing ≥10 patients with gMG/year (≥10 mg CS for ≥1 month).

RESULTS: Neurologists reported that ~60% of their patients have been treated with CSs and ~40% with nonsteroidal immunosuppressants. Regarding CS dose and duration, ~50% of neurologists said they consider CS dose ≤10 mg/day (prednisone equivalent) well tolerated in long-term use (≥6 months) but that ~50% of their patients are unable to taper to <10 mg/day. 77% of neurologists reported being very/extremely familiar with CS toxicity; they identified increased appetite/weight gain (58%), insulin resistance (50%), decreased bone density (48%), and immunosuppression (45%) as the most-common adverse effects of long-term CS use. The neurologists said they typically monitor CS toxicity alone (84%) or in conjunction with primary care providers (41%). To balance effectiveness and toxicity, 48% rely on clinical experience/training alone, and 53% use recommendations from guideline(s). Most neurologists (88%) said a tool for systematically monitoring CS toxicity would be valuable.

SUMMARY/CONCLUSION: Responses show that although more than three-fourths of neurologists monitor and manage CS toxicity in patients with gMG, approximately half use guidelines to do so. This suggests that clearer guidance on how to administer CSs and manage toxicities would be welcomed by neurologists, with potential for benefit to patient care.

Disclosures:

Neelam Goyal - Consultant/advisor for argenx, Alexion, UCB, Janssen, Amgen, and Lycia Therapeutics and receives or has received grant support from argenx.

Gil Wolfe - Consultant/advisor for Alexion, argenx, BPL, Cartesian, Grifols, Janssen, Takeda, and UCB and receives or has received research support from Alexion, argenx, Immunovant, Roche, UCB, and the Myasthenia Gravis Foundation of America.

Deborah Gelinas - Employee of argenx.

Tom Hughes - Employee of argenx.

Vijayaraghava Rao - Employee of argenx.

Paul Nisbet - Employee of One Research, LLC, which was paid by argenx to conduct the survey and analyze the data.

John Stone - Consultant to argenx on glucocorticoid toxicity and is the chair of the Scientific Advisory Board at Steritas.

Pushpa Narayanaswami - Consultant/advisor for argenx, Alexion, UCB, Janssen, Dianthus, GSK, and Novartis; has served on a data safety monitoring board for Sanofi; receives or has received research support from PCORI, Alexion, Janssen, Dianthus, and UCB; receives or has received royalties from Springer Nature.

RECESSIVE SYT2-CONGENITAL MYASTHENIC SYNDROME CAUSED BY A MATERNAL UNIPARENTAL DISOMY OF CHROMOSOME 1

Rebecca Dutta (West Sacramento, CA), Alex Govorukhin (Sacramento, CA), Kristen Fishler (Omaha, NE), Chris Cummings (Oma, NE), Marie Rickard (Omaha, NE), Ricardo Maselli (Sacramento, CA)

INTRODUCTION: Synaptotagmins (Syt) are a family of synaptic proteins that participate in calcium-regulated synaptic vesicle (SV) exocytosis. Synaptotagmin 2 encoded by SYT2 is the Syt isoform that is expressed at the neuromuscular junction. Dominant SYT2 mutations are linked with either a Lambert-Eaton-like congenital myasthenic syndrome (CMS) or a motor axonal neuropathy. Recently, recessive biallelic SYT2 mutations causing severe CMS have also been described.

OBJECTIVE: Here we report a case of an infant with recessively inherited SYT2-CMS resulting from uniparental disomy of chromosome 1.

METHODS: Not available (case report)

RESULTS: A 2-month-old infant born with severe hypotonia and weakness from a non-consanguineous couple developed an episode of respiratory arrest and cyanosis, which responded to resuscitation. The neurologic examination revealed intact ocular movements but profound hypotonia and weakness. The EMG showed extreme reduction of compound muscle action potential (CMAP) amplitudes, with more than 600% increment of CMAP amplitudes with repetitive stimulation at 50 Hz. A rapid genome trio identified that the patient carried a homozygous pathogenic variant in SYT2 (c.852dup, p.G285Rfs*11). This was further identified to be due to uniparental disomy of chromosome 1. Treatment with Firdapse (3,4 diaminopyridine, 1 mg/kg) in addition to Pyridostigmine and BiPAP resulted in striking improvement of muscle power.

SUMMARY/CONCLUSION:

1) Rarely, cases of recessive variants in genes associated with CMS may result from uniparental disomies.

2) Firdapse plays a fundamental role in the treatment of the recessive form of SYT2-CMS.

PHASE 3 TRIAL INVESTIGATING IMPACT OF INTRAVENOUS EFGARTIGIMOD IN ANTI-ACETYLCHOLINE RECEPTOR ANTIBODY NEGATIVE GENERALIZED MYASTHENIA GRAVIS

James F. Howard Jr (Chapel Hill, NC), Jeffrey Guptill (Raleigh, NC), Rosa H. Jimenez (Hingham, MA), Fien Gistelinck (Ghent, Belgium), Sophie Steeland (Ghent, Belgium)

INTRODUCTION: Approximately 15%-20% of patients with generalized myasthenia gravis (gMG) are anti-acetylcholine receptor antibody negative (AChR-Ab-). Lack of approved treatment options for the AChR-Ab- gMG population represents an unmet need in the gMG treatment landscape. Efgartigimod is a human immunoglobulin G (IgG)1 antibody Fc-fragment that reduces IgG levels (including pathogenic autoantibodies) through blockade of the neonatal Fc receptor. This phase 3 (NCT06298552) trial will investigate the efficacy and safety of efgartigimod in participants with AChR-Ab- gMG.

OBJECTIVE: To determine the efficacy and safety of 10 mg/kg IV efgartigimod compared with placebo in AChR-Ab- participants with gMG.

METHODS: Adult participants with AChR-Ab- gMG who have a Myasthenia Gravis Activities of Daily Living (MG-ADL) total score of ≥5 (with >50% of the score due to nonocular symptoms) and are on a stable dose of ≥1 concomitant gMG treatment will be included. One hundred ten adjudicated participants will be randomized 1:1 to either receive 10 mg/kg IV efgartigimod or placebo. The study has 2 stages: the double-blinded placebo-controlled part A, consisting of 4 once-weekly infusions and 5 weeks of follow-up, and the open-label extension part B, consisting of varying number and frequency of cycles for ≤2 years.

RESULTS: The primary endpoint is the change in MG-ADL total score from study baseline to Day 29 in part A. Additional efficacy outcomes (QMG, MG-QoL15r, EQ-5D-5L), safety/tolerability, and pharmacokinetic/pharmacodynamic effects are also being assessed.

SUMMARY/CONCLUSION: This phase 3 trial will provide important data on the efficacy and safety of efgartigimod IV in the treatment of AChR-Ab- gMG.

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Jeffrey Guptill - Employee of argenx (2010 MGFA and ABF Clinician-Scientist Development Award in Myasthenia Gravis Recipient)

Rosa H. Jimenez -Employee of argenx.

Fien Gistelinck - Employee of argenx.

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A RETROSPECTIVE CASE SERIES OF MYASTHENIA GRAVIS ASSOCIATED WITH IMMUNE CHECKPOINT INHIBITORS

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INTRODUCTION: Immune checkpoint inhibitor (ICI) therapy is a revolutionary cancer treatment. However, it could lead to neuromuscular complications including myasthenia gravis (MG).

OBJECTIVE: Characterize the clinical features of ICI associate MG

METHODS: From Jan 2020 to Jan 2024,1388 patients received ICIs at our institution. Twelve cases with neuromuscular complications after initiation of ICI therapy were identified.

RESULTS: The patients' mean age was 64.7 years, nine of twelve were men. The most common cancer was renal cell carcinoma (33.3%). The most commonly used ICI was Nivolumab (41.7%). Four cases underwent dual ICIs. The time range from initial ICI to symptom onset was 3 days to 32 weeks. Two cases had Guillain Barre syndrome, one had chronic sensorimotor axonal polyneuropathy, one had Bell's palsy. Eight patients had clinical diagnosis of MG. Two had positive acetylcholine receptor antibodies, all were negative for MuSK and LRP4 antibodies. Three of the MG cases presented with overlap myositis, two MG cases had myocarditis and myositis, one MG case had myocarditis and hepatitis. Five patients with MG received electrophysiological study: four demonstrated myopathy, two exhibited decrements to low frequency repetitive stimulation test, one of which also showed myopathic changes. High-dose steroids, IV immunoglobulin, pyridostigmine were the most commonly used treatments. Despite mild to moderate clinical improvement (62.5%), the mortality for ICI-related MG was 58.3%.

SUMMARY/CONCLUSION: The ICI case series indicates: the rates of positive MG antibodies and of abnormal repetitive nerve stimulation responses are lower than in spontaneously occurring MG; overlap syndromes are common in ICI associated MG, along with increased mortality.

NMD670, A FIRST-IN-CLASS SKELETAL MUSCLE CLC-1 INHIBITOR IN MYASTHENIA GRAVIS: THE SYNAPSE-MG DOSE-FINDING STUDY

Vera Kiyasova (Aarhus, Denmark), Thomas S Grønnebæk (Aarhus, Denmark), Teresa Gidaro (Aarhus, Denmark), Thomas Breuer (Aarhus, Denmark), Jitendra Gupte (Aarhus, Denmark), Claire Sampson (Aarhus, Denmark), Thomas H. Pedersen (Aarhus, Denmark), Jorge A. Quiroz (Aarhus, Denmark)

INTRODUCTION: NMD670 is an inhibitor of skeletal muscle-specific chloride channel protein 1 (CIC-1) that enhances neuromuscular transmission and is being developed for the treatment of neuromuscular diseases, including myasthenia gravis (MG), in which neuromuscular junction (NMJ) transmission is impaired. Despite available treatments, MG patients struggle with symptoms of prominent muscle weakness and fatigue. In a recent phase 1 proof-of-mechanism study in 12 MG patients with mild symptoms, a single dose of NMD670 led to significant and clinically meaningful improvements as assessed with the Quantitative MG (QMG) score. It was shown to be safe and well tolerated thus supporting further clinical development in MG (Sci Transl Med. 2024). Therefore, a dose finding study in adult patients with MG who have antibodies against Muscle Specific Kinase (MuSK) or the Acetylcholine Receptor (AchR) was initiated in June 2024.

OBJECTIVE: The aim of this study is to evaluate the efficacy and safety of 3 dose levels of NMD670, administered twice a day for 21 days vs. placebo.

METHODS: Male and female patients, aged 18-75 years, diagnosed with MG, Myasthenia Gravis Foundation of America (MGFA) class II-IV, a QMG score of 11 or more and an MG-Activities of Daily-Living score of 6 or more at screening are planned to be enrolled at 40 sites across Europe and North America. Endpoints of this study include changes in the QMG total score MG-ADL, MG Composite (MGC), MG Quality of Life 15 revised (QOL15r), and Neuro Qol Fatigue Short Form total scores.

SUMMARY/CONCLUSION: Study key updates will be presented in October 2024.

DISEASE BURDEN IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS

Nicholas Silvestri (Buffalo, NY), Maria Ait-Tihyaty (Titusville, NJ), Kavita Gandhi (Titusville, NJ), Ibrahim Turkoz (Titusville, NJ), Mehmet Daskiran (Titusville, NJ), Bonnie C. Shaddinger (Titusville, NJ), Ewa Lindenstrom (Titusville, NJ)

INTRODUCTION: Despite newer treatments for generalized myasthenia gravis (gMG), many patients continue to experience inadequately controlled symptoms. This study investigates the burden of gMG using recent US medical claims data.

METHODS: Adult patients diagnosed with gMG (ICD-10 codes G70.00/G70.01), from 01/01/2022-12/31/2023 were identified from the Optum Clinformatics database. Data on patient demographics, treatment characteristics, and clinical events were collected for a 12-month baseline and 24-month follow-up period. Disease burden was assessed through the incidence of MG-related hospitalizations and emergency room (ER) visits, acute respiratory failure, mechanical ventilation, gastrostomy tube insertion, intensive care unit (ICU) stay, any use of corticosteroids and rescue treatments (immunoglobulin or plasma exchange).

RESULTS: A total of 6480 gMG patients were identified and followed for up to 24 months (median: 556 days). The proportion of patients with at least one event and, among them, the frequency of all events per patient-year, respectively, were 26.9% and 3.65 for exacerbations; 39.2%/1.53 for MG-related hospitalizations; 12.2%/1.55 for acute respiratory failure; 5.2%/1.16 for mechanical ventilation; 1.0%/1.29 for gastrostomy tube insertion; 22.0%/1.30 for MG-related ICU stay; 23.4%/1.15 for MG-related ER visits; and 7.8%/2.77 for use of rescue treatments. Corticosteroid use was recorded in 50.2% of patients, with 50.5% of these receiving prednisone equivalent doses >10 mg/day. Among 482 patients who received targeted immunotherapy, the disease burden remained high.

SUMMARY/CONCLUSION: Despite recent therapeutic advancements, a significant disease burden persists in gMG patients, highlighting an ongoing unmet medical need.

Disclosures:

Nicholas Silvestri - Consultant/advisor for argenx, Alexion, Amgen, Annexon, Immunovant, Janssen, and UCB. Speaker for argenx, Alexion, Takeda, UCB.

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Mehmet Daskiran - Is or was employee, contractor or consultant for Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

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Ewa Lindenstrom - Is or was employee, contractor or consultant for Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER PHASE 3 STUDY OF INEBILIZUMAB IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS (MINT): TOPLINE EFFICACY AND SAFETY FINDINGS

Richard Nowak (New Haven, CT), Kimiaki Utsugisawa (Hanamaki, Japan), Michael Benatar (Miami, FL), Emma Ciafaloni (Rochester, NY), M Isabel Leite (Oxford, United Kingdom), John Vissing (Copenhagen, Denmark), Fengming Tang (Rockville, MD), Yanping Wu (Rockville, MD), Mikhail Rojavin (Rockville, MD), Nishi Rampal (Branford, CT), James Howard, Jr (Chapel Hill, NC)

INTRODUCTION: Generalized myasthenia gravis (gMG) is an autoimmune disorder of the postsynaptic neuromuscular junction. Most patients have autoantibodies against the acetylcholine receptor (AChR), and less frequently, against muscle-specific kinase (MuSK); these are produced by plasma cells and plasmablasts.

OBJECTIVE: Since B-cells are central in MG pathogenesis, inebilizumab, a monoclonal antibody that targets CD19+ B-cells, including plasmablasts and some plasma cells, was assessed for efficacy/safety in the Myasthenia Gravis INebilizumab Trial (MINT, NCT04524273).

METHODS: Patients with anti-AChR or anti-MuSK antibody positive gMG, MGFA classification II-IV, MG-Activities of Daily Living (MG-ADL) score 6-10 with

>50% attributed to non-ocular items, or an MG-ADL score ≥11, Quantitative MG (QMG) score ≥11, and on oral standard-of-care at the time of screening and randomization were included. Randomized control period (RCP) was 52-weeks for the AChR+ population and 26-weeks for the MuSK+ population. Patients were given 300mg of inebilizumab or placebo on Day1, Day15, and every 6 months thereafter. Oral prednisone was tapered to 5mg/day starting at Week-4. The primary endpoint was change from baseline (CFB) in MG-ADL score at Week-26 in overall population. Secondary endpoints included CFB in QMG score in overall population, MG-ADL/QMG-scores in AChR+ and MuSK+ populations at Week-26 and safety/tolerability.

RESULTS: 237 patients were randomized and included in the analysis (60.8% female, 47.5±15.3years); 189 (79.7%) were AChR+ and 48 (20.3%) were MuSK+. Both groups had similar gMG duration (mean±SD; AChR+ 6.7±7.4 years, MuSK+ 5.2±5.5 years) and MG-ADL/QMG baseline scores.

SUMMARY/CONCLUSION: Topline results will be presented at the Congress.

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Nishi Rampal - Was an employee and stockholder in Amgen Inc. at the time of the study.

James Howard, Jr - Receives research funding from Ad Scientiam, Alexion, argenx, Cartesian, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, and UCB Pharma; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics (now Amgen Inc.), Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, UCB Pharma, and Zai Labs; non-financial support from Alexion, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Pharma and Zai Labs.

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

Lauren Williams (Lexington, KY), Nakul Katyal (Lexington, KY), Raghav Govindarajan (Fairview Heights, IL)

INTRODUCTION: Rozanolixizumab is a subcutaneous neonatal Fc receptor (FcRn) antagonist approved for treatment of acetylcholine receptor antibody-positive generalized myasthenia gravis (AChR+ gMG).

OBJECTIVE: To describe clinical experience with use of rozanolixizumab in clinic practice

METHODS: Retrospective review

RESULTS: Three patients diagnosed with AChR+ gMG were treated with rozanolixizumab. Among them were two females and one male, with mean (SD) age of 62.33 (7.5) years. Prior to initiating rozanolixizumab treatment, the mean MG-ADL score (SD) was 10.66 (1.15). Two patients were transitioned from efgartigimod to rozanolixizumab. Both completed two cycles of efgartigimod without any change in their MG-ADL scores (12 and 10, respectively). Following the completion of six weekly infusions of rozanolixizumab, the mean MG-ADL score (SD) improved to 6.66 (1.15). All patients demonstrated clinically significant improvements in MG-ADL scores (>2 points). The second cycle of rozanolixizumab was initiated 10 weeks after the commencement of the first infusion in the initial cycle. Following the completion of the second cycle, the mean MG-ADL score (SD) remained stable at 5.66 (0.57). One patient experienced infusion-related side effects, including nausea and headache, after the first infusion of rozanolixizumab. Subsequently, this patient was premedicated with acetaminophen, diphenhydramine, and famotidine before subsequent infusions, and did not experience similar side effects. The other two patients were premedicated prior to their infusions and did not experience any side effects.

SUMMARY/CONCLUSION: Patients with AChR+ gMG had clinically meaningful improvement in MG-ADL scores after treatment with rozanolixizumab including those who did not respond to efgartigimod.

Disclosures:

Raghav Govindarajan - Served on ad board for Argenx, UCB, Janssen, Roche, and speakers bureau for Argenx and Alexion.

EFFICACY AND SAFETY OF NIPOCALIMAB IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: TOPLINE RESULTS FROM THE DOUBLE-BLIND, PLACEBO-CONTROLLED, RANDOMIZED PHASE 3 VIVACITY-MG3 STUDY

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INTRODUCTION: Monoclonal antibodies or fragments targeting neonatal Fc receptors (FcRn) have been approved for reducing generalized myasthenia gravis (gMG) manifestations; however, persisting safety concerns and flexible dosing schedules that require patients to deteriorate before re-dosing, create uncertainty. Nipocalimab, an FcRn blocker that is molecularly unique from marketed anti-FcRns and has predictable dosing, has the potential to deeply lower IgG and provide sustained disease control.

OBJECTIVE: To assess the efficacy and safety of nipocalimab in patients with gMG.

METHODS: Seropositive (anti-AChR+/MuSK+/LRP4+) and seronegative patients with gMG (MGFA Class II-IV) inadequately controlled on SOC therapy were enrolled in a 24-week double-blind placebo-controlled study. Randomization was 1:1 (nipocalimab+SOC, or placebo+SOC). The primary endpoint was mean change in MG-ADL score from baseline over weeks 22, 23 and 24 in seropositive patients. Secondary endpoints included change in QMG score.

RESULTS: Of 199 patients enrolled, 153 were seropositive. Baseline demographics were balanced (77 nipocalimab, 76 placebo). Nipocalimab showed statistically significant improvement in clinical efficacy with mean change in MG-ADL score of -4.70 (SE 0.329) from baseline over weeks 22-24 on nipocalimab vs. -3.25 (SE 0.335) on placebo (difference of LS means -1.45; p=0.002). Statistically significant improvement was seen in mean change in QMG score of -4.86 (SE 0.504) from baseline over weeks 22-24 on nipocalimab vs. -2.05 (SE 0.499) on placebo (difference of LS means -2.81, p<0.001). Nipocalimab was well-tolerated with incidence of adverse events comparable to placebo.

SUMMARY/CONCLUSION: Nipocalimab treatment demonstrated sustained efficacy and safety in this trial of adult seropositive patients with gMG.

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Sarah Hoffmann - Received speakers´ honoraria from Alexion, argenx, UCB, Grifols and Roche and honoraria for attendance at advisory boards from Alexion, argenx and Roche. SH is member of the medical advisory board of the German Myasthenia Society, DMG.

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Keith Karcher - Employee of Janssen Pharmaceuticals; may hold stock or stock options in Johnson & Johnson.

Yaowei Zhu - Employee of Janssen Pharmaceuticals; may hold stock or stock options in Johnson & Johnson.

Carlo Antozzi - Funding travel, meeting attendance & advisory board participation: Alexion, argenx, Momenta, Sanofi, UCB.

Leona Ling - Employee of Janssen Pharmaceuticals; may hold stock or stock options in Johnson & Johnson.

Hong Sun - Employee of Janssen Pharmaceuticals; may hold stock or stock options in Johnson & Johnson.

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Jan De Bleecker - Served on advisory boards for Alexion, Alnylam, Amicus Pharma, argenx, CSL Behring, Janssen Pharmaceuticals, Roche, UCB, Sanofi.

THE MYASTHENIA GRAVIS PATIENT REGISTRY: CHARACTERISTICS, INSIGHTS, AND LEARNINGS AFTER A DECADE (2013-23)

Kelly Gwathmey (Charlottesville, VA), Oshin Sangha (Vancouver, Canada), Minjee Park (Basel, Switzerland), Renee Willmon (Toronto, Canada), Paul Strumph (Moneta, VA), Richard Nowak (New Haven, CT)

INTRODUCTION: The Myasthenia Gravis Foundation of America (MGFA) Patient Registry was initiated with the purpose of assessing disease progression, management, clinical trial recruitment, and to provide an educational platform. The registry is funded by the MGFA and previously the Coordinating Center located at the University of Alabama at Birmingham. In 2022, the next iteration of the registry, the MGFA Global MG Patient Registry (MGFAPR), was developed in partnership with Alira Health.

OBJECTIVE: To report the baseline demographics and disease characteristics of the MGFAPR, including insights/learnings from a patient-reported registry.

METHODS: The MGFAPR is an online longitudinal registry with information collected at enrollment and then at 6-month intervals. Subjects are >/=18 years at enrollment, with self-reported MG. Descriptive analyses were conducted on key clinical features/variables. Enrolled subjects are contacted biannually to provide updates.

RESULTS: 3556 subjects (95% Non-Hispanic; 87% White; 61% female) were enrolled from July 2013 through June 2023. The mean age at enrollment was 55.8 years and at diagnosis was 49.4 years. Of the 1814 reporting serostatus: 62.8% AChR antibody-positive, 5.2% MuSK antibody-positive, 0.4% LRP4 antibody-positive, and 31.6% seronegative. Enrollment and follow-up remain ongoing.

SUMMARY/CONCLUSION: The MGFAPR represents the largest existing MG-specific registry which has captured data on over thirty-five hundred individuals. The advantages of this registry include the volume of the data collected, the completeness of the dataset, and the unique perspective into the MG disease impact with patient-reported outcomes and healthcare resource utilization. While there are clear limitations, unique insights and learnings over the past decade support its ongoing utility and value.

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Oshin Sangha - Employee of Alira Health.

Minjee Park - Employee of Alira Health.

Renee Willmon - Employee of Alira Health.

Richard Nowak - Research support from the National Institutes of Health, Genentech, Inc., Alexion Pharmaceuticals, Inc., argenx, Annexon Biosciences, Inc., Ra Pharmaceuticals, Inc. (now UCB S.A.), the Myasthenia Gravis Foundation of America, Inc., Momenta Pharmaceuticals, Inc. (now Janssen), Immunovant, Inc., Grifols, S.A., and Viela Bio, Inc. (Horizon Therapeutics, now Amgen Inc.). Served as a consultant and advisor for Alexion Pharmaceuticals, Inc., argenx, Cabaletta Bio, Inc., Cour Pharmaceuticals, Ra Pharmaceuticals, Inc. (now UCB S.A.), Immunovant, Inc., Momenta Pharmaceuticals, Inc. (now Janssen), and Viela Bio, Inc. (Horizon Therapeutics, now Amgen Inc.).

ELEVATED C1S/C1-INH IN SERUM AND PLASMA OF MYASTHENIA GRAVIS PATIENTS

Anna Punga (Uppsala, Sweden), Yu-Fang Huang (Uppsala, Sweden), Caitlin Briggs (Raleigh, NC), Sankalp Gokhale (New York, NY)

INTRODUCTION: The C1-inhibitor (C1-INH) regulates the classical complement pathway and has emerged as a promising marker in various autoimmune disorders. While complement inhibitors are a treatment option for acetylcholine receptor antibody-positive myasthenia gravis (AChR+ MG), the specifics of early pathway activation in MG remain unclear.

OBJECTIVE: Our objective in this study was to measure the C1s/C1-INH complex levels in the sera and plasma of patients with MG and compare these with matched healthy controls (HC).

METHODS: Sera were collected from 73 Swedish MG patients, including 50 AChR+ patients, with plasma available from 23 of these individuals. Disease severity was assessed using the Myasthenia Gravis Composite (MGC) score and the Myasthenia Gravis Activities of Daily Living (MG-ADL) scale. Sera and plasma samples from 74 age- and sex-matched HC were also collected. The C1s/C1-INH complex was detected using a commercially available C1s/C1-INH human sandwich ELISA.

RESULTS: Serum C1s-C1-INH levels were significantly higher in MG patients compared to HC ($p=0.0102$), with no significant difference between patients receiving standard immunosuppression and those who did not ($p=0.4634$). C1s/C1-INH levels did not vary significantly across different MG subgroups categorized by clinical severity, acetylcholine receptor antibody titer, or age of onset.

SUMMARY/CONCLUSION: These findings indicate early activation of the classical pathway in most MG patients, suggesting that activated C1s may serve as a potential treatment target and biomarker in MG.

Disclosures:

Anna Punga - The study was sponsored by Dianthus Therapeutics and received consultancy fees from Dianthus Therapeutics. (2024 MGFA High Impact Pilot Project Grant Award Recipient)

Yu-Fang Huang - The study was sponsored by Dianthus Therapeutics.

Caitlin Briggs - Dianthus employee and shareholder.

Sankalp Gokhale - Dianthus employee and shareholder.

ENHANCED LABORATORY DETECTION OF ANTI-ACETYLCHOLINE RECEPTOR ANTIBODY CONTRIBUTES TO RISING INCIDENCE MYASTHENIA GRAVIS

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INTRODUCTION: While the detection of Acetylcholine receptor antibodies (AChR Abs) by the radioimmunoprecipitation assay (RIPA) serves as a reliable marker for diagnosing MG, fixed and live Cell-Based Assays (L-CBA) can enhance the detection of AChR Abs. The annual incidence of MG ranges from 0.41 to 3 per 100,000. Prior studies investigated AChR Ab seropositivity as a surrogate marker for MG epidemiology.

OBJECTIVE: We evaluated the incidence and epidemiologic characteristics of AChR Ab seropositivity using both RIPA and L-CBA over time in British Columbia (BC), Canada.

METHODS: We performed a population-based study of the incidence of AChR Abs seropositivity in BC for the 30 years of 1993 to 2023. Incident cases were determined by retrospectively identifying all first-time seropositive tests by RIPA and/or L-CBA. Incidence rates (IRs) were calculated as the annual number of first-time AChR Abs seropositive cases per 1 million population based on annual population estimates done in July by the BC government.

RESULTS: We identified 2646 new AChR Ab seropositive individuals (f = 1229). 53% of seropositive cases were aged 65 and older, 26.4% were 45 to 64 years, 15.4% were 20 to 44 years, and 5.3% were 19 and younger. The overall mean IRs of AChR Ab seropositivity was estimated at 20.6 /1 million. Since 2019, when L-CBA was added to the AChR Ab diagnostic algorithm, it has increased the IR of seropositivity by 1.2/1,000,000.

SUMMARY/CONCLUSION: The overall average AChR Ab seropositivity IRs in BC is among the highest reported rates. Further, the L-CBA has increased its incidence by 1.2 per million/year.

Disclosures:

Ali Mousavi - Staff at BC Neuroimmunology Lab.

Pankaj Kumar - Director of BC Neuroimmunology Lab.

Tariq Aziz - Staff at BC Neuroimmunology Lab.

Harvir Sodhi - Lab technician at BC Neuroimmunology Lab.

Navpreet Kaur - Lab technician at BC Neuroimmunology Lab.

Hans Frykman - Owner and director of BC Neuroimmunology Lab.

A SERUM INFLAMMATORY PROTEIN BIOMARKER PROFILE DEFINES ACETYLCHOLINE RECEPTOR ANTIBODY SEROPOSITIVE MYASTHENIA GRAVIS

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INTRODUCTION: There is a significant unmet need for objective Myasthenia Gravis (MG)-specific biomarkers to monitor patients over time, particularly with the emergence of novel immunosuppressive treatments entering clinical trials. Ideally, an MG biomarker should distinctly differentiate MG patients from healthy individuals and accurately reflect the underlying pathophysiology.

OBJECTIVE: To define a serum protein profile that separates acetylcholine receptor antibody seropositive (AChR+) MG patients from healthy controls (HCs).

METHODS: Proteomics analysis using proximity extension assay of 92 inflammatory proteins was performed in the sera of 98 AChR+ MG patients and 77 matched HC. Logistic regression and the Boruta algorithm ranked proteins according to their confirmed status as biomarkers in MG. Clinical severity was assessed based on MG-Activities-of-Daily-living (MG-ADL) and MG Composite (MGC) scores.

RESULTS: This cross-sectional study identified a signature of 23 inflammatory serum proteins that distinguish MG patients from HC. CCL28 (p=1.70E-10), TNFSF14 (p=2.20E-11), 4E-BP1 (p=2.30E-09), TGF-alpha (p=8.80E-11), and ST1A1 (p=5.30E-12) ranked top biomarkers. TGF-β1 and OPG differed between early- and late-onset MG, whereas CXCL10, TNFSF14, CCL11, IL-17C, and TGF-alpha differed significantly with immunosuppressive treatment.

SUMMARY/CONCLUSION: An inflammatory protein biomarker signature defined AChR+ MG patients from healthy controls. MG subgroup-specific biomarkers were identified. These findings allow prospective validation studies for patient subgroup stratification.

DESIGN OF KYSA-6, A PHASE 2, OPEN-LABEL, ULTICENTER STUDY OF KYV-101, A NOVEL FULLY HUMAN ANTI-CD19 CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY IN REFRACTORY GENERALIZED MYASTHENIA GRAVIS

Aiden Haghikia (Magdeburg, Germany), Dominic Borie (Emeryville, CA), James Chung (Emeryville, CA), Ralf Gold (Bochum, Germany)

INTRODUCTION: Myasthenia gravis (MG) is a B-cell-mediated autoimmune disease for which new therapeutic paradigms are needed that can improve disease activity control in refractory patients and enable sustained treatment-free remission. KYV-101 is a first-in-class, fully human autologous anti-CD19 CAR T-cell therapy containing a CAR demonstrated to have a favorable clinical safety profile in oncology. In the named patient setting, KYV-101 demonstrated rapid, profound improvements in disease severity and was well-tolerated in patients with severe refractory MG. KYV-101 is being investigated in KYSA-6, a multicenter, open-label, phase 2 study in MG (NCT06193889).

OBJECTIVE: Primary objectives are to evaluate the safety and efficacy of KYV-101, assessing adverse events and MG Activities of Daily Living (MG-ADL) at 24 weeks. Secondary objectives include evaluation of further efficacy, disease-related autoantibodies, and patient-reported outcomes.

METHODS: Twenty patients 18–75 years old, with generalized MG (class IIB-IV per MG Foundation of America), disease-related autoantibodies, an MG-ADL score ≥6, and who failed prior immunosuppressive/immunomodulatory therapy, are eligible. After lymphodepletion (fludarabine 30 mg/m^2/day, cyclophosphamide 300 mg/m^2/day; 3 days), patients will receive a single infusion of 1×10^8 CAR T cells. Descriptive statistics will be provided.

RESULTS: KYV-101 received FDA fast track designation for MG. KYSA-6 is being initiated in the US and other regions.

SUMMARY/CONCLUSION: KYV-101 is a novel therapy with the potential to change the treatment paradigm through deep B-cell depletion and immune reset with a single infusion in patients with B-cell driven autoimmune diseases like MG. KYV-101 is also under investigation in additional neurologic and rheumatologic diseases.

Disclosures:

Dominic Borie - Employee of Kyverna Therapeutics, Inc.

James Chung - Employee of Kyverna Therapeutics, Inc.

Ralf Gold - Holds stock and received honorarium from Kyverna Therapeutics.

TREATMENT STRATEGY TOWARDS MYASTHENIA GRAVIS WITH GAD65-IGG ASSOCIATED NEUROLOGICAL DISORDERS

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INTRODUCTION: Here, we report and describe a case affected by both acetylcholine receptor (AChR)-seropositive generalized myasthenia gravis (MG) and antibodies to glutamic acid decarboxylase associated neurological disorders (GADAD) with an anterior mediastinal teratoma.

OBJECTIVE: We aim to reveal the underlying pathogenic mechanisms and explore the immunotherapy strategy of MG with GADAD to gain better outcomes.

METHODS: We applied cell-based assays to detect GAD-IgG and tissue-based assay to determine the specific location of immunoreactivity. Images of computed tomography and magnetic resonance were presented to show the abnormalities in the brain and mediastinum. The immunohistochemical stainings were performed to uncover the histological and immunological characteristics of the anterior mediastinal tumor.

RESULTS: The pathogenic link between neurological disorders and GAD autoimmunity was established by the intrathecal synthesis of GAD65 antibodies in our case. Due to unsatisfied alleviation of intravenous immunoglobulin (IVIG) and tacrolimus, the new neonatal Fc receptor (FcRn) blocker was administered 21 days after IVIG infusion to gain a better post-intervention status(PIS) of MG, thus lowering the risk of myasthenic exacerbation under high-dose corticosteroids for GADAD and facilitating the subsequent corticosteroids tapering to enable an earlier mediastinal tumor resection. In addition, the CD20-positive B-lymphocytes depleting agent, was given after a reasonable time of FcRn blockade to suppress the autoimmune pathogenic mechanisms upstream of autoantibodies. Eventually, the symptoms of MG and GADAD were both significantly alleviated in our case.

SUMMARY/CONCLUSION: The anterior mediastinal teratoma provided a pathogenetic niche shared by multiple autoimmune diseases. Early and efficient immunotherapy is important and might be associated with better outcomes.

THE MITOCHONDRIAL QUALITY CONTROL MECHANISM OF STATINS AFFECTING MYASTHENIA GRAVIS PATIENTS WITH HYPERLIPIDEMIA

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INTRODUCTION: Previous reports showed patients with hyperlipidemia who use statins may be at risk of triggering or exacerbating myasthenia gravis (MG). Synaptic formation, Ca2+ influx, vesicle generation and recycling, and postsynaptic potential generation are all dependent on the local recruitment of mitochondria at the neuromuscular junction. Statins can cause mitochondrial membrane potential reduction, declination of coenzyme Q10 levels, an increase in reactive oxygen species production, and induce apoptosis.

OBJECTIVE: To explore how statins affect the mitochondrial quality control (MQC) system in MG patients with hyperlipidemia.

METHODS: This is a prospective cohort study. Patients were recruited from 2018 to 2022, grouped as “Statin group” and “Non-statin group”. Four serum biomarkers are tested by ELISA, respectively: 1) Synthesis: PGC-1α; 2) Fusion: Mfn2; 3) Fission: Fis1; 4) Autophagy: Parkin protein.

RESULTS: Both the statin group and the non-statin group included 26 patients. There were no significant differences in the four MQC-related biomarkers levels between the two groups (PGC-1α 2046.1±932.3 vs. 2537.1±1706.3, p=0.195; MFN-2 1462.1±705.0 vs. 1313.4±562.5, p=0.380, Fis1 4.5±4.7 vs. 5.4±5.5, p=0.546; Parkin 61.1±84.9 vs 221.8±633.8, units ng/ml). However, it was observed that the levels of PGC-1α, Fis1, and Parkin in the statin group were lower than non-statin group. The levels of PGC-1α, Fis1, and Parkin in the 20mg/d atorvastatin group were lower than those in the 10mg/d atorvastatin group.

SUMMARY/CONCLUSION: It is suggested that increasing the dosage of statins may have certain effects on mitochondrial fusion, division and autophagy. Dynamic monitoring of serum MQC-related biomarker levels may be considered to explore the mechanism of statins' impact on MG.

EFFECT OF ROZANOLIXIZUMAB ON MYASTHENIA GRAVIS–SPECIFIC OUTCOME SUBDOMAIN SCORES: POST HOC ANALYSES FROM THE PHASE 3 MYCARING STUDY

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INTRODUCTION: The Phase 3 MycarinG study (NCT03971422) demonstrated that rozanolixizumab significantly improved Myasthenia Gravis Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) total scores in patients with generalized myasthenia gravis (gMG) versus placebo.

OBJECTIVE: Treatment may have differential effects across the different muscle groups; the objective of this analysis was to evaluate the effect of rozanolixizumab treatment on MG-ADL and QMG subdomain scores assessing ocular, bulbar, respiratory and limb weakness/gross motor muscle groups.

METHODS: Adults with acetylcholine receptor or muscle-specific kinase autoantibody-positive gMG were randomized to weekly rozanolixizumab 7 mg/kg, rozanolixizumab 10 mg/kg or placebo for 6 weeks (one cycle). This post hoc analysis assessed change from baseline (CFB) to Day 43 in MG-ADL and QMG subdomain scores.

RESULTS: Overall, 200 patients received rozanolixizumab 7 mg/kg (n=66), 10 mg/kg (n=67) or placebo (n=67). Mean (standard deviation [SD]) CFB in MG-ADL subdomain scores in the rozanolixizumab 7 mg/kg, rozanolixizumab 10 mg/kg and placebo groups: ocular, −0.8 (1.3), −1.0 (1.2) and −0.1 (0.9), respectively; bulbar, −1.3 (1.7), −1.3 (1.5) and −0.2 (1.4), respectively; respiratory, −0.3 (0.6), −0.3 (0.7) and 0.0 (0.5), respectively; limb weakness, −1.0 (1.3), −0.7 (1.1) and −0.3 (1.0), respectively. Similar trends were observed for mean (SD) CFB in the QMG subdomain scores (ocular, bulbar, respiratory and gross motor muscle groups). Rozanolixizumab was generally well tolerated, and most adverse events were mild/moderate.

SUMMARY/CONCLUSION: Rozanolixizumab treatment led to improvements across all MG-ADL and QMG subdomain scores, representing the ocular, bulbar, respiratory and limb weakness/gross motor muscle groups, in patients with gMG. Funding: UCB Pharma.

Disclosures:

Robert M. Pascuzzi - Professor Emeritus of Neurology at Indiana University and receives compensation for his professional work from Indiana University Health. He has no financial relationship with any pharmaceutical company and receives no compensation from any pharmaceutical company (present or past). Robert M. Pascuzzi speaks at educational seminars on a broad variety of general neurology topics for primary care physicians through the organisation Medical Education Resources (an educational organisation with no links or ties to any pharmaceutical or healthcare business company). Therefore, Robert M. Pascuzzi has no conflicts of interest related to this research, manuscript, presentation, or publication.

Ali A. Habib - Received research support from Alexion Pharmaceuticals, argenx, Cabaletta Bio, Genentech/Roche, Immunovant, Regeneron Pharmaceuticals, UCB Pharma and Viela Bio (now Amgen). He has received honoraria from Alexion Pharmaceuticals, Alpine Immune Sciences, argenx, Genentech/Roche, Immunovant, Inhibrx, Regeneron Pharmaceuticals, NMD Pharma and UCB Pharma.

John Vissing - Consultant on advisory boards for Amicus Therapeutics, Arvinas, Biogen, Fulcrum Therapeutics, Genethon, Horizon Therapeutics (now Amgen), Lupin, ML Biopharma, Novartis, Regeneron, Roche, Sanofi Genzyme (now Sanofi), Sarepta Therapeutics and UCB Pharma. He has received research, travel support and/or speaker honoraria from Alexion Pharmaceuticals, argenx, Biogen, Edgewise Therapeutics, Fulcrum Therapeutics, Lupin, Sanofi Genzyme (now Sanofi) and UCB Pharma. He is a Principal Investigator in clinical trials for Alexion Pharmaceuticals, argenx, Genethon, Horizon Therapeutics (now Amgen), Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), ML Biopharma, Novartis, Regeneron Pharmaceuticals, Roche, Sanofi Genzyme (now Sanofi) and UCB Pharma.

Tuan Vu - USF Site Principal Investigator for MG clinical trials sponsored by Alexion Pharmaceuticals, Amgen, argenx, Cartesian Therapeutics, Dianthus Therapeutics, Immunovant, Johnson & Johnson, Regeneron Pharmaceuticals, RemeGen, and UCB Pharma, and has served as a speaker for Alexion Pharmaceuticals, Allergan (now AbbVie), argenx, and CSL Behring. He performed consulting work for Alexion Pharmaceuticals, argenx, Dianthus Therapeutics, ImmunAbs, RemeGen, and UCB Pharma.

Asha Hareendran - Employee and shareholder of UCB Pharma.

Francesca Pannullo - Contractor for UCB Pharma.

Thaïs Tarancón - Employee and shareholder of UCB Pharma.

Vera Bril - Consultant for Akcea, Alexion Pharmaceuticals, Alnylam, argenx, CSL, Grifols, Ionis, Immunovant, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), Momenta (now Johnson & Johnson), Novo Nordisk, Octapharma, Pfizer, Powell Mansfield, Roche, Sanofi, Takeda Pharmaceuticals and UCB Pharma. She has received research support from Akcea, Alexion Pharmaceuticals, argenx, CSL, Grifols, Immunovant, Ionis, Momenta (now Johnson & Johnson), Octapharma, Takeda Pharmaceuticals, UCB Pharma and Viela Bio (now Amgen).

SWITCHING TO SUBCUTANEOUS ZILUCOPLAN FROM IV COMPLEMENT COMPONENT 5 INHIBITORS IN MYASTHENIA GRAVIS: A PHASE 3B STUDY

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INTRODUCTION: Zilucoplan, a peptide complement component 5 (C5) inhibitor, is a self-administered subcutaneous (SC) injection, which presents an alternative to IV infusion of antibody-based C5 inhibitors eculizumab and ravulizumab.

OBJECTIVE: We aimed to evaluate SC zilucoplan in adults with acetylcholine receptor autoantibody-positive generalized myasthenia gravis who switched from IV C5 inhibitors to zilucoplan.

METHODS: MG0017 (NCT05514873) is a Phase 3b, open-label, single-arm study with a 12-week treatment period, with daily SC zilucoplan 0.3 mg/kg. Eligible patients had clinically stable disease on an IV C5 inhibitor and were willing to switch to zilucoplan. Incidence of treatment-emergent adverse events (TEAEs; primary endpoint), and change from baseline in Myasthenia Gravis Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) scores were assessed. Complement inhibition was measured by the sheep red blood cell lysis assay.

RESULTS: In total, 26 patients enrolled and received zilucoplan; 16 switched from eculizumab and 10 from ravulizumab. Of these, 23 patients completed the main treatment period and 3 discontinued. TEAEs occurred in 19/26 (73.1%) patients and were mostly mild in severity. At Week 12, least squares mean (SE) MG-ADL scores were improved from baseline by −1.15 (0.46) and QMG scores by −1.24 (0.67), with greater improvements in patients who switched from ravulizumab (−2.41 [0.89] and −3.52 [1.13], respectively). Complement inhibition increased with zilucoplan treatment (baseline 93.5% inhibition to Week 12 98.5% inhibition), particularly after switching from ravulizumab (87.3% to 98.9%).

SUMMARY/CONCLUSION: Zilucoplan demonstrated a favorable safety profile. Myasthenia gravis symptoms improved during zilucoplan treatment; this was clinically meaningful for those switching from ravulizumab.

Disclosures:

Miriam Freimer - Served as a paid Consultant for Alexion Pharmaceuticals, argenx and UCB Pharma. Receives research support from Alnylam Pharmaceuticals, Avidity Biosciences, Fulcrum Therapeutics, Janssen Pharmaceuticals, the NIH and UCB Pharma.

Michael D. Weiss - Received honoraria for serving on scientific advisory boards for Alexion Pharmaceuticals, Immunovant, Ra Pharmaceuticals (now UCB Pharma), argenx, Biogen, Mitsubishi Tanabe Pharma and Amylyx Pharmaceuticals; consulting honoraria from Cytokinetics and CSL Behring; speaker honoraria from Soleo Health; serves as a special government employee for the Food and Drug Administration.

Babak Boroojerdi - Employee and shareholder of UCB Pharma.

Eumorphia Maria Delicha - Employee and shareholder of UCB Pharma.

Brittany Harvey - Employee and shareholder of UCB Pharma.

Andreea Lavrov - Employee and shareholder of UCB Pharma.

Puneet Singh - Employee of UCB Pharma and shareholder of UCB Pharma and GSK.

Urvi Desai - Served on advisory boards for argenx, Alnylam Pharmaceuticals, Biogen, Catalyst, CSL Behring, Fulcrum Therapeutics, Sarepta, Takeda Pharmaceuticals and UCB Pharmal; served on speaker bureaus for Alexion Pharmaceuticals, Alnylam Pharmaceuticals, argenx and CSL Behring; institution has received research support from Mitsubishi Tanabe Pharma.

Raghav Govindarajan - Served on advisory boards for argenx, Janssen Pharmaceuticals, Roche and UCB Pharma and participated in speaker bureaus for Alexion Pharmaceuticals, argenx and UCB Pharma.

Min K. Kang - Receives research support from UCSF and has served on advisory boards for UCB Pharma.

Shaida Khan - Served as a paid Consultant for UCB Pharma and has served on advisory boards for argenx and UCB Pharma; receives research support from the Fichtenbaum Charitable Trust.

Bhupendra Khatri - Received research and/or consulting financial compensation from Alexion Pharmaceuticals, argenx, Biogen, Bristol Myers Squibb, EMD Serono, Genentech, Novartis, Sanofi Genzyme (now Sanofi), Terumo BCT, TG Therapeutics and UCB Pharma.

Samir Macwan - Received personal compensation for serving as a Consultant for Alexion Pharmaceuticals, argenx, Kabafusion and UCB Pharma; received personal compensation for serving on a Speakers Bureau for Abbvie, Alexion Pharmaceuticals, argenx and Grifols; institution has received research support from Alexion Pharmaceuticals, Disimmune Disease Foundation.

James F. Howard, Jr - Received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention (Atlanta, GA, USA), the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health (including the National Institute of Neurological Disorders and Stroke and the National Institute of Arthritis and Musculoskeletal and Skin Diseases), PCORI, and UCB

Pharma; has received honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-La Roche, Horizon Therapeutics (now Amgen), Medscape CME, Merck EMD Serono, NMD Pharma, Novartis, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, UCB Pharma, Regeneron Pharmaceuticals, Sanofi US, and Zai Labs; and has received non-financial support from Alexion AstraZeneca Rare Disease, argenx, Toleranzia AB and UCB Pharma.

ROZANOLIXIZUMAB IN PATIENTS AGED ≥65 YEARS WITH GENERALIZED MYASTHENIA GRAVIS: A POST HOC ANALYSIS OF THE PHASE 3 MYCARING STUDY

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INTRODUCTION: Patients with generalized myasthenia gravis (gMG) aged ≥65 years are often underrepresented in clinical studies.

OBJECTIVES: Evaluate rozanolixizumab in patients with gMG aged ≥65 years.

METHODS:In the Phase 3 MycarinG (NCT03971422) study, adults with acetylcholine receptor or muscle-specific tyrosine kinase autoantibody-positive gMG were randomized 1:1:1 to weekly subcutaneous placebo, rozanolixizumab 7mg/kg or rozanolixizumab 10mg/kg for 6 weeks. Primary endpoint: change from baseline (CFB) to Day 43 in Myasthenia Activities of Daily Living (MG-ADL) score. Baseline characteristics and incidence of treatment-emergent adverse events (TEAEs) were analyzed by age (<65 and ≥65 years) post hoc.

RESULTS: Overall, 200 patients received placebo (<65 years: n=51; ≥65 years: n=16) or rozanolixizumab (n=100; n=33). Baseline characteristics were broadly similar between subgroups. Concomitant medications were used by 98.0% (n=148/151) of patients aged <65 years and all patients aged ≥65 years. Comorbidities, including cardiac and vascular disorders, were generally more common in the older subgroup than the younger subgroup. Mean (SD) CFB to Day 43 in MG-ADL scores for placebo- and rozanolixizumab-treated patients aged <65 years: −1.1 (2.7) and −3.7 (3.2), respectively; ≥65 years: 0.7 (2.8) and −2.1 (4.0). TEAEs occurred in 60.8% (n=31/51) and 85.0% (n=85/100) of placebo- and rozanolixizumab-treated patients aged <65 years, respectively, and 87.5% (n=14/16) and 72.7% (n=24/33) of patients aged ≥65 years. Headache, the most common TEAE, was more common in the younger subgroup (placebo: 21.6% [n=11/51]; rozanolixizumab: 49.0% [n=49/100]) than the older subgroup (12.5% [n=2/16]; 18.2% [n=6/33]).

SUMMARY/CONCLUSION: Rozanolixizumab was well tolerated and efficacious in patients with gMG aged ≥65 years. Funding: UCB Pharma.

Disclosures:

Tuan Vu - Is the USF Site Principal Investigator for MG clinical trials sponsored by Alexion Pharmaceuticals, Amgen, argenx, Cartesian Therapeutics, Dianthus Therapeutics, Immunovant, Johnson & Johnson, Regeneron Pharmaceuticals, RemeGen, and UCB Pharma, and has served as a speaker for Alexion Pharmaceuticals, Allergan (now AbbVie), argenx, and CSL Behring. He performed consulting work for Alexion Pharmaceuticals, argenx, Dianthus Therapeutics, ImmunAbs, RemeGen, and UCB Pharma.

Ali A. Habib - Received research support from Alexion Pharmaceuticals, argenx, Cabaletta Bio, Genentech/Roche, Immunovant, Regeneron Pharmaceuticals, UCB Pharma and Viela Bio (now Amgen). He has received honoraria from Alexion Pharmaceuticals, Alpine Immune Sciences, argenx, Genentech/Roche, Immunovant, Inhibrx, Regeneron Pharmaceuticals, NMD Pharma and UCB Pharma.

Fiona Grimson - Employee and shareholder of UCB Pharma.

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Thaïs Tarancón - Employee and shareholder of UCB Pharma.

Vera Bril - Consultant for Akcea, Alexion Pharmaceuticals, Alnylam, argenx, CSL, Grifols, Ionis, Immunovant, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), Momenta (now Johnson & Johnson), Novo Nordisk, Octapharma, Pfizer, Powell Mansfield, Roche, Sanofi, Takeda Pharmaceuticals and UCB Pharma. She has received research support from Akcea, Alexion Pharmaceuticals, argenx, CSL, Grifols, Immunovant, Ionis, Momenta (now Johnson & Johnson), Octapharma, Takeda Pharmaceuticals, UCB Pharma and Viela Bio (now Amgen).

IS RESIDUAL SERUM FIBRINOGEN A BIOMARKER FOR MYASTHENIA GRAVIS?

Taylor Bauman (Washington, DC), Sean Lee (Washington, DC), Jiaxin Chen (Washington, DC), Linda Kusner (Washington, DC), Henry Kaminski (Washington, DC)

INTRODUCTION: Fibrinogen, a soluble protein produced in the liver, is crucial for blood clot formation. Beyond its role in hemostasis, fibrinogen is also linked to inflammation and recognized as a proinflammatory mediator in other diseases. Hussain et al. (Sci Rep. 2023) identified residual serum fibrinogen as a potential biomarker for myasthenia gravis (MG) after finding its levels to be over 1000-fold higher in MG patients compared to controls. However, the pathophysiological mechanism for the elevated residual serum fibrinogen levels in MG patients remains unclear.

OBJECTIVE: The aim of our study was to validate the use of fibrinogen as a biomarker for MG.

METHODS: Serum samples from 52 MG patients and 14 non-autoimmune controls were assessed for fibrinogen levels using enzyme-linked immunosorbent assays (ELISAs) (Abcam, ab241383). The MG patients were from independent cohorts, including patients with anti-AChR antibodies (N=31), anti-MuSK antibodies (N=10), and double-seronegative patients (N=11). To test for differences between MG and control groups, we fitted a lognormal regression to fibrinogen levels data as a function of group.

RESULTS: Predicted mean fibrinogen levels did not differ between groups (MG=1,037ng/mL [95%CI 718-1,507]; control=887ng/mL [95%CI 639-1,230]; p=0.389).

SUMMARY/CONCLUSION: Our results indicate that residual serum fibrinogen is not significantly elevated in MG patients compared to controls. We conclude that residual serum fibrinogen is not a biomarker for MG. We will confirm our results of serum fibrinogen with serum proteomic profile analyses.

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INCIDENCE AND OUTCOME OF MENINGOCOCCAL INFECTION WITH ECULIZUMAB OR RAVULIZUMAB IN PATIENTS WITH GMG OR NMOSD: AN ANALYSIS OF US CLINICAL PRACTICE

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INTRODUCTION: Eculizumab and ravulizumab are effective treatments for generalized myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD). Safety mitigations, including vaccinations, are used to reduce the risk of Neisseria meningitidis (Nm) infection associated with these treatments.

OBJECTIVE: To evaluate US exposure-adjusted Nm infection and mortality in eculizumab- or ravulizumab-treated patients with gMG and NMOSD using postmarketing pharmacovigilance data (Nm case counts) and commercial data (exposure).

METHODS: The US Alexion safety database was searched for eculizumab and ravulizumab (data cutoff: December 2022) across approved indications (gMG, NMOSD, paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome) using the MedDRA High Level Term “Neisseria infection.” Only Nm-associated cases were included. Reporting rates were calculated cumulatively per 100 patient-years (PY).

RESULTS: US Nm infection and mortality annual reporting rates in eculizumab-treated patients remained stable over 15 years across approved indications (2022: 0.13 and 0.01, respectively; exposure: 29,758.4 PY). In 2022, US postmarketing Nm infection reporting rates in eculizumab-treated patients with gMG and NMOSD were 0.02 (exposure: 8,042.0 PY) and 0.07 (exposure: 1,470.1 PY), respectively. At data cutoff, there were no Nm infections among ravulizumab-treated patients with gMG. No Nm fatalities were noted for eculizumab- or ravulizumab-treated patients with gMG and NMOSD.

SUMMARY/CONCLUSION: Nm infection and mortality reporting rates for patients with gMG and NMOSD remained stable despite increasing eculizumab and ravulizumab exposure over time. These results suggest US Nm-related risk mitigation strategies are effective in patients receiving eculizumab or ravulizumab.

Disclosures:

Shirali Pandya - Employee of, and holds stock in, Alexion, AstraZeneca Rare Disease.

Lokesh Jha - Employee of, and holds stock in, Alexion, AstraZeneca Rare Disease.

Imad Al-Dakkak - Employee of, and holds stock in, Alexion, AstraZeneca Rare Disease.

Feifei Yang - Employee of, and holds stock in, Alexion, AstraZeneca Rare Disease.

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PATTERNS OF EFGARTIGIMOD DOSING IN CLINICAL PRACTICE IN THE UNITED STATES

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INTRODUCTION: Efgartigimod is approved in the US for the treatment of anti-acetylcholine receptor antibody positive generalized myasthenia gravis. Efgartigimod is administered in cycles of 4 weekly infusions, with subsequent cycles initiated based on clinical evaluation.

OBJECTIVE: To evaluate efgartigimod dosing patterns.

METHODS: Patients in the US who initiated efgartigimod by September 26, 2023, were identified from the “My VYVGART Path” dataset. Efgartigimod infusion dates were captured through phone contact. Patients who initiated ≥2 cycles were identified to analyze time between cycles. Patients who initiated ≥6 cycles were identified to analyze treatment cadence beyond Cycle 3. Patients were considered to have fixed dosing if >66.6% of their gaps between cycles were ±7 days of their median gap length from Cycle 3 onward. Those with >±7 day’s deviation were considered to have flexible dosing.

RESULTS: Among 3961 patients who initiated efgartigimod, 2616 (66%) had ≥2 cycles. The most common gap length among 7341 total gaps between cycles was 4 weeks (22.8%), with 10.1% of gaps being <4 weeks, 48.2% being 4-6 weeks, and 41.7% being >6 weeks (range, 0-68 weeks). Among 490 patients (12%) who initiated ≥6 cycles, more had fixed (n=357/490 [73%]) vs flexible (n=133/490 [27%]) dosing. Gaps between cycles among this cohort were most commonly 4 weeks regardless of treatment cadence, with the majority of gaps being 4-6 weeks (range, 0-43 weeks).

SUMMARY/CONCLUSION: Among patients who initiated efgartigimod, gaps between treatment cycles were most commonly 4-6 weeks. Among those with ≥6 cycles, the majority followed a fixed dosing cadence from Cycle 3 onward.

Disclosures:

Ratna Bhavaraju-Sanka - Served on advisory boards for argenx and is a consultant to Sanofi.

Cynthia Qi - Employee of argenx.

Matthew Jefferson - Employee of argenx.

Eddie Brauer - Employee of argenx.

Deborah Gelinas - Employee of argenx.

Tharun Balaji Suthagar - Employee of ZS Associates and serve as paid consultants for argenx.

Rohit R Menon - Employee of ZS Associates and serve as paid consultants for argenx.

Mai Sato - Employee of ZS Associates and serve as paid consultants for argenx.

A. Gordon Smith - Paid consultant for argenx, Alexion, UCB, and Seismic.

SELF-ADMINISTRATION OF SUBCUTANEOUS ROZANOLIXIZUMAB IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: CLINICAL STUDY DESIGN

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INTRODUCTION: Generalized myasthenia gravis (gMG) is a chronic autoimmune disease requiring long-term therapy. Rozanolixizumab, indicated for the treatment of adults with acetylcholine receptor or muscle-specific tyrosine kinase receptor autoantibody-positive gMG, is currently administered subcutaneously by healthcare professionals (HCPs) using a programmable syringe driver.

OBJECTIVE: The MG0020 study aims to demonstrate whether patients can safely self-administer rozanolixizumab using the syringe driver and manual push methods.

METHODS: MG0020, a Phase 3, open-label, randomized, crossover study, will include patients aged ≥18 years with gMG. In total, 75 patients have been screened and 55 will be randomized. Patients will receive once-weekly rozanolixizumab for 18 consecutive weeks consisting of a 6-week self-administration training period followed by two 6-week self-administration periods (at clinic and unsupervised at home). After training, patients will be randomized 1:1 to the syringe driver or manual push self-administration method, subsequently crossing over to the alternative method. A safety follow-up period of up to 7-weeks will follow. Primary endpoint: successful self-administration of rozanolixizumab (choosing the correct infusion site, administering subcutaneously and delivering intended dose) by syringe driver and manual push, evaluated by an HCP at Weeks 12 and 18. Secondary endpoints are occurrence of treatment-emergent adverse events, local site reactions and medication errors resulting in adverse reactions. Additional endpoints include patient preference for subcutaneous infusions performed by an HCP versus self-administration, and preference for manual push versus syringe driver self-administration.

SUMMARY/CONCLUSION: MG0020 will evaluate the safety and success of self-administration of rozanolixizumab using the syringe driver and manual push methods in patients with gMG. Funding: UCB Pharma.

Disclosures:

Rachana K. Gandhi Mehta - Received research support from Akcea (now Ionis Pharmaceuticals, Inc.), Graticule and UCB Pharm; site Investigator for the Rare Disease Network for Myasthenia Gravis (MGNet) National Institute of Neurological Disorders & Stroke; participated in advisory boards for UCB Pharma and has received speaker honoraria from UCB Pharma; served as a NEJM Group Clinical Reasoning Contributing Editor for NEJM Healer.

Mark Morris - Employee and shareholder of UCB Pharma.

Puneet Singh - Employee and shareholder of UCB Pharma.

Rose Snipes - Employee and shareholder of UCB Pharma.

M. Isabel Leite - Funded by the NHS (Myasthenia and Related Disorders Service and National Specialised Commissioning Group for Neuromyelitis Optica, UK) and by the University of Oxford, UK. She has been awarded research grants from UK associations for patients with myasthenia and with muscular disorders (Myaware and Muscular Dystrophy UK, respectively) and the University of Oxford. She has received speaker honoraria or travel grants from Biogen, the Guthy-Jackson Charitable Foundation, Novartis and UCB Pharma. She serves on scientific or educational advisory boards for argenx, Horizon Therapeutics (now Amgen) and UCB Pharma.

Carlo Antozzi - Received funding for congress and Institutional Review Board participation from argenx, Alexion, Biogen, Janssen, Momenta and UCB Pharma.

Vera Bril - Consultant for Akcea, Alexion Pharmaceuticals, Alnylam, argenx, CSL, Grifols, Ionis, Immunovant, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), Momenta (now Johnson and Johnson), Novo Nordisk, Octapharma, Pfizer, Powell Mansfield, Roche, Sanofi, Takeda and UCB Pharma. She has received research support from Akcea, Alexion Pharmaceuticals, argenx, CSL, Grifols, Immunovant, Ionis, Momenta (now Johnson and Johnson), Octapharma, Takeda, UCB Pharma and Viela Bio (now Amgen).

Zabeen K. Mahuwala - Received funding for advisory board participation from Alexion Pharmaceuticals.

Jana Zschüntzsch - Has been awarded research grants from the Innovative Medicines Initiative 2 Joint Undertaking (IMI JU) of the European Commission (grant number: 101034427-2), German Society for Muscle Disease (DGM) and the German Innovationfond. She has received speaker honoraria or travel grants from argenx, Alexion, Sanofi, Kedrion and Roche. She serves on scientific or educational advisory boards for UCB Pharma, argenx, Alexion, Sanofi, Amicus, Kedrion and iThera. She has received research support from argenx and UCB Pharma. She is a member of the European Reference Network for Rare Neuromuscular Diseases (ERN EURO-NMD) and a member of the medical advisory boards of the German Myasthenia Gravis Society and the DGM.

Denis Flemm - Employee and shareholder of UCB Pharma.

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SIMULTANEOUS MYASTHENIA GRAVIS-POLYMYOSITIS OVERLAP SYNDROME, A CASE REPORT

Alexandra McMillan (Albany, NY), Kimberly Robeson-Gewuerz (Albany, NY)

INTRODUCTION: Over the last two decades there has been a growing body of literature in case series and case reports of myasthenia gravis (MG) and inflammatory myositis (IM) overlap syndromes, most with years between diagnoses. More recently, the focus has been on these overlap cases in the setting of immune checkpoint inhibitor therapies.

OBJECTIVE: To add to the growing literature by presenting a case of MG-IM overlap syndrome with simultaneous diagnosis in the setting of thymoma, without exposure to checkpoint-inhibitors.

METHODS: Identifying a case of simultaneous thymomatous MG and granulomatous polymyositis (PM) at a tertiary care center in New York.

RESULTS: A single patient was identified with MG-IM overlap syndrome and is presented here.

SUMMARY/CONCLUSION: 58yo female with no prior autoimmune history or use of checkpoint inhibitors presenting with generalized weakness including bulbar weakness that was worse in the evenings, elevated Creatine Kinase (CK), and magnetic resonance imaging consistent with diffuse active myositis, who was found to have thymoma during malignancy work-up and subsequently tested positive for Acetylcholine receptor antibodies. Muscle biopsy was consistent with granulomatous polymyositis. Thymoma pathology was consistent with Masuoka grade II thymoma. She was treated immediately with intravenous immunoglobulin with only partial improvement in symptoms. Steroids caused an initial worsening but did resolve her myalgia and normalize her CK, although her severe bulbar symptoms persisted. She did not have response to pyridostigmine. She underwent thymic resection and was eventually started on mycophenolate in the outpatient setting with good improvement over the following months.

Disclosures:

Kimberly Robeson-Gewuerz - Paid as a consultant as part of the speakers bureau for Alexion Pharmaceuticals.

EXPLORING THE IMPACT OF NONSTEROIDAL IMMUNOSUPPRESSIVE DRUGS AND STEROIDS ON THE DEVELOPMENT OF COMORBIDITIES IN PATIENTS WITH MYASTHENIA GRAVIS IN THE NATIONAL VETERANS AFFAIRS HEALTH NETWORK

Cynthia Qi (Boston, MA), Yilu Lin (New Orleans, LA), Yuebing Li (Clevland, OH), Tuan Vu (Lutz, FL), Deborah Gelinas (Durham, NC), Femke De Ruyck (Ghent, Belgium), Lizheng Shi (New Orleans, LA)

INTRODUCTION: Myasthenia gravis (MG) is an autoimmune neuromuscular disorder characterized by muscle weakness and fatigue that significantly impacts the quality of life. While considerable progress has been made in understanding the pathophysiology of MG, understanding the relationship between treatment strategies and the prevalence of comorbidities in MG can help to inform treatment decisions.

OBJECTIVE: To examine the impact of nonsteroidal immunosuppressants (NSISTs) and steroids on the development of comorbidities in MG.

METHODS: Deidentified data from the National Veterans Affairs Health Care Network's database was extracted between January 1999 and March 2022 on patients who had ≥2 MG-related diagnostic claims. The impact of NSISTs and steroids on comorbidity development in MG while adjusting for patient demographic and other disease-related characteristics was evaluated.

RESULTS: A total of 10,632 patients with MG were identified with a mean age at diagnosis of 70.5 years. Patients were followed for a median of 7 years. Among the 14 comorbidities examined in the study, use of steroids was associated with a significantly higher risk of developing osteoporosis (hazard ratio [HR]:1.35); autoimmune conditions (HR:1.23), glaucoma (HR:1.22), diabetes (HR:1.22), malignancy (HR:1.19), infection (HR:1.18), thyroid disorders (HR:1.17), and depression (HR:1.15) (all P<.05). Conversely, NSISTs were associated with a significantly elevated risk of anxiety (HR:1.26) and sleep disorders (HR:1.28) (all P<.05).

SUMMARY/CONCLUSION: The study found that when treating MG, conventional immunosuppressive therapies including steroids and NSISTS significantly increased the risk of developing several comorbidities. This result suggests it is important to consider the potential impact of comorbidities in the treatment selection for patients with MG.

Disclosures:

Cynthia Qi - Employee of argenx.

Yilu Lin - Received research support through a contract from argenx to Tulane University and also received research support from NIH and PCORI.

Yuebing Li - Served as a consultant for argenx, UCB Pharma, Alexion, Catalyst, and Immunovant, and received grant support from argenx.

Tuan Vu - Speaker for Alexion, argenx, and CSL Behring; performed consulting work for argenx, Alexion/Astra Zeneca, Dianthus, ImmunAbs, and UCB; and participated in trials in MG sponsored by Alexion/Astra Zeneca, argenx, UCB, Amgen, Immunovant, Regeneron, Johnson & Johnson, Dianthus, and Cartesians Therapeutics.

Deborah Gelinas - Employee of argenx.

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Lizheng Shi - Received research support through a contract from argenx to Tulane University and also received research support from NIH and CDC.

UNMET NEEDS IN MYASTHENIA GRAVIS: PATIENT AND PHYSICIAN PERSPECTIVES

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INTRODUCTION: Progress has been made in the development of new immunomodulatory medications for generalized myasthenia gravis (gMG), 1,2 Yet, recent U.S. and international publications found patients report high levels of burdensome symptoms and overall unmet needs.3-5 It is not known if treating physicians also perceive areas of unmet need and how they would prioritize addressing these gaps.

OBJECTIVE: The goal of this study was to elicit whether US clinicians recognize important unmet clinical needs for gMG patients, despite recent therapeutic approvals.

METHODS: A research study in February 2024 with 50 U.S. based neurologists, 38% (n=19) from Academic Institution/Hospitals; 8% (n=4) from Non-Academic Institution/Hospitals; 54% (n=27) from individual or community private practice groups (from 21 states, representing 68% of the US population) was conducted. The average annual gMG patient volumes ranged from 80 (Academic) to 53 (non-academic/community). Distribution of gMG patients based on severity was reported as follows:

• Mild 46% (academic); 55% (non-academic)

• Moderate to severe 54% (academic); 45% (non-academic)

RESULTS: Neurologists in this study reported the top three unmet clinical needs across all gMG subtypes were better efficacy, safety, and dosing. Respondents were asked what percentage of gMG patients experience the following problems:

• Fluctuating symptoms (47% academic; 35% non-academic)

• Persistent symptoms (40% academic; 24% non-academic)

• Severe and debilitating muscle function impairment (20% academic; 17% non-academic).

SUMMARY/CONCLUSION: Physician responses in this study aligned with prior patient-centric research; academic and non-academic views were consistent. Despite availability of new physician-preferred treatments, there is apparently still a need for additional treatments across all gMG patient subtypes.

Disclosures:

Martin Brandhoj Skov – Employee of NMD Pharma.

Ali Habib - Receiving research support from Alexion/Astra Zeneca, argenx, UCB, Immunovant, Regeneron, CabalettaBio, VielaBio/Horizon, and Genentech/Roche and honoraria from UCB, argenx, Alexion, Immunovant, Regeneron, and Genentech/Roche.

Srikanth Muppidi - Served on advisory board meetings for Argenx, Alexion/AZ, Amgen, and UCB.

Tuan Vu - Received research support from Alexion/AstraZeneca Rare Disease, Amgen, Amylyx, argenx, Cartesians, CSL Behring, Dianthus, Healy Platform Trials, Immunovant, Ipsen, Johnson & Johnson, PTC Therapeutics, Regeneron, Sanofi, UCB, and Woolsey Pharma; served on speakers bureaus for Alexion, AstraZeneca Rare Disease, argenx, and CSL Behring; served on ad boards or as consultant for Alexion/AstraZeneca Rare Disease, Amgen, argenx, ImmunAbs, John & Johnson, and UCB.

Daniel Brennan - Employee of NMD Pharma.

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CORTICOSTEROID DOSE TAPERING DURING TREATMENT WITH ZILUCOPLAN IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: 120-WEEK FOLLOW-UP OF RAISE-XT

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INTRODUCTION: The efficacy and safety of zilucoplan in patients with acetylcholine receptor autoantibody-positive generalized myasthenia gravis (gMG) were assessed in two double-blind studies (NCT03315130/NCT04115293). During these studies, and the first 12 weeks of the ongoing, open-label extension study, RAISE-XT (NCT04225871), corticosteroid dose was kept stable. Thereafter, corticosteroid dose could be changed at the investigator's discretion.

OBJECTIVE: Evaluate corticosteroid dose changes in patients with gMG during zilucoplan treatment in RAISE-XT.

METHODS: In RAISE-XT, adults who completed a qualifying double-blind study self-administered once-daily subcutaneous zilucoplan 0.3mg/kg. Primary outcome: incidence of treatment-emergent adverse events (TEAEs). This post hoc interim analysis (November 11, 2023) assessed the proportion of patients who reduced, discontinued, or increased their corticosteroid dose relative to double-blind baseline and change from baseline (CFB) in Myasthenia Gravis Activities of Daily Living (MG-ADL) score after 120 weeks.

RESULTS: Overall, 200 patients enrolled. Of patients on corticosteroids at double-blind baseline with Week 120 data, 61.1% (n=33/54) had reduced or discontinued corticosteroids (mean 15.5mg dose reduction from 23.0mg at baseline); mean CFB in MG-ADL score: −6.6 (standard deviation [SD] 3.6). Amongst all patients with Week 120 data, 9.3%
(n=8/86) increased or started corticosteroids relative to double-blind baseline (mean dose increase: 11.6mg); mean CFB in MG-ADL score: −7.4 (SD 4.6). At Week 120, 32% of patients with a ≥7.5mg dose at double-blind baseline had reduced their dose to a dose <7.5mg. TEAEs occurred in 97.0% (n=194/200) of patients.

SUMMARY/CONCLUSION: Treatment with zilucoplan allowed for reduction or discontinuation of corticosteroids in the majority of patients, while demonstrating sustained efficacy. Funding: UCB Pharma.

Disclosures:

Miriam Freimer - Served as a paid Consultant for Alexion Pharmaceuticals, argenx and UCB Pharma. She receives research support from Alnylam Pharmaceuticals, Avidity Biosciences, Fulcrum Therapeutics, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), the NIH and UCB Pharma.

Mark Vanderkelen - Employee and shareholder of UCB Pharma.

James F. Howard Jr. - Received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention (Atlanta, GA, USA), the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health (including the National Institute of Neurological Disorders and Stroke and the National Institute of Arthritis and Musculoskeletal and Skin Diseases), PCORI, and UCB Pharma; received honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-La Roche, Horizon Therapeutics (now Amgen), Medscape CME, Merck EMD Serono, NMD Pharma, Novartis, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, UCB Pharma, Regeneron Pharmaceuticals, Sanofi US, and Zai Labs; and received non-financial support from Alexion AstraZeneca Rare Disease, argenx, Toleranzia AB and UCB Pharma.

Angela Genge - Served as a paid Consultant for Alexion Pharmaceuticals, ALS Pharmaceuticals, Amicus Therapeutics, Amylyx Pharmaceuticals, Anelixis Pharmaceuticals, Anexon Biosciences, Apellis Pharmaceuticals, Atlantic Research Group, Biogen, Calico, Cytokinetics, Eli Lilly, Ionis Pharmaceuticals, Medtronic, Mitsubishi Tanabe Pharma, Orion, QurAlis, Ra Pharmaceuticals (now UCB Pharma), Roche, Sanofi Genzyme (now Sanofi), UCB Pharma and Wave Life Sciences.

Channa Hewamadduma - Received funding for consultancy on scientific or educational advisory boards for argenx, Biogen, Lupin, Roche and UCB Pharma; has received an investigator-led research grant from UCB Pharma; and study activities were supported by a Sheffield NIHR BRC UK centre grant.

M. Isabel Leite - Funded by the NHS (Myasthenia and Related Disorders Service and National Specialised Commissioning Group for Neuromyelitis Optica, UK) and by the University of Oxford, UK; has been awarded research grants from UK associations for patients with myasthenia and with muscular disorders (Myaware and Muscular Dystrophy UK, respectively) and the University of Oxford. She has received speaker honoraria or travel grants from Biogen, the Guthy-Jackson Charitable Foundation, Novartis and UCB Pharma. She serves on scientific or educational advisory boards for argenx, Horizon Therapeutics (now Amgen) and UCB Pharma.

Kimiaki Utsugisawa - Served as a paid Consultant for argenx, Chugai Pharmaceutical, HanAll Biopharma, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), Merck, Mitsubishi Tanabe Pharma, UCB Pharma and Viela Bio (now Amgen); and received speaker honoraria from Alexion Pharmaceuticals, argenx, the Japan Blood Products Organization and UCB Pharma.

Tuan Vu - USF Site Principal Investigator for MG clinical trials sponsored by Alexion Pharmaceuticals, Amgen, argenx, Cartesian Therapeutics, Dianthus Therapeutics, Immunovant, Johnson & Johnson, Regeneron Pharmaceuticals, RemeGen, and UCB Pharma; has served as a speaker for Alexion Pharmaceuticals, Allergan (now AbbVie), argenx, and CSL Behring; and performed consulting work for Alexion Pharmaceuticals, argenx, Dianthus Therapeutics, ImmunAbs, RemeGen, and UCB Pharma.

Babak Boroojerdi - Employee and shareholder of UCB Pharma.

Fiona Grimson - Employee and shareholder of UCB Pharma.

Natasa Savic - Employee and shareholder of UCB Pharma.

CONCOMITANT INTRAVENOUS IMMUNOGLOBULIN OR PLASMA EXCHANGE HAS NO EFFECT ON COMPLEMENT INHIBITION BY ZILUCOPLAN

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INTRODUCTION: Macrocyclic peptide complement component 5 inhibitor, zilucoplan, significantly improved myasthenia gravis (MG)-specific outcomes in the Phase 3 RAISE study (NCT04115293). An open-label extension, RAISE-XT (NCT04225871), is ongoing.

OBJECTIVE: Evaluate the impact of rescue therapy (intravenous immunoglobulin [IVIg] or plasma exchange [PLEX]) on zilucoplan concentration and complement inhibition in RAISE and RAISE-XT.

METHODS: In RAISE, adults with acetylcholine receptor autoantibody-positive generalized MG were randomized 1:1 to daily subcutaneous zilucoplan 0.3mg/kg or placebo for 12 weeks. Patients completing qualifying double-blind studies (NCT03315130/NCT04115293) could enter RAISE-XT to receive zilucoplan 0.3mg/kg daily. RAISE-XT primary outcome: incidence of treatment-emergent adverse events (TEAEs). Zilucoplan plasma concentration was measured pre- and post-administration on the day of rescue therapy by liquid chromatography-tandem mass spectrometry. Complement activity was measured by sheep red blood cell lysis assay, with post-measurement taken ≤1 day after rescue.

RESULTS: In patients with ≥1 week of zilucoplan 0.3mg/kg exposure during RAISE and RAISE-XT (N=200), 21 (10.5%) received IVIg and 10 (5.0%) received PLEX. Where available, zilucoplan steady-state concentrations were comparable between patients with and without rescue therapy. Mean (standard deviation) complement inhibition remained complete (>95%) pre- and post-rescue: 97.1% (0.80) and 97.4% (0.63) for IVIg (10 events with data), respectively. Pre- and post-rescue complement inhibition was 96.3% and 95.9% for PLEX (1 event with data), respectively. TEAEs occurred in 188 (94.0%) patients (data cutoff: September 08, 2022).

SUMMARY/CONCLUSION: Complete complement inhibition was maintained with rescue therapy during zilucoplan treatment, confirming that zilucoplan can be used concomitantly with IVIg and PLEX without the need for supplemental dosing. Funding: UCB Pharma.

Disclosures:

Michael D. Weiss - Received honoraria for serving on scientific advisory boards for Alexion Pharmaceuticals, Immunovant, Ra Pharmaceuticals (now UCB Pharma), argenx, Biogen, Mitsubishi Tanabe Pharma and Amylyx Pharmaceuticals, 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.

Anna Nordmark - Contractor for UCB Pharma.

Natasa Savic - Employee and shareholder of UCB Pharma.

James F. Howard Jr. - Received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention (Atlanta, GA, USA), the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health (including the National Institute of Neurological Disorders and Stroke and the National Institute of Arthritis and Musculoskeletal and Skin Diseases), PCORI, and UCB Pharma; has received honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-La Roche, Horizon Therapeutics (now Amgen), Medscape CME, Merck EMD Serono, NMD Pharma, Novartis, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, UCB Pharma, Regeneron Pharmaceuticals, Sanofi US, and Zai Labs; and has received non-financial support from Alexion AstraZeneca Rare Disease, argenx, Toleranzia AB and UCB Pharma.

Channa Hewamadduma - Received funding for consultancy on scientific or educational advisory boards for argenx, Biogen, Lupin, Roche and UCB Pharma; and received an investigator-led research grant from UCB Pharma; study activities were supported by a Sheffield NIHR BRC UK centre grant.

M. Isabel Leite - Funded by the NHS (Myasthenia and Related Disorders Service and National Specialised Commissioning Group for Neuromyelitis Optica, UK) and by the University of Oxford, UK; awarded research grants from UK associations for patients with myasthenia and with muscular disorders (Myaware and Muscular Dystrophy UK, respectively) and the University of Oxford; received speaker honoraria or travel grants from Biogen, the Guthy-Jackson Charitable Foundation, Novartis and UCB Pharma; serves on scientific or educational advisory boards for argenx, Horizon Therapeutics (now Amgen) and UCB Pharma.

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Tuan Vu - USF Site Principal Investigator for MG clinical trials sponsored by Alexion Pharmaceuticals, Amgen, argenx, Cartesian Therapeutics, Dianthus Therapeutics, Immunovant, Johnson & Johnson, Regeneron Pharmaceuticals, RemeGen, and UCB Pharma; served as a speaker for Alexion Pharmaceuticals, Allergan

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Babak Boroojerdi - Employee and shareholder of UCB Pharma.

René Bouw - Employee and shareholder of UCB Pharma.

Fiona Grimson - Employee and shareholder of UCB Pharma.

REAL-WORLD REDUCTION IN ORAL CORTICOSTEROID UTILIZATION AT 1-YEAR FOLLOWING EFGARTIGIMOD INITIATION

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OBJECTIVE: To evaluate oral corticosteroid (OCS) usage at 1-year following efgartigimod (EFG) initiation.

METHODS: Patients with generalized myasthenia gravis (gMG) using OCS pre-EFG initiation were identified from a United States medical and pharmacy claims database (based on information licensed from IQVIA: Longitudinal Access and Adjudication Data [LAAD] for the period April 2016−December 2023, reflecting estimates of real-world activity [all rights reserved]). Mean (SD) average daily dose (ADD) of OCS was evaluated during the 3-months prior to, and at 6- and 12-months post-EFG initiation. To assess outcomes, de-identified Myasthenia Gravis Activities of Daily Living (MG-ADL) data collected in the “My VYVGART Path” patient support program was tokenized and integrated into the primary dataset.

RESULTS: A total of 169 adults (aged ≥18 years) who were using chronic OCS pre-EFG initiation, initiated EFG by December 31, 2022, and continued EFG for at least 12 months were included in the analysis. At 6- and 12-months post-EFG, respectively, 31 (18%) and 45 (27%) patients had no OCS usage. Overall mean (SD) OCS ADD was significantly reduced at 6-months (13.2 [13.9] mg/day, P<0.001), and at 12-months (10.2 [12.1] mg/day, P<0.001) post-EFG initiation compared with baseline (17.2 [13.7] mg/day). Among a subset of 72 patients (43%) who had both pre- and post-EFG MG-ADL scores available, best-follow up mean (SD) MG-ADL was significantly reduced (from 8.3 [3.7] to 3.4 [2.8], P<0.001).

SUMMARY/CONCLUSION: : The significant reduction of OCS usage observed at 6-months post-EFG initiation was retained at 12-months, while demonstrating MG-ADL response expected from EFG treatment.

Disclosures:

Neelam Goyal - Served as a paid consultant for argenx, UCB, Janssen, and Alexion, and has grant support from argenx.

Cynthia Qi - Employee of argenx.

John Stone - Consulted for argenx on glucocorticoid toxicity.

Edward Brauer - Employee of argenx.

Matthew Jefferson - Employee of argenx.

Tharun Balaji Suthagar - Employee of ZS Associates and serves as a paid consultant for argenx.

Rohit R Menon - Employee of ZS Associates and serves as a paid consultant for argenx.

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TREATMENT RELATED INFECTION IN MYASTHENIA GRAVIS

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INTRODUCTION: Myasthenia Gravis (MG) is an autoimmune disorder of the neuromuscular junction treated with immunosuppressants. It is important to assess infection risk in MG due to increased morbidity and mortality in chronically treated patients.

OBJECTIVE: To characterize infection risk in patients with MG on chronic immunosuppression.

METHODS: Retrospective chart review of 101 patients from 2021-2023 at Houston Methodist Hospital with MG on immunosuppression, including prednisone. Patients on IVIG only were excluded.

RESULTS: Out of 101 patients, 67 (66%) had an infection with 30 (45%) having more than one infection. Mean age of patients with infection was 64 ±16 and most were female (41, 61%). Comorbidities included 20 (30%) diabetes, 16 (24%) malignancy, and Hashimoto's thyroiditis (5, 7%). Thirty-eight (57%) were on prednisone, 29 (43%) were on mycophenolate mofetil, 17 on azathioprine (25%), and 16 on rituximab (24%). Twenty (30%) patients were on more than one immunosuppressant and 63 (94%) were on immunosuppression for 1 year. Thirty-four (51%) had infections of upper respiratory tract (URI), 9 of urinary tract (13%) and 9 had pneumonia (13%). Twenty (30%) experienced worsening of their MG symptoms and 20 (30%) patients were hospitalized. Of those hospitalized, the mean length of stay (LOS) was 5 days (range 2-62).

SUMMARY/CONCLUSION: Two thirds of treated MG patients had an infection. Most patients were older and female. Mycophenolate mofetil, prednisone, and more than one immunosuppressant were associated with infection. URI was the most common infection. Mean hospitalization LOS was 5 days. Ongoing research will compare groups with and without infection.

Disclosures:

Ericka Greene - Avidity Biosciences -Advisor Strategic Working Group, Alexion Inc Advisor, Ionis ALS Fus DSBM member.

SAFETY AND EFFECTIVENESS OF NIPOCALIMAB IN ADOLESCENT PARTICIPANTS IN THE OPEN LABEL PHASE 2/3 VIBRANCE-MG CLINICAL STUDY

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INTRODUCTION: Nipocalimab is a fully human, effectorless IgG1 anti-neonatal Fc receptor (FcRn) monoclonal antibody. Nipocalimab may ameliorate generalized myasthenia gravis (gMG) disease manifestations by selectively targeting FcRn IgG recycling and lowering IgG, including pathogenic autoantibodies in gMG.

OBJECTIVE: To evaluate the effectiveness and safety of intravenous nipocalimab added to background standard-of-care therapy in adolescents with gMG.

METHODS: Seropositive patients (12-<18 years) with gMG (MGFA Class II-IV) on stable therapy but inadequately controlled, were enrolled in a 24-week open label study. Nipocalimab was administered as a 30 mg/kg IV loading dose followed by 15 mg/kg IV every 2 Weeks. The primary endpoint was change in total serum IgG. Secondary endpoints included change in MG-ADL and QMG scores. Safety was assessed.

RESULTS: Seven adolescents were enrolled, 5 have completed 24 weeks. Mean (SD) age was 14.1 (1.86) years; seven were anti-AChR+, six were female. Mean (SD) baseline scores were 4.29 (2.430) for MG-ADL, and 12.50 (3.708) for QMG. Nipocalimab showed a statistically significant reduction in total serum IgG at week 24; the mean (SD) percent change from baseline to week 24 for total serum IgG was -68.98% (7.561). The mean (SD) change at week 24 in MG-ADL was -2.40 (0.418) and in QMG was -3.80 (2.683); 4 of 5 patients achieved minimum symptom expression (MG-ADL score 0-1) by week 24. Nipocalimab was well-tolerated; there were no serious adverse events and no discontinuations due to an adverse event.

SUMMARY/CONCLUSION: Nipocalimab demonstrated efficacy and safety in this 6-month trial in seropositive adolescents with gMG.

Disclosures:

Jonathan Strober - Consultant fees from Pfizer; advisory/data monitoring board fees from Scholar Rock, Argenyx; speaker bureau fees from Biogen; research support from Anonymous, PTC, Fibrogen, Janssen, Biohaven; paid editor, associate editor, or editorial advisory board member for Pediatric Neurology; Expert Witness fees from many law firms

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Hong Sun - Employees of Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

Shawn Black - Employees of Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

Sindhu Ramchandren - Employees of Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

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Dan Huang - Employees of Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

LEVERAGING AI TO CHARACTERIZE MENTAL HEALTH EXPERIENCES THROUGHOUT THE MYASTHENIA GRAVIS DIAGNOSIS JOURNEY

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INTRODUCTION: Individuals living with Myasthenia Gravis (MG) have higher rates of anxiety and depression compared to the general US population.

OBJECTIVE: To characterize mental health experiences of anxiety, fear, depression, and hopelessness, as well as potential triggers for individuals throughout management and later stages of the MG diagnosis journey via MG digital conversations using AI.

METHODS: Proprietary AI-powered methodology was used to examine US MG-related English-language public-domain online conversations (August 2022-August 2023).

RESULTS: Among 9901 identified discussions capturing the MG diagnosis journey, 21% described pre-diagnosis, 33% diagnosis, 35% management, and 11% ongoing assessment of MG (stages 1-4, respectively). Posts reporting self-described anxiety decreased during management and ongoing-assessment stages from the pre-diagnosis and diagnosis stages (6% and 5% from 48% and 36%, respectively). Self-described fear decreased to 16% in stage-4 conversations from 38%, 43%, and 40%, respectively, from stages 1-3 conversations. Conversely, increasing proportions of posts indicating depressive feelings (14%, 21%, 43%, and 55%, stages 1-4) and hopelessness (0%, 0%, 11%, and 24%) were identified. Triggers for fear and anxiety included symptoms, uncertainty, fatigue, catastrophizing thoughts, and physical, financial, and relationship impacts. Depressive feelings were mainly triggered by impacts on quality-of-life, ineffective treatment, and lack of control.

SUMMARY/CONCLUSION: This digital conversation study identified decreasing rates of self-described anxiety and fear as individuals progressed to maintenance/ongoing-assessment stages, contrasting with increasing proportions of depressive feelings and hopelessness during the same stages. These AI-leveraged insights highlight the importance of establishing effective holistic treatment plans early to support patients with MG.

Disclosures:

Raghav Govindarajan - Served on ad board for Argenx, UCB, Janssen, Roche, and speakers bureau for Argenx and Alexion and UCB .

Ashley Anderson - Speakers Bureau member for Alexion Pharmaceuticals and Consultant for Janssen Pharmaceuticals.

Rachelle D. Rodriguez - Employee of Janssen Global Services, and a Johnson & Johnson stockholder.

Zia Choudhry - Works for Janssen full time as Senior Medical Director Autoantibody Rare Diseases, Immunology, and owns Takeda and Janssen stock.

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UNCONTROLLED MYASTHENIA GRAVIS CAN CONTRIBUTE TO ADDITIONAL STRESS BURDEN AND ADVERSE MENTAL HEALTH EXPERIENCES

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INTRODUCTION: Individuals with generalized myasthenia gravis (gMG) have higher rates of anxiety/depression than the general population.

OBJECTIVE: To investigate potential factors that may contribute to adverse mental-health in individuals with gMG.

METHODS: Twelve individuals with self-reported gMG diagnosis from a Patient Engagement Research Council (PERC; US-based/demographically-diverse) participated in the first two of three, two-hour, virtual focus-groups in February 2023. They described personal experiences from symptom-onset through recent-treatments. Transcripts were analyzed to identify stressors affecting mental-health.

RESULTS: All participants described stressors affecting mental-health experiences, including nine describing challenges associated with uncontrolled symptoms. These stressors were categorized into four themes: Treatments and Barriers (Healthcare-Providers [HCPs], Insurance, Medications, Other); Activities of Daily Living ([ADL] Work, Family, Personal-Care); Social-Support and Loneliness; and Discrimination (Body-Type, LGBTQ+, Race/Ethnicity, Other). Stressors generally adversely impacted mental-health, though some had a positive impact. Specific gMG-related stressors appear to contribute to adverse mental-health in individuals with gMG, which in turn can adds/worsens their gMG symptoms. Six individuals referred to the negative impact of stress/emotions on gMG symptoms. Two had experienced depression, five experienced anxiety, and each experienced trauma, guilt, and controlling emotions. A participant described their experience: “…I would get stressed out and upset when I couldn't do things…stress makes the myasthenia worse. If I get stressed out, I'm definitely going to get worse [symptomatically]. Have a lot of anxiety.” Seven referred to resilience regarding impacts of stressors in positive/negative terms (hopefulness/despair).

SUMMARY/CONCLUSION: Uncontrolled gMG contributes to the stress and mental-health burden that individuals experience. Stressors were related to gMG treatment, ADL, social-support, and discrimination.

Disclosures:

Kelly Gwathmey - Consulting for Argenx, UCB, and Alexion, and speaking engagements for Alexion.

Rachelle D. Rodriguez - Employee of Janssen Global Services, and a Johnson & Johnson stockholder.

Zia Choudhry - Works for Janssen full time as Senior Medical Director Autoantibody Rare Diseases, Immunology, and owns Takeda and Janssen stock.

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Neelam Goyal - Employee of Stanford Neuroscience Health Center, Palo Alto, CA, USA, and reports advisory and consulting engagements from Alexion, Argenx, UCB/Ra Pharma, Janssen, Amgen, and Lycia, and grant support from Argen.

SENTIMENT ANALYSIS OF DIGITAL CONVERSATIONS RELATED TO MYASTHENIA GRAVIS BY RACE/ETHNICITY

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INTRODUCTION: Myasthenia gravis (MG) is a rare neuromuscular disease characterized by muscle-weakness and fatigue, which imposes profound patient burden. Digital conversations can provide unprompted insights into perceptions, highlighting areas of greatest patient concern. There is a lack of data focusing on race/ethnicity.

OBJECTIVE: To describe sentiments/barriers/drivers related to MG through analyzing conversations by race/ethnicity.

METHODS: US-based public-domain patient-conversations focusing on MG and posted online from August 2022–2023 were mined. Content contributors were patients self-identified as White/Black/Hispanic/Asian within the conversations or public-profiles. Advanced-search techniques and artificial intelligence-powered algorithms were used to extract/organize data by topics. Natural-language-processing was conducted to identify sentiments, mindsets, and drivers/barriers towards treatment.

RESULTS: 13,163 conversations were extracted/segmented by patient race/ethnicity. Among 1,678 conversations by Black patients, 67% were negative-led by “misdiagnosis problems” (23%) and "impact on life (23%). “Uncertain” mindsets were more frequent among Black/Hispanics than White/Asian patients (47% and 55% vs. 39% and 40%). Frequent themes related to “barriers to treatment” were lack of efficacy and side-effects. "Level of relief", "duration", and "symptom relief" were the most frequent themes within the efficacy category for all groups. Cost/insurance was a more dominant theme for Black/Hispanic than Asian/White patients (15% and 18% vs. 4% and 5%).

SUMMARY/CONCLUSION: Conversations by race/ethnicity may indicate relevant differences in experiences of people living with MG. Black/Hispanic patients more frequently discuss misdiagnosis, which is often a challenge in the patient journey. Additionally, conversations highlighting cost/insurance issues may point to health disparities for persons of color. This data informs management strategies personalized to individual patients’ needs and priorities.

Disclosures:

Alex Lorenzo - Employee of CulturIntel, a research company paid by Janssen Pharmaceuticals to undertake the analyses for this study.

Ashley Anderson – Speaker Bureau member for Alexion Pharmaceuticals and Consultant for Janssen Pharmaceuticals.

Caroline Brethenoux - Employee of CulturIntel, a research company paid by Janssen Pharmaceuticals to undertake the analyses for this study.

Alyssa DeLuca - Employee of CulturIntel, a research company paid by Janssen Pharmaceuticals to undertake the analyses for this study.

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Rosario Alvarez - Employee of CulturIntel, a research company paid by Janssen Pharmaceuticals to undertake the analyses for this study.

Laura González Quijano - Employee of CulturIntel, a research company paid by Janssen Pharmaceuticals to undertake the analyses for this study.

FACTORS INFLUENCING EXACERBATIONS AND CRISES IN GENERALIZED MYASTHENIA GRAVIS: FINDINGS FROM A CLAIMS DATABASE STUDY

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INTRODUCTION: Generalized myasthenia gravis (gMG) is a rare, chronic autoantibody disease characterized by muscle weakness and fatigue; worsening symptoms can manifest as exacerbations and/or life-threatening crisis.

OBJECTIVE: Explore the relationship between select patient characteristics and exacerbations/crises among gMG patients.

METHODS: Newly diagnosed (incident) and prevalent gMG patients were identified within Optum's de-identified Clinformatics® Data Mart Database (01/2017-3/2023) for this retrospective cohort study. Associations between baseline characteristics and exacerbations/crises were assessed using case-control methods nested in the gMG cohort: patients who developed event(s) during follow up were classified as cases, and patients without events were controls, with relevant patient characteristics collected over the 12-months preceding the event (cases), or the 12-months preceding the follow-up end date (controls).

RESULTS: 12,813 prevalent and 3,748 incident gMG patients were identified. Rates of exacerbations and crises were 19.2 and 3.5 per 100 patient-years for prevalent patients and 33.9 and 7.5 per 100 patient-years for incident patients, respectively. Among prevalent gMG patients, prior exacerbation was significantly associated with future exacerbation (odds ratio [OR] 7.05, 95% confidence interval [CI]: 4.24-11.71); prior crisis was significantly associated with future crises (OR 3.29, 95% CI: 2.05-5.28). Among incident patients, late-onset MG (onset after age 50) was significantly associated with exacerbation events (OR 2.89, 95% CI: 1.40-5.95).

SUMMARY/CONCLUSION: Exacerbations/crises occur at a notable rate among patients with gMG, particularly patients with late-onset MG, and prior history of an exacerbation/crisis is a strong predictor of future occurrences. These findings suggest that an outstanding need remains for gMG treatments that provide stable disease control and avoidance of exacerbations/crises.

Disclosures:

Louis Jackson – Employee of Janssen Scientific Affairs, LLC and a Johnson & Johnson stockholder.

Zhiwen Liu - Employee of Janssen Scientific Affairs, LLC and a Johnson & Johnson stockholder.

Jacqueline Pesa - Employee of Janssen Pharmaceuticals US, Inc., Titusville, NJ, USA.

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IMPACT OF RACE AND SOCIAL DETERMINANTS OF HEALTH ON EXACERBATIONS IN GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: Generalized myasthenia gravis (gMG), a rare, chronic autoantibody disease characterized by muscle weakness and fatigue, can manifest as exacerbations when symptoms are uncontrolled.

OBJECTIVE: Explore the relationship between race and exacerbations in patients with gMG.

METHODS: This retrospective cohort study used US claims data from HealthVerity to identify adults with gMG (ICD-10-CM: G70.00, G70.01) between 1/2017-6/2023, 12 months continuous enrollment, and race information (White, Black, Asian, Hispanic). Exacerbation was defined as an inpatient episode with gMG diagnosis at admission. Inverse probability of treatment weighting was the method used to remove confounding and control for selection bias and estimate the probability of the exacerbation by race. To estimate social determinants of health (SDoH), Agency for Healthcare Research and Quality county-level estimates of percentage insured and income was assigned to individuals in the cohort using provider zip codes to further assess robustness of the effect of race on exacerbations after adjusting for SDoH factors for a subset of patients.

RESULTS: 10,981 eligible gMG patients were included. During follow-up, risk of exacerbation was significantly higher among Black vs White patients (incidence rate ratio 1.21; 95% confidence interval 1.03-1.42) and the association remained after controlling for percentage insured and income in the subset who could be linked to SDoH (n=5,147).

SUMMARY/CONCLUSION: Black gMG patients may be at higher risk of exacerbations even after controlling for SDoH and warrants further investigation. At-risk populations should be a focus for healthcare providers, disease management efforts, and patient support entities.

Disclosures:

Zhiwen Liu - Employee of Janssen Scientific Affairs, LLC and a Johnson & Johnson stockholder

Jacqueline Pesa - Employee of Janssen Pharmaceuticals US, Inc., Titusville, NJ, USA.

Louis Jackson - Employee of Janssen Scientific Affairs, LLC and a Johnson & Johnson stockholder

Alicia Campbell - Employee of Janssen Scientific Affairs, LLC and a Johnson & Johnson stockholder.

Ashley Anderson - Speakers Bureau member for Alexion Pharmaceuticals and Consultant for Janssen Pharmaceuticals.

COMPARATIVE RISK-BENEFIT PROFILES OF IMMUNOMODULATORY THERAPIES FOR PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS

A. Gordon Smith (Richmond, VA), Gil Wolfe (Buffalo, NY), Ali A. Habib (Irvine, CA), Cynthia Qi (Boston, MA), Hongbo Yang (Boston, MA), Mandy Du (Boston, MA), Xin Chen (Boston, MA), Deborah Gelinas (Boston, MA), Eddie Brauer (Boston, MA), Glenn Phillips (Boston, MA), Francesco Saccà (Naples, Italy)

INTRODUCTION: Several novel therapies have been recently approved in the United States for generalized myasthenia gravis (gMG), although their risk-benefit profiles have not yet been fully compared.

OBJECTIVE: To evaluate relative benefits and risks of treatments for anti-acetylcholine receptor antibody-positive (AChR Ab+) gMG.

METHODS: Clinical trials of neonatal Fc receptor inhibitors (efgartigimod intravenous [IV], rozanolixizumab) and complement inhibitors (ravulizumab, zilucoplan) vs. placebo were included in the primary network meta-analysis (NMA) comparing efficacy and safety outcomes. Efficacy outcomes included ≥3- and ≥5-point reduction from baseline for Myasthenia Gravis-Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) scores. Safety outcomes included serious, treatment-emergent, and commonly reported adverse events. For each treatment, the number needed to treat (NNT) and number needed to harm (NNH) vs. placebo were estimated from NMA outputs. A sensitivity analysis added efgartigimod subcutaneous (SC) and eculizumab to the NMA.

RESULTS: In the primary analysis, efgartigimod IV had the lowest NNT vs. placebo for achieving ≥5-point reduction in MG-ADL and ≥3-point reductions in QMG (significantly lower vs. ravulizumab and zilucoplan), and ≥5-point reduction in QMG (significantly lower than zilucoplan). Rozanolixizumab had the lowest NNT for ≥3-point reduction in MG-ADL (not statistically lower than other treatments). Sensitivity analyses indicated that efgartigimod SC and IV had comparable NNT, whereas eculizumab had comparable NNT to other complement inhibitors. The NNHs vs. placebo were similar across most safety outcomes assessed.

SUMMARY/CONCLUSION: Fc receptor inhibitors, in particular efgartigimod IV and SC, were associated with a favorable benefit-risk profiles compared to ravulizumab, zilucoplan, and eculizumab.

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A. Gordon Smith - Consulting fees from Abalone, Alexion, argenx, Disarm Therapeutics, Eidos, Lexicon, and Sangamo.

Glenn Phillips - Employee of argenx and holds stock/options.

Francesco Saccà - Public speaking honoraria from Alexion, argenx, Biogen, Genpharm, Medpharma Madison Pharma, Zai Lab; Advisory boards or consultation fees from Alexion, argenx, Biogen, Dianthus, Lexeo Therapeutics, Novartis, Reata, Sandoz; PI in clinical trials for Alexion, argenx, Immunovant, Lediant, Novartis, Prilenia, Remgen, Sanofi.

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SAFETY AND EFFICACY OF SUBCUTANEOUS IMMUNOGLOBULIN IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: Recent studies suggest subcutaneous immunoglobulin (SCIG) can reduce disability in generalized myasthenia gravis (GMG) or maintain stability induced by intravenous immunoglobulin (IVIG).

OBJECTIVE: This study evaluates the efficacy and safety of SCIG in GMG patients over six months using SCIG alone and IVIG followed by SCIG.

METHODS: A phase 2, open-label, randomized study (NCT04728425) enrolled patients over 18 with MGFA Class II-IV GMG. Arm 1 received IVIG for three months, followed by SCIG for three months. Arm 2 received SCIG alone for six months. The primary outcome was the change in MG impairment index (MGII). Secondary outcomes included MG-ADL, QMG, MGC, and MG-QOL15 scores.

RESULTS: Thirty patients were equally divided between Arm 1 (SCIG alone) and Arm 2 (IVIG followed by SCIG). The mean age was 57±15 years; 48% were female; the mean disease duration was 8±10 years; 82% were acetylcholine receptor antibody positive; and 52% were on prednisone. There were no significant baseline differences between arms in demographics or MGII scores. The overall mean improvement in MGII at six months was 6.4±7.3
(p=0.010), with no significant difference between the treatment groups. Secondary outcomes showed slight improvement but were not statistically significant. Most adverse events were mild or moderate, with common SCIG-related issues being local reactions. Three patients exited due to severe adverse events.

CONCLUSION: SCIG is well-tolerated and effective in GMG over six months. Additional evidence is needed to confirm if SCIG alone is sufficient for sustained clinical response.

Disclosures:

Hans Katzberg - Consultant and has received clinical trial support for the current study by Takeda Pharmaceuticals. Unrelated to the current work, he has been a consultant to Octapharma,UCB, Alnylam, CSL Behring, Alexion, ArgenX, Dyne, Roche, Dianthus, Merz, he has been on the DSMB for Alexion, UCB, Abcuro, Octapharma and ArgenX and has received clinical trial support from CSL Behring, Roche and ArgenX.

Carolina Barnett - Advisory board for argenx, Alexion, UCB and Janssen. She has been a consultant for argenx Janssen and UCB; received research support from US Department of Defense, Muscular Dystrophy Canada and MGNet. Grifols and Octapharma; is the primary developer of the MGII and may receive royalties.

Vera Bril - Consultant : Akcea Therapeutics, Inc.; AZ-Alexion Pharmaceuticals, Inc.; Alnylam Pharmaceuticals, Inc.; argenX; CSL; F. Hoffmann-La Roche Ltd; Grifols; Immunovant, Inc.; Ionis Pharmaceuticals; Janssen Global Services, LLC; Japan Tobacco; Johnson & Johnson Services, Inc.; Novo Nordisk A/S; Octapharma USA, Inc.; Pfizer Inc.; Powell Mansfield Inc.; Sanofi; Takeda Pharmaceutical Company Limited. Research support: Akcea Therapeutics, Inc.; Alexion Pharmaceuticals, Inc.; argenx; AstraZeneca; CSL; Grifols; Immunovant, Inc.; Ionis Pharmaceuticals; Johnson & Johnson Services, Inc.; Momenta; Octapharma USA, Inc.; Takeda Pharmaceutical Company Limited; UCB S.A.

LONG-TERM SAFETY AND EFFICACY OF ZILUCOPLAN IN GENERALIZED MYASTHENIA GRAVIS: 120-WEEK INTERIM ANALYSIS OF RAISE-XT

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INTRODUCTION: RAISE-XT (NCT04225871), an ongoing, Phase 3, open-label extension study, will further enhance understanding of the safety and efficacy of zilucoplan, a macrocyclic peptide complement component 5 inhibitor, in patients with acetylcholine receptor autoantibody-positive generalized myasthenia gravis (gMG).

OBJECTIVE: Evaluate the long-term safety, and efficacy up to 120 weeks, of zilucoplan treatment in patients with gMG in an interim analysis of RAISE-XT.

METHODS: RAISE-XT enrolled adults with gMG who completed a qualifying double-blind study (NCT03315130/NCT04115293). Patients self-administered daily subcutaneous injections of zilucoplan 0.3mg/kg. Primary outcome was incidence of treatment-emergent adverse events (TEAEs). Change from double-blind baseline to Week 120 in Myasthenia Gravis Activities of Daily Living (MG-ADL) score was analyzed for pooled data from participants who received zilucoplan 0.3mg/kg or placebo in the qualifying studies.

RESULTS: Overall, 200 patients enrolled in RAISE-XT. At data cutoff (November 11, 2023), median (range) exposure to zilucoplan was 2.2 (0.11-5.6) years. TEAEs occurred in 194 (97.0%) patients; 81 (40.5%) experienced a serious TEAE. The most common TEAEs were COVID-19 and myasthenia gravis worsening, occurring in 71 (35.5%) and 59 (29.5%) patients, respectively. Of 183 patients who received zilucoplan 0.3mg/kg or placebo in the qualifying study, 93 continued zilucoplan 0.3mg/kg and 90 switched from placebo to zilucoplan 0.3mg/kg. At Week 120, mean reduction from double-blind baseline in MG-ADL score in pooled zilucoplan 0.3mg/kg patients was 7.14 (standard error 0.44).

SUMMARY/CONCLUSION: In this RAISE-XT interim analysis, zilucoplan demonstrated a favorable long-term safety profile with sustained efficacy up to 120 weeks of treatment. Funding: UCB Pharma.

Disclosures:

James F. Howard Jr. - Received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention (Atlanta, GA, USA), the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health (including the National Institute of Neurological Disorders and Stroke and the National Institute of Arthritis and Musculoskeletal and Skin Diseases), PCORI, and UCB Pharma; has received honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-La Roche, Horizon Therapeutics (now Amgen), Medscape CME, Merck EMD Serono, NMD Pharma, Novartis, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, UCB Pharma, Regeneron Pharmaceuticals, Sanofi US, and Zai Labs; and has received non-financial support from Alexion AstraZeneca Rare Disease, argenx, Toleranzia AB and UCB Pharma.

Michael D. Weiss - Received honoraria for serving on scientific advisory boards for Alexion Pharmaceuticals, Immunovant, Ra Pharmaceuticals (now UCB Pharma), argenx, Biogen, Mitsubishi Tanabe Pharma and Amylyx Pharmaceuticals, consulting honoraria from Cytokinetics and CSL Behring, and speaker honoraria from Soleo Health. He also serves as a special government employee for the Food and Drug Administration.

Babak Boroojerdi - Employee and shareholder of UCB Pharma.

Petra W. Duda - Employee and shareholder of UCB Pharma.

Fiona Grimson - Employee and shareholder of UCB Pharma.

Mark Vanderkelen - Employee and shareholder of UCB Pharma.

M. Isabel Leite - Funded by the NHS (Myasthenia and Related Disorders Service and National Specialised Commissioning Group for Neuromyelitis Optica, UK) and by the University of Oxford, UK. She has been awarded research grants from UK associations for patients with myasthenia and with muscular disorders (Myaware and Muscular Dystrophy UK, respectively) and the University of Oxford. She has received speaker honoraria or travel grants from Biogen, the Guthy-Jackson Charitable Foundation, Novartis and UCB Pharma. She serves on scientific or educational advisory boards for argenx, Horizon Therapeutics (now Amgen) and UCB Pharma.

Miriam Freimer - Consultant for Alexion Pharmaceuticals, argenx and UCB Pharma. She receives research support from Alnylam Pharmaceuticals, Avidity Biosciences, Fulcrum Therapeutics, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), the NIH and UCB Pharma.

Angela Genge - Consultant for Alexion Pharmaceuticals, ALS Pharmaceuticals, Amicus Therapeutics, Amylyx Pharmaceuticals, Anelixis Pharmaceuticals, Anexon Biosciences, Apellis Pharmaceuticals, Atlantic Research Group, Biogen, Calico, Cytokinetics, Eli Lilly, Ionis Pharmaceuticals, Medtronic, Mitsubishi Tanabe Pharma, Orion, QurAlis, Ra Pharmaceuticals (now UCB Pharma), Roche, Sanofi Genzyme (now Sanofi), UCB Pharma and Wave Life Sciences.

Channa Hewamadduma - Received funding for consultancy on scientific or educational advisory boards for argenx, Biogen, Lupin, Roche and UCB Pharma; and has received an investigator-led research grant from UCB Pharma. His study activities were supported by a Sheffield NIHR BRC UK centre grant.

Angelina Maniaol - Received payment for travel, meeting attendance, consulting honoraria or advisory board participation from argenx, Biogen, CSL Behring, Novartis and UCB Pharma.

Renato Mantegazza - Received funding for travel and meeting attendance or advisory board participation from Alexion Pharmaceuticals, argenx, BioMarin, Catalyst, Sanofi, Regeneron Pharmaceuticals and UCB Pharma.

Kimiaki Utsugisawa - Consultant for argenx, Chugai Pharmaceutical, HanAll Biopharma, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), Merck, Mitsubishi Tanabe Pharma, UCB Pharma and Viela Bio (now Amgen); and he has received speaker honoraria from Alexion Pharmaceuticals, argenx, the Japan Blood Products Organization and UCB Pharma.

Tuan Vu - USF Site Principal Investigator for MG clinical trials sponsored by Alexion Pharmaceuticals, Amgen, argenx, Cartesian Therapeutics, Dianthus Therapeutics, Immunovant, Johnson & Johnson, Regeneron Pharmaceuticals, RemeGen, and UCB Pharma, and has served as a speaker for Alexion Pharmaceuticals, Allergan (now AbbVie), argenx, and CSL Behring. He performed consulting work for Alexion Pharmaceuticals, argenx, Dianthus Therapeutics, ImmunAbs, RemeGen, and UCB Pharma.

DEVELOPING NEEDS-DRIVEN MEDICAL EDUCATION FOR HEALTHCARE PROFESSIONALS IN MYASTHENIA GRAVIS

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INTRODUCTION: An analysis of the global myasthenia gravis (MG) educational landscape highlighted a lack of robustly designed ongoing education for the MG medical community.

OBJECTIVE: To cultivate an international MG community and provide a forum for knowledge translation, providing needs-based, outcomes-focused learning.

METHODS: Physician learning needs were identified through advisory boards, literature searches and a comprehensive needs assessment. A backward-planning model was used to establish educational program goals, a 10-year ambition and metrics for success at the outset. Touchpoints across the first 24 months were planned by a Steering Committee and mapped to priority learning outcomes based on identified learning needs. Educational content was designed to meet learning objectives, laddering up to the overarching learning outcomes. Learning transfer was sought by applying proven instructional design models and active learning techniques. To foster continued learning throughout the year, educational content was made available online.

RESULTS: The resulting product-agnostic educational program, Rare Disease Connect in Neurology, was initiated in 2021 with a 3-day virtual meeting attended by 127 healthcare professionals (HCPs) globally. Across all 3 days, the average HCP Impact Score was 8.6 (scores ≥7 indicate that HCPs find the education valuable). Overall, 91% of evaluation form respondents indicated intent to change their clinical practice (score of ≥3 on a 4-point scale). Now in its fourth year, 500 global HCPs are registered members of this MG community.

SUMMARY/CONCLUSION: This program supports robust education in MG. Metrics to assess implementation of learning are being evaluated. Learning needs assessments for the wider MG community are ongoing. Funding: UCB Pharma.

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argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention (Atlanta, GA, USA), the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health (including the National Institute of Neurological Disorders and Stroke and the National Institute of Arthritis and Musculoskeletal and Skin Diseases), PCORI, and UCB Pharma; has received honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-La Roche, Horizon Therapeutics (now Amgen), Medscape CME, Merck EMD Serono, NMD Pharma, Novartis, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, UCB Pharma, Regeneron Pharmaceuticals, Sanofi US, and Zai Labs; and has received non-financial support from Alexion AstraZeneca Rare Disease, argenx, Toleranzia AB and UCB Pharma.

Renato Mantegazza - Received funding for travel and meeting attendance or advisory board participation from Alexion Pharmaceuticals, argenx, BioMarin, Catalyst, Sanofi, Regeneron Pharmaceuticals and UCB Pharma.

Pushpa Narayanaswami - Received grant support from the Agency for Healthcare Research and Quality (AHRQ), the Patient-Centered Outcomes Research Institute (PCORI), UCB Pharma and Alexion and consultation fees from argenx, Alexion, UCB Pharma, Janssen, Sarepta, GSK and Dianthus and is a member of the Data and Safety Monitoring Board for Sanofi.

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Heinz Wiendl - Scientific Advisor for Abbvie, Alexion Pharmaceuticals, argenx, Bristol Myers Squibb/Celgene, Janssen, Merck, Novartis and Sandoz. He has received speaker honoraria and travel support from Alexion Pharmaceuticals, Biogen, Bristol Myers Squibb, Genzyme, Merck, Neurodiem, Novartis, Ology, Roche, TEVA and WebMD Global and is a paid Consultant for Abbvie, Actelion, argenx, BD, Biogen, Bristol Myers Squibb, EMD Serono, Fondazione Cariplo, Gossamer Bio, Idorsia, Immunic, Immunovant, Janssen Pharmaceuticals, Lundbeck, Merck, NexGen, Novartis, PSI CRO, Roche, Sanofi, the Swiss Multiple Sclerosis Society, UCB Pharma and Worldwide Clinical Trials. His research is funded by the German Ministry for Education and Research, Deutsche Forschungsgesellschaft, Deutsche Myasthenie Gesellschaft e.V., Alexion Pharmaceuticals, Amicus Therapeutics Inc., argenx, Biogen, CSL Behring, F. Hoffmann-La Roche, Genzyme, Merck KgaA, Novartis, Roche and UCB Pharma.

Sophie Barry - Employee of UCB Pharma.

Michelle Mackechnie - Employee of UCB Pharma.

PERINATAL TREATMENT PATTERNS IN MYASTHENIA GRAVIS

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INTRODUCTION: Clinical management of myasthenia gravis (MG) during pregnancy is complex, as both the disease and available treatments may have adverse effects on the mother and/or infant. Although clinical guidelines have been established, few studies of real-world medication utilization have been conducted in this population.

METHODS: We conducted a retrospective cohort study in the United States (US) Marketscan Commercial Claims and Encounters database between 2000-2023. Pregnancies in females aged 18-49 were identified. MG was defined by ≥1 inpatient or ≥2 outpatient diagnoses within a 365-day period, with ≥1 diagnosis required before pregnancy end. Prescription fills were summarized at the class level in preconception, pregnancy, and postpartum and included corticosteroids, rapid-acting immunotherapies, acetylcholinesterase inhibitors, steroid-sparing immunosuppressants, and monoclonal antibodies

RESULTS: Among 647 women with MG, 54.3% were untreated in the six months before pregnancy, 61.2% in pregnancy (68.8% in the first trimester), and 57.8% in the six months postpartum. The most common medication class was acetylcholinesterase inhibitors (31.2% before pregnancy, 26.9% in pregnancy, and 26.7% in postpartum) followed by corticosteroids (24.4%, 19.6%, and 24.0%, respectively). Those taking acetylcholinesterase inhibitors or corticosteroids before pregnancy were more likely to continue a medication in the class during pregnancy (67.3% and 53.8%, respectively) than those taking steroid-sparing immunosuppressants before pregnancy (42.5%). Of those taking acetylcholinesterase inhibitors or corticosteroids in pregnancy, 21.8% and 33.1% of them had not been taking them before pregnancy, respectively.

SUMMARY/CONCLUSION: Though most patients with MG did not receive treatment in the perinatal period, those who did showed dynamic patterns.

Disclosures:

Melanie H. Jacobson - Employed by, and hold stock in, Johnson & Johnson.

Rupa Makadia - Employed by, and hold stock in, Johnson & Johnson.

Anna Ostropolets - Employed by, and hold stock in, Johnson & Johnson.

John Sheehan - Employed by, and hold stock in, Johnson & Johnson.

Sicong Huang - Employed by, and hold stock in, Johnson & Johnson.

Rebecca Zaha - Employed by, and hold stock in, Johnson & Johnson.

Alexis A. Krumme - Employed by, and hold stock in, Johnson & Johnson.

ADVERSE PREGNANCY OUTCOMES IN MYASTHENIA GRAVIS: A RETROSPECTIVE COHORT STUDY IN A US HEALTH INSURANCE CLAIMS DATABASE

Melanie H. Jacobson (Raritan, NJ), Rupa Makadia (Raritan, NJ), John Sheehan (Pennington, NJ), Nathan Hall (Raritan, NJ), Jill Hardin (Raritan, NJ), Sicong Huang (Titusville, NJ), Ran Sun (Raritan, NJ), Rebecca Zaha (Raritan, NJ), Alexis A. Krumme (Raritan, NJ)

INTRODUCTION: Pregnancy is common among individuals with autoantibody conditions and adverse perinatal outcomes have been documented. However, previous studies in myasthenia gravis (MG) have produced mixed results

METHODS: We conducted a retrospective cohort study in the United States (US) Marketscan Commercial Claims and Encounters database between 2000-2023. Pregnancies in females aged 18-49 were identified and among live births, maternal and infant records were linked. MG was defined by ≥1 inpatient or ≥2 outpatient diagnoses within a 365-day period, with ≥1 diagnosis required before pregnancy end. The prevalence of six perinatal outcomes was calculated in the MG and total populations: live birth, spontaneous abortion, Cesarean section, preeclampsia, preterm birth, and small for gestational age (SGA). Outcome prevalence in the total population was standardized to the MG population age distribution.

RESULTS: A total of 694 individuals with MG had 900 pregnancies and 3,928,256 individuals in the total population had 5,185,726 pregnancies. The prevalence of live birth (75.0% vs. 72.6%) and spontaneous abortion (20.4% vs. 22.2%) was similar in the MG and age-adjusted total population, respectively. Preeclampsia and Cesarean section were more frequent among MG than the total population (10.7% vs. 7.1%; 42.9% and 36.7%, respectively). The largest relative differences were noted for preterm birth and SGA, which were more prevalent among MG than the total population (18.0% vs. 9.9%; 4.3% vs. 1.7%, respectively)

SUMMARY/CONCLUSION: MG was associated with a greater burden of certain adverse perinatal outcomes, occurring in both mother and infant. Further research is needed to understand drivers of pregnancy outcomes in MG

Disclosures:

Melanie H. Jacobson - Employed by, and hold stock in, Johnson & Johnson.

Rupa Makadia - Employed by, and hold stock in, Johnson & Johnson.

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Sicong Huang - Employed by, and hold stock in, Johnson & Johnson.

Ran Sun - Employed by, and hold stock in, Johnson & Johnson.

Rebecca Zaha - Employed by, and hold stock in, Johnson & Johnson.

Alexis A. Krumme - Employed by, and hold stock in, Johnson & Johnson.

PARTNERING WITH PATIENTS AND CAREGIVERS TO GUIDE THE DEVELOPMENT OF IMPACTFUL STUDY ENGAGEMENT TOOLS IN A GENERALIZED MYASTHENIA GRAVIS REAL WORLD STUDY

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INTRODUCTION: In recent years, research in myasthenia gravis (gMG) has seen significant advances. Clinical trials are conducted to advance new therapies while real-world studies are conducted to understand unmet needs. In rare diseases like gMG, patient recruitment and retention (R&R) is key to successful study completion. Within MGNation, a prospective real-world study, a Patient Engagement Research Council (PERC), comprised of gMG patients and caregivers was formed and focus groups were conducted to advise on the study R&R plans.

METHODS: The gMG PERC is a diverse group of patients and caregivers with respect to time since diagnosis, disease severity, serostatus, treatments, age, gender, and race/ethnicity. Nine gMG patients and 5 caregivers from the gMG PERC participated in 4 virtual, 2-hour semi-structured focus groups. Sessions focused on reviewing recruitment materials, accessibility, engagement, and retention strategies.

RESULTS: Insights gathered on recruitment materials provided actionable changes such as enlarging and standardizing text fonts to support patients with ocular MG symptoms while creating concise materials with easy-to-understand language for the end-user. Feedback on retention tactics was also assessed, such as interest in receiving a newsletter for study patients and desired frequency and channel of study reminders. Additional suggestions were also collected to better understand motivation and retention of patients in an ongoing 2-year study.

SUMMARY/CONCLUSION: Including patient and caregiver perspectives in the development and review of study recruitment material is key to creating thoughtfully designed and impactful engagement tools. This work highlights how patients and caregivers can contribute to scientific advancements and help better understand MG.

Disclosures:

Maria Ait-Tihyaty - Is or was employee, contractor or consultant for Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

Brindley Rospars - Is or was employee, contractor or consultant for Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

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Zia Choudhry - Is or was employee, contractor or consultant for Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

Lisa Shea - Is or was employee, contractor or consultant for Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

NON-STEROIDAL IMMUNOSUPPRESSANT THERAPY CHANGES DURING TREATMENT WITH ZILUCOPLAN IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: 120-WEEK FOLLOW-UP OF RAISE-XT

Tuan Vu (Tampa, FL), Miriam Freimer (Columbus, OH), Angela Genge (Montreal, Canada), Channa Hewamadduma (Sheffield, United Kingdom), M. Isabel Leite (Oxford, United Kingdom), Kimiaki Utsugisawa (Hanamaki, Japan), Babak Boroojerdi (Monheim, Germany), Fiona Grimson (Slough, United Kingdom), Natasa Savic (Bulle, Switzerland), James F. Howard Jr. (Chapel Hill, NC)

INTRODUCTION: The efficacy and safety of zilucoplan in patients with acetylcholine receptor autoantibody-positive generalized myasthenia gravis (gMG) were assessed in two double-blind studies (NCT03315130/NCT04115293). During these studies, and the first 12 weeks of the ongoing open-label extension RAISE-XT (NCT04225871), baseline non-steroidal immunosuppressant therapies (NSISTs) remained unchanged. Thereafter, NSISTs could be changed at the investigator's discretion.

OBJECTIVE: Evaluate NSIST changes in patients with gMG during zilucoplan treatment in RAISE-XT.

METHODS: In RAISE-XT, adults self-administered once-daily subcutaneous zilucoplan 0.3mg/kg. This post hoc analysis assessed the proportion of patients who changed NSIST relative to double-blind baseline, and change from baseline (CFB) in Myasthenia Gravis Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) scores at Week 120 (interim data cut: November 11, 2023).

RESULTS: In RAISE-XT, 200 patients enrolled. Of patients on NSISTs at double-blind baseline with Week 120 data, 29.8% (n=14/47) had decreased NSIST dose, including seven patients (14.9%) who discontinued NSIST. Mean (standard deviation [SD]) CFB in MG-ADL score at Week 120: −7.57 (4.69, decreased dose) and −7.00 (6.08, discontinuation); mean (SD) CFB in QMG score: −12.14 (6.30, decreased dose) and −13.00 (9.02, discontinuation). Amongst all patients with Week 120 data, only two increased NSIST dose (2.4%), including one patient who initiated a new NSIST; mean (SD) CFB in MG-ADL and QMG score: −6.50 (4.95) and −11.50 (0.71). Over a median of 2.2 years' follow-up, treatment-emergent adverse events occurred in 97.0% (n=194/200) of patients.

SUMMARY/CONCLUSION: Treatment with zilucoplan permitted discontinuation or dose reduction of NSIST

for some patients while demonstrating sustained efficacy.

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Tuan Vu - USF Site Principal Investigator for MG clinical trials sponsored by Alexion Pharmaceuticals, Amgen, argenx, Cartesian Therapeutics, Dianthus Therapeutics, Immunovant, Johnson & Johnson, Regeneron Pharmaceuticals and UCB Pharma, and has served as a speaker for Alexion Pharmaceuticals, argenx, and CSL Behring. He performed consulting work for Alexion Pharmaceuticals, argenx, Dianthus Therapeutics, ImmunAbs and UCB Pharma.

James F. Howard Jr. – Received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention (Atlanta, GA, USA), the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health (including the National Institute of Neurological Disorders and Stroke and the National Institute of Arthritis and Musculoskeletal and Skin Diseases), PCORI, and UCB Pharma; has received honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-La Roche, Horizon Therapeutics (now Amgen), Medscape CME, Merck EMD Serono, NMD Pharma, Novartis, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, UCB Pharma, Regeneron Pharmaceuticals, Sanofi US, and Zai Labs; and has received non-financial support from Alexion AstraZeneca Rare Disease, argenx, Toleranzia AB and UCB Pharma.

Miriam Freimer - Consultant for Alexion Pharmaceuticals, argenx and UCB Pharma. She receives research support from Alnylam Pharmaceuticals, Avidity Biosciences, Fulcrum Therapeutics, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), the NIH and UCB Pharma.

Angela Genge – Consultant for Alexion Pharmaceuticals, ALS Pharmaceuticals, Amicus Therapeutics, Amylyx Pharmaceuticals, Anelixis Pharmaceuticals, Anexon Biosciences, Apellis Pharmaceuticals, Atlantic Research Group, Biogen, Calico, Cytokinetics, Eli Lilly, Ionis Pharmaceuticals, Medtronic, Mitsubishi Tanabe Pharma, Orion, QurAlis, Ra Pharmaceuticals (now UCB Pharma), Roche, Sanofi Genzyme (now Sanofi), UCB Pharma and Wave Life Sciences.

Channa Hewamadduma - Received funding for consultancy on scientific or educational advisory boards for argenx, Biogen, Lupin, Roche and UCB Pharma; and has received an investigator-led research grant from UCB Pharma. His study activities were supported by a Sheffield NIHR BRC UK centre grant.

M. Isabel Leite - Funded by the NHS (Myasthenia and Related Disorders Service and National Specialised Commissioning Group for Neuromyelitis Optica, UK) and by the University of Oxford, UK. She has been awarded research grants from UK associations for patients with myasthenia and with muscular disorders (Myaware and Muscular Dystrophy UK, respectively) and the University of Oxford. She has received speaker honoraria or travel grants from Biogen, the Guthy-Jackson Charitable Foundation, Novartis and UCB Pharma. She serves on scientific or educational advisory boards for argenx, Horizon Therapeutics (now Amgen) and UCB Pharma.

Kimiaki Utsugisawa - Consultant for argenx, Chugai Pharmaceutical, HanAll Biopharma, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), Merck, Mitsubishi Tanabe Pharma, UCB Pharma and Viela Bio (now Amgen); and he has received speaker honoraria from Alexion Pharmaceuticals, argenx, the Japan Blood Products Organization and UCB Pharma.

Babak Boroojerdi - Employee and shareholder of UCB Pharma.

Fiona Grimson - Employee and shareholder of UCB Pharma.

Natasa Savic - Employee and shareholder of UCB Pharma.

QUALITY OF LIFE OF OCULAR MG PATIENTS WITH PERSISTENT SYMPTOMS: COMPARISON WITH THE GENERAL POPULATION

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INTRODUCTION: Myasthenia Gravis (MG) is a rare autoimmune disorder associated with fatigue and muscle weakness.

OBJECTIVE: The objective was to compare the health-related quality-of-life (HRQoL) of ocular MG patients with persistent symptoms (POMG) to the general population. POMG patients were defined as having MGFA Class I, and daily/constant eyelid droop and/or daily/constant double vision, as reported by the patient.

METHODS: We used data from two multinational digital observation studies: MyRealWorld-MG (people with MG ; n=2424) and POPUP (people without MG ; n=9000). Study measurements included EQ-5D-5L, MG-QoL-15r (modified for the POPUP study), caregiver burden and sick leave. POPUP was used to estimate population norms.

RESULTS: The mean utility value was significantly lower for POMG patients (n=72) than for the general population (0.754 versus 0.799, p=0.023). POMG patients reported more problems in the EQ-5D-5L dimensions “pain/discomfort” and “performing usual activities”, and with bolt-on questions on tiredness and vision.

The mean MG-QoL-15r score was significantly worse for POMG patients than for the general population (9.2 versus 4.9, p<0.0001). POMG patients reported more severe problems on most items of the MG-QoL-15r, including frustration, losing independence and limitations in performing work and enjoying hobbies.

Compared to the general population, significantly more POMG patients took sick leave (28.2% versus 13.2%, p<0.0001). More POMG patients needed regular help from a caregiver but this difference was not significant (14% versus 8%, p=0.118).

CONCLUSION: MG patients in MGFA Class I with persistent ocular problems have significantly lower utility values, higher MG-QoL-15r scores and take more sick leave than the general population.

Disclosures:

Cynthia Qi - Employee of argenx, the sponsor of the MRW and POPUP study.

Febe Brackx - Received honoraria for data analysis and reporting.

Sarah Dewilde - Received honoraria for the analysis of the data and reporting.

Femke De Ruyck - Employee of argenx, the sponsor of the MRW and POPUP study.

Carolina Barnett - Served as member of the advisory board for argenx, Alexion, UCB and Janssen. She has been a consultant for argenx, Janssen and UCB. She has received research support from US Department of Defense, Muscular Dystrophy Canada and MGNet. Grifols and Octapharma. She is the primary developer of the MGII and may receive royalties.

Sui Wong - Has done consultancy work for argenx and Immunovant.

Rosa Jimenez - Employee of argenx, the sponsor of the MRW and POPUP study.

Jeffrey Guptill - Employee of Argenx, the sponsor of the MRW and POPUP study. (2010 MGFA and ABF Clinician-Scientist Development Award in Myasthenia Gravis Recipient)

ROZANOLIXIZUMAB TREATMENT PATTERNS IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: POST HOC ANALYSIS

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INTRODUCTION: In MycarinG (NCT03971422; Phase 3), adults with generalized myasthenia gravis (gMG) received one 6-week rozanolixizumab treatment cycle. All patients who enrolled in the open-label extension, MG0007 (NCT04650854), received one further treatment cycle with subsequent need-based cycles initiated at the investigator's discretion. This led to variability in treatment-free intervals and number of cycles received per patient.

OBJECTIVE: To describe the range of rozanolixizumab treatment patterns and assess their associations with baseline patient characteristics.

METHODS: We conducted a clustering analysis of the number of cycles per year using data from patients with ≥1 cycle from MycarinG and MG0007 (data cutoff: July 08, 2022). Baseline characteristics were assessed for association with number of cycles per year using multivariate regression models. Treatment-emergent adverse events were compared among the clusters.

RESULTS: The most balanced clustering and optimal goodness-of-fit was achieved using three clusters to describe number of cycles per year (low: <2.59; medium: 2.59–4.64; high: >4.64). Mean (standard deviation) number of cycles per year in each cluster was 1.50 (0.53, n=74), 3.59 (0.60, n=64) and 5.82 (0.72, n=50), respectively. Overall, baseline characteristics were balanced between the clusters and did not predict in which cluster a patient would be. Rozanolixizumab was generally well tolerated across the three clusters.

SUMMARY/CONCLUSION: These three treatment clusters demonstrate that rozanolixizumab cycle cadence varies between patients, from 1–7 cycles per year. This suggests that each patient takes an individualized approach to rozanolixizumab treatment based on their own gMG experience, as the study included a broad, adult gMG population.

Disclosures:

Funding: UCB Pharma.

Ali A. Habib - Received research support from Alexion Pharmaceuticals, argenx, Cabaletta Bio, Genentech/Roche, Immunovant, Regeneron Pharmaceuticals, UCB Pharma and Viela Bio (now Amgen). He has received honoraria from Alexion Pharmaceuticals, Alpine Immune Sciences, argenx, Genentech/Roche, Immunovant, Inhibrx, Regeneron Pharmaceuticals, NMD Pharma and UCB Pharma.

Thaïs Tarancón - Employee and shareholder of UCB Pharma.

Vera Bril - Consultant for Akcea, Alexion Pharmaceuticals, Alnylam, argenx, CSL, Grifols, Ionis, Immunovant, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), Momenta (now Johnson & Johnson), Novo Nordisk, Octapharma, Pfizer, Powell Mansfield, Roche, Sanofi, Takeda Pharmaceuticals and UCB Pharma. She has received research support from Akcea, Alexion Pharmaceuticals, argenx, CSL, Grifols, Immunovant, Ionis, Momenta (now Johnson & Johnson), Octapharma, Takeda Pharmaceuticals, UCB Pharma and Viela Bio (now Amgen).

Tuan Vu - USF Site Principal Investigator for MG clinical trials sponsored by Alexion Pharmaceuticals, Amgen, argenx, Cartesian Therapeutics, Dianthus Therapeutics, Immunovant, Johnson & Johnson, Regeneron Pharmaceuticals and UCB Pharma, and has served as a speaker for Alexion Pharmaceuticals, argenx, and CSL Behring. He performed consulting work for Alexion Pharmaceuticals, argenx, Dianthus Therapeutics, ImmunAbs and UCB Pharma.

Kimiaki Utsugisawa - Consultant for argenx, Chugai Pharmaceutical, HanAll Biopharma, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), Merck, Mitsubishi Tanabe Pharma, UCB Pharma and Viela Bio (now Amgen); and he has received speaker honoraria from Alexion Pharmaceuticals, argenx, the Japan Blood Products Organization and UCB Pharma.

Julian Grosskreutz - Consultant for Alexion Pharmaceuticals, Biogen and UCB Pharma, and his institution has received research support from the Boris Canessa Foundation.

John Vissing - Consultant on advisory boards for Amicus Therapeutics, Arvinas, Biogen, Fulcrum Therapeutics, Genethon, Horizon Therapeutics (now Amgen), Lupin, ML Biopharma, Novartis, Regeneron, Roche, Sanofi Genzyme (now Sanofi), Sarepta Therapeutics and UCB Pharma. He has received research, travel support and/or speaker honoraria from Alexion Pharmaceuticals, argenx, Biogen, Edgewise Therapeutics, Fulcrum Therapeutics, Lupin, Sanofi Genzyme (now Sanofi) and UCB Pharma. He is a Principal Investigator in clinical trials for Alexion Pharmaceuticals, argenx, Genethon, Horizon Therapeutics (now Amgen), Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), ML Biopharma, Novartis, Regeneron Pharmaceuticals, Roche, Sanofi Genzyme (now Sanofi) and UCB Pharma.

Marion Boehnlein - Employee and shareholder of UCB Pharma.

Fiona Grimson - Employee and shareholder of UCB Pharma.

Irene Pulido-Valdeolivas - Employee and shareholder of UCB Pharma.

CLC-1 INHIBITION IMPROVES SKELETAL MUSCLE FUNCTION IN RAT MODELS AND PATIENTS WITH MYASTHENIA GRAVIS.

Martin Skov (Aarhus N, Denmark), Thomas S Grønnebæk (Aarhus N, Denmark), Marianne Skals (Aarhus N, Denmark), Nete Huus (Aarhus N, Denmark), Martin Gruwier Broch-Lips (Aarhus N, Denmark), Thomas K. Petersen (Aarhus N, Denmark), Jorge A. Quiroz (Boston, MA), Thomas H. Pedersen (Aarhus N, Denmark)

INTRODUCTION: ClC-1 is a Cl- ion channel specifically expressed in skeletal muscle cells. The channel stabilizes the resting membrane potential and dampens muscle fiber excitability and is involved in regulating muscle fiber excitability during intense exercise. Recently, it was shown that inhibition of the ClC-1 channel improves neuromuscular transmission in isolated rat muscle exposed to a neuromuscular blocking agent. This pharmacological approach mimics a neuromuscular transmission failure, suggesting that ClC-1 inhibition could be a possible mechanism to improve neuromuscular transmission in diseases with neuromuscular transmission failure. While neuromuscular transmission is reliable in healthy individuals, transmission failure causes weakness and fatigue in a range of neuromuscular diseases including Myasthenia Gravis (MG).

OBJECTIVE: In the present study we investigated the effect of ClC-1 inhibition in pre-clinical models of neuromuscular dysfunctions. Two animal models were used; a pharmacological model induced in healthy rats and an actively immunized MG rat model

RESULTS: Our results show that pharmacological inhibition of ClC-1 restores synaptic transmission and skeletal muscle function leading to marked improvements in muscle strength in both the pharmacological model of neuromuscular dysfunction as well as in the MG rat model. Specifically, we found that compound muscle actions potentials and stimulated muscle force were both markedly improved when animals were dosed with the ClC-1 inhibitor NMD670, and that this translated to improved running performance and grip strength.

SUMMARY/CONCLUSION: These findings suggest ClC-1 inhibition as a potential novel approach to enhancing neuromuscular transmission, thereby leading to improved muscle function and restored mobility, in disorders where neuromuscular transmission is compromised.

Disclosures:

Martin Skov - Employed at NMD Pharma.

Thomas S Grønnebæk - Employed at NMD Pharma.

Marianne Skals -Employed at NMD Pharma.

Nete Huus - Employed at NMD Pharma.

Martin Gruwier Broch-Lips - Employed at NMD Pharma.

Thomas K. Petersen - Employed by NMD Pharma.

Jorge A. Quiroz - Employed by NMD Pharma.

Thomas H. Pedersen - Employed by NMD Pharma.

DETERMINATION OF THE OPTIMAL COMPOUND MUSCLE ACTION POTENTIAL AMPLITUDE DECREMENT CUTOFF VALUES IN THE DIAGNOSIS OF MYASTHENIA GRAVIS USING REPETITIVE NERVE STIMULATION STUDIES

Alexandra Bonner (Cleveland, OH), John Morren (Cleveland, OH), John Bireley (Cleveland, OH)

INTRODUCTION: Repetitive nerve stimulation (RNS) is used to assess transmission at the neuromuscular junction in disorders such as Myasthenia Gravis (MG). RNS is considered abnormal when there is a reproducible compound muscle action potential (CMAP) amplitude decrement that exceeds a prespecified cutoff value.

OBJECTIVE: In this study we aim to assess the sensitivity and specificity of a range of CMAP amplitude decrement cutoff values during RNS in the electrodiagnosis of MG to determine if a decrement cutoff below the accepted standard of 10% significantly affects the diagnostic yield of RNS testing.

METHODS: RNS data from 241 adults [57 with MG (44 generalized, 13 ocular) and 184 without MG] evaluated at the Cleveland Clinic Neuromuscular Center between April 2020 - April 2022 were reviewed retrospectively. The Youden index was calculated across five muscles at seven timepoints (1 baseline, and 6 postexercise values) to determine the value at which sensitivity and specificity for the diagnosis of MG were optimized (described as the “optimal amplitude decrement cutoff”).

RESULTS: Only 2/35 (6%) optimal amplitude decrement cutoff values were greater than the standard 10% cutoff. Despite an overall mean decrement cutoff value of <5% in our data, the sensitivity and specificity for the diagnosis of MG is 54% on average (range: 30-89%), and 85% on average (range: 50-100%) respectively, which is comparable to previously published data.

SUMMARY/CONCLUSION: These data support that lowering the amplitude decrement cutoff value from 10% to 5% for a diagnosis of MG using RNS maintains sensitivity with little effect on specificity, thereby facilitating increased diagnostic yield.

CLC-1 INHIBITION IMPROVES QMG SCORE AND SKELETAL MUSCLE FUNCTION IN PATIENTS WITH MYASTHENIA GRAVIS

Vera Kiyasova (Aarhus, Denmark), Titia Q. Ruijs (Leiden, Netherlands), Thomas S Grønnebæk (Aarhus N, Denmark), Martin Skov (Aarhus N, Denmark), Jan Verschuuren (Leiden, Netherlands), W. David Arnold (Pickerington, OH), Geert J. Groeneveld (Leiden, Netherlands), Thomas K. Petersen (Aarhus N, Denmark), Jorge A. Quiroz (Boston, MA), Thomas H. Pedersen (Aarhus N, Denmark)

INTRODUCTION: ClC-1 is a Cl- ion channel specifically expressed in skeletal muscle cells. The channel stabilizes the resting membrane potential and dampens muscle fiber excitability and is involved in regulating muscle fiber excitability during intense exercise. Recently, it was shown that inhibition of the ClC-1 channel improves neuromuscular transmission in isolated rat muscle exposed to a neuromuscular blocking agent. This pharmacological approach mimics a neuromuscular transmission failure, suggesting that ClC-1 inhibition could be a possible mechanism to improve neuromuscular transmission in diseases with neuromuscular transmission failure. While neuromuscular transmission is reliable in healthy individuals, transmission failure causes weakness and fatigue in a range of neuromuscular diseases including Myasthenia Gravis (MG).

OBJECTIVE: In the present study we investigated the effect of the ClC-1 inhibitor NMD670 in MG patients

METHODS: A 3-way, cross-over design in 12 patients, each patient was administered a single dose of either placebo, 400 mg NMD670 or 1200 mg NMD670.

RESULTS: The study showed that NMD670 improved Quantitative Myasthenia Gravis (QMG) scale in patients with mild symptoms by 2 points, compared to placebo, in 42 to 50 % of the patients in both doses and at both the 3- and 5-hour time points post administration. Individual functional tests comprising the QMG scale, such as hand grip strength, ptosis, and dysarthria also showed improvement in patients receiving NMD670 compared to placebo treatment.

SUMMARY/CONCLUSION:These findings suggest ClC-1 inhibition as a potential novel approach to enhancing neuromuscular transmission, thereby leading to improved muscle function and restored mobility, in disorders where neuromuscular transmission is compromised.

Disclosures:

Vera Kiyasova - Employed by NMD Pharma.

Thomas H. Pedersen - Employed by NMD Pharma.

Thomas S Grønnebæk - Employed by NMD Pharma.

Martin Skov - Employed by NMD Pharma.

W. David Arnold - Received travel grants from NMD Pharma,

Thomas K. Petersen - Employed by NMD Pharma.

Jorge A. Quiroz - Employed by NMD Pharma.

OUTCOMES FOR PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS PRESCRIBED RAVULIZUMAB, ECULIZUMAB, OR EFGARTIGIMOD TREATMENT: INTERIM ANALYSIS OF A RETROSPECTIVE MEDICAL RECORD ANALYSIS (ELEVATE)

Christopher A. Scheiner (Knoxville, TN), Samir P. Macwan (Palm Springs, CA), Nicholas Streicher (Washington, DC), Karen S. Yee (Boston, MA), Chloe Sader (New York, NY), Michael Blackowicz (Boston, MA), Nana Numapau (Chandler, AZ), Danielle Gentile (Charlotte, NC), Jason Sharpe (Durham, NC), Prathamesh Pathak (Dublin, OH), Michael T. Pulley (Jacksonville, FL)

INTRODUCTION: Targeted therapies such as ravulizumab and eculizumab (terminal complement inhibitors) and efgartigimod (neonatal Fc receptor blocker) are approved to treat anti-acetylcholine receptor antibody-positive (AChR-Ab+) generalized myasthenia gravis (gMG). However, there is a lack of real-world data assessing clinical outcomes among patients treated with these therapies.

OBJECTIVE: Evaluate outcomes among patients with gMG treated with ravulizumab, eculizumab, or efgartigimod as first targeted immunotherapy.

METHODS: Physician-abstracted electronic medical records were included for adults with AChR-Ab+ gMG in Cardinal Health's Neurology Provider Extended Network who initiated targeted immunotherapy on or after December 1, 2021. Outcomes included clinical characteristics and Myasthenia Gravis Activities of Daily Living (MG-ADL) total scores ≥2 years pre-initiation and MG-ADL total scores ≥2 years following initiation. Interim results are included here (≥3- to 6-month follow-up post treatment initiation).

RESULTS: Data were available for 109 patients (ravulizumab, n=37; eculizumab, n=12; efgartigimod, n=60). Mean±SD age at initiation was 62.0±14.0 years for ravulizumab, 58.8±14.8 for eculizumab, and 52.0 ±16.5 for efgartigimod. Pre-initiation, mean±SD MG-ADL total scores were 8.7±2.7 in the ravulizumab group, 7.7±1.8 in the eculizumab group, and 9.3±3.3 in the efgartigimod group. Mean±SD MG-ADL total scores at 3 months post-initiation were 4.5±3.2, 3.5±3.0, and 6.3±3.2 with ravulizumab, eculizumab, and efgartigimod, respectively, and at 6 months post initiation, total scores were 0.4±0.5, 3.1±4.2, and 2.6 ±2.8, respectively.

SUMMARY/CONCLUSION: Although patient characteristics differed between targeted immunotherapy groups, interim results suggest that

ravulizumab may provide greater symptom control benefit than alternative therapies as measured by MG-ADL. Currently, patient accrual is ongoing, and additional outcomes with extended follow-up will be presented

Disclosures:

Christopher A. Scheiner - Consulted for Alexion and CSL Behring.

Prathamesh Pathak - Employee of Cardinal Health, which received funding to conduct this research.

Michael T. Pulley - Received compensation for medical advisory board membership or regional advisory board participation from Alexion, AstraZeneca Rare Disease, argenx, Catalyst, CSL Behring, Immunovant, and UCB.

Samir P. Macwan - Consultant for Abbvie, Alexion, argenx, Catalyst, Grifols, KabaFusion, Supernus, and UCB.

Nicholas Streicher - Speaker for Alexion and Catalyst.

Karen S. Yee - Employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.

Chloe Sader - Employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.

Michael Blackowicz - Employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.

Nana Numapau - Employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.

Danielle Gentile - Employee of Cardinal Health, which received funding to conduct this research.

Jason Sharpe – Employee of Cardinal Health, which received funding to conduct this research.

CHANGE IN CONCOMITANT IMMUNOSUPPRESSIVE THERAPIES FOR GENERALIZED MYASTHENIA GRAVIS IN PATIENTS RECEIVING COMPLEMENT C5 INHIBITOR THERAPIES: A RETROSPECTIVE ANALYSIS OF REGISTRY DATA

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INTRODUCTION: Complement C5 inhibitor therapies (C5ITs) eculizumab and ravulizumab are approved for anti-acetylcholine receptor antibody-positive generalized myasthenia gravis (gMG). Although immunosuppressive therapies (ISTs) can be effective in gMG, high doses may be associated with adverse events. The global MG SPOTLIGHT Registry is assessing C5IT safety/effectiveness and concomitant IST (con-IST) use in adults with gMG in clinical practice.

OBJECTIVE: Describe changes in con-IST use after initiation of eculizumab and/or ravulizumab treatment.

METHODS: The current analysis included registry patients who transitioned from eculizumab to ravulizumab, had available con-IST (azathioprine, mycophenolate mofetil, intravenous immunoglobulin/plasma exchange, oral corticosteroid [OCS]) data, and received eculizumab and ravulizumab for ≥1y. Frequency/type of serious adverse events were assessed.

RESULTS: Of 226 gMG patients in the SPOTLIGHT Registry (Oct-2-2023), 61 had received eculizumab and ravulizumab (male: 60.7%; mean±SD ages: 56.2 ±20.4y [MG diagnosis]; 61.9±16.8y [eculizumab initiation]; 64.8±17.1y [eculizumab-to-ravulizumab transition]), with treatment durations of 2.8±1.8y (eculizumab) and 0.8±0.4y (ravulizumab). At eculizumab initiation, 61.9%/35.7%/2.4% were receiving 1/2/3 con-ISTs; after C5IT, the number of con-ISTs used decreased in 16/42 patients (38.1%), increased in 4/42 (9.5%), and was unchanged in 22/42 (52.4%). OCS dose (mg/day) decreased from eculizumab initiation (14.5±15.0; n=32) to last ravulizumab dose assessed (6.2±7.0). The proportion of patients receiving ≤5/≤10mg/day OCS increased from 37.5%/62.5% to 68.8%/81.3% after C5IT. C5ITs were well tolerated, consistent with previous analyses, including clinical trial data.

SUMMARY/CONCLUSION: These descriptive registry results represent clinical practice and demonstrate reduced OCS burden in patients with gMG receiving eculizumab and ravulizumab. No adjustment for confounders was performed. Data for patients receiving ravulizumab only are forthcoming.

Disclosures:

Richard J. Nowak - Received research support from Alexion, AstraZeneca Rare Disease, Annexon Biosciences, Inc., argenx, Genentech, Inc., Grifols, S.A., Immunovant, Inc., Momenta Pharmaceuticals, Inc., the Myasthenia Gravis Foundation of America, Inc., the National Institutes of Health, Ra Pharmaceuticals, Inc. (now UCB S.A.), and Viela Bio, Inc. (Horizon Therapeutics plc, now Amgen); has served as consultant/advisor for Alexion, AstraZeneca Rare Disease, argenx, Cabaletta Bio, Inc., Cour Pharmaceuticals, Grifols, S.A., Immunovant, Inc., Momenta Pharmaceuticals, Inc., Ra Pharmaceuticals, Inc. (now UCB S.A.), and Viela Bio, Inc. (Horizon Therapeutics plc, now Amgen).

Ali A. Habib - Received research support from Alexion, AstraZeneca Rare Disease, argenx, Cabaletta Bio, Genentech/Roche, 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.

Christopher A. Scheiner - Received compensation for medical advisory board membership and/or serving as a speaker for Alexion, AstraZeneca Rare Disease, argenx, and CSL Behring.

Lida Zeinali - Employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.

Michael T. Pulley - Received compensation for medical advisory board membership or regional advisory board participation from Alexion, AstraZeneca Rare Disease, argenx, Catalyst, CSL Behring, Immunovant, and UCB.

Chuang Liu - Employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.

Andrew J. Gordon - Received honoraria from Alexion, AstraZeneca Rare Disease, argenx, Janssen, and UCB.

Ashley Yegin - Employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.

Pushpa Narayanaswami - Received research support from, served on advisory boards or as Data Monitoring Committee Chair for, or been speaker for Alexion, AstraZeneca Rare Disease, argenx, Momenta/Janssen, PCORI, Ra Pharmaceuticals Inc, Sanofi, and UCB.

ORAL CLADRIBINE CAPSULES FOR GENERALIZED MYASTHENIA GRAVIS: DESIGN OF AN ACTIVELY-RECRUITING PHASE 3 CLINICAL STUDY – THE MYCLAD STUDY

Henry Kaminski (Washington, DC), James F. Howard Jr (Chapel Hill, NC), Gary Cutter (Birmingham, AL), Kevin C. O'Connor (New Haven, CT), Mazen M. Dimachkie (Kansas City, MO), Jacqueline Palace (Oxford, United Kingdom), Andreas Meisel (Berlin, Germany), Renato Mantegazza (Milan, Italy), Axel Nolting (Darmstadt, Germany), Sathej Gopalakrishnan (Darmstadt, Germany), Claire Le Bolay (Lyon, France), Andrija Javor (Eysins, Switzerland), Nektaria Alexandri (Darmstadt, Germany), Dominic Jack (Middlesex, United Kingdom), Konrad Rejdak (Lublin, Poland)

INTRODUCTION: Myasthenia Gravis (MG) is an autoimmune disorder of neuromuscular junction transmission, characterized by fluctuating muscle weakness, often beginning in ocular muscles and progressing to generalized MG (gMG). Cladribine targets B and T cells and has shown efficacy in a pilot study of participants with gMG. We present the design of MyClad; an actively-recruiting Phase 3 trial of cladribine capsules (CladC) in gMG.

OBJECTIVE: To evaluate efficacy and safety of CladC versus placebo in gMG.

METHODS: MyClad is a 3-year Phase 3 trial that aims to recruit participants with gMG Class II-IVa (MG Foundation of America Classification). In the first double-blind placebo-controlled period of 24 weeks, participants will be randomized 1:1:1 to two short courses of placebo or one of two CladC doses. In the following blinded extension period of 24 weeks, placebo recipients will be re-randomized to one of two CladC doses. During this period and a third double-blind follow-up period of 96 weeks, any participant may be retreated with CladC if clinically needed.

RESULTS: MyClad plans to recruit 240 participants. The primary endpoint is change from baseline (CFB) to Week 24 in MG-Activities of Daily Living score for each CladC dose versus placebo. Secondary endpoints include CFB to Week 24 in Quantitative MG, MG Composite and MG 15-Item Quality of Life Scale revised scores, time from CladC full dose to retreatment or rescue treatment, safety, and CladC pharmacokinetics.

SUMMARY/CONCLUSION: MyClad will actively recruit and seeks to establish meaningful clinical benefits of CladC in gMG by targeting B and T cell-mediated autoimmunity.

Disclosures:

Henry Kaminski - Principal investigator for the Rare Disease Network, MGNet, supported by NIH grant U54NS115054 and a consultant for R43NS12432; is a consultant for Canopy Immuno Therapeutics, Roche, Takeda, Cabaletta Bio, UCB Pharmaceuticals, EMD Serono, Ono Pharmaceuticals, ECoR1, Gilde Healthcare, and Admirix, Inc. Argenix provides an unrestricted educational grant to George Washington University. Dr Kaminski has equity interest in Mimivax, LLC.

Sathej Gopalakrishnan - Employee of Merck Healthcare KGaA, Darmstadt, Germany.

Claire Le Bolay - Employee of Merck Santé S.A.S., Lyon, France, an affiliate of Merck KGaA, Darmstadt, Germany.

Andrija Javor - Employee of Ares Trading SA, Eysins, Switzerland, an affiliate of Merck KGaA, Darmstadt, Germany.

Nektaria Alexandri - Employee of Merck Healthcare KGaA, Darmstadt, Germany.

Dominic Jack - Employee of Merck Serono Ltd., Middlesex, United Kingdom, an affiliate of Merck KGaA, Darmstadt, Germany.

Konrad Rejdak - Received speaking honoraria and travel expenses for participation in scientific meetings, and participated in advisory boards in the past years with Bayer, Biogen, Merck Healthcare KGaA, Novartis, Roche, Sanofi Genzyme, and Teva Pharmaceutical.

James F. Howard Jr - Research funding (paid to institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, Ra Pharmaceuticals/UCB Bioscience, and Takeda Pharmaceuticals; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biohaven Ltd, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc (now Amgen), Medscape CME, Merck EMD Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Ra Pharmaceuticals/UCB Bioscience, Regeneron Pharmaceuticals, Sanofi US, and Zai Labs; non-financial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Bioscience, and Zai Labs.

Gary Cutter - Data and Safety Monitoring Boards: Applied Therapeutics, AI therapeutics, AMO Pharma, AstraZeneca, Avexis Pharmaceuticals, Bristol Meyers Squibb/Celgene, CSL-Behring, Cynata Therapeutics, Horizon Pharmaceuticals, Immunic, Karuna Therapeutics, Kezar Life Sciences, Mapi Pharmaceuticals LTD, Merck, Mitsubishi Tanabe Pharma Holdings, Opko Biologics, Prothena Biosciences, Novartis, Pipeline Therapeutics, Regeneron, Sanofi-Aventis, Reata Pharmaceuticals, Teva Pharmaceuticals, United BioSource LLC, University of Texas Southwestern, University of Pennsylvania, Visioneering Technologies, Inc. Consulting or Advisory Boards: Alexion, Antisense Therapeutics, Avotres, Biogen, Clene Nanomedicine, Clinical Trial Solutions LLC, Endra Life Sciences, Cognito Therapeutics, Entelexo Biotherapeutics, Inc., Genzyme, Genentech, GW Pharmaceuticals, Hoya Corporation, Immunic, Immunosis Pty Ltd, Klein-Buendel Incorporated, Linical, Merck/Serono, Novartis, Perception Neurosciences, Protalix Biotherapeutics, Regeneron, Roche, SAB Biotherapeutics, Sapience Therapeutics. Dr Cutter is employed by the University of Alabama at Birmingham and President of Pythagoras, Inc., a private consulting company located in Birmingham AL.

Kevin C. O'Connor - Research support from Alexion Rare Disease, Seismic Therapeutics, Horizon (Amgen), and argenx; and is an equity shareholder of Cabaletta Bio.

Mazen M. Dimachkie - Serves or recently served as a consultant for Abcuro, Amicus, argenx, Astellas, Cabaletta Bio, Catalyst, CNSA, Covance/Labcorp, CSL-Behring, Dianthus, Horizon, EMD Serono/Merck, Fortrea, Ig Society, Inc, Ipsen, Janssen, Medlink, Nuvig, Octapharma, Priovant, Sanofi Genzyme, Shire Takeda, TACT/Treat NMD, Abata/Third Rock, UCB Biopharma, Valenza Bio, and Wolters Kluwer Health/UpToDate. Dr. Dimachkie received research grants or contracts or educational grants from Alexion/AstraZeneca, Alnylam Pharmaceuticals, Amicus, argenx, Bristol Myers Squibb, Catalyst, CSL-Behring, FDA/OOPD, GlaxoSmithKline, Genentech, Grifols, Mitsubishi Tanabe, MDA, NIH, Novartis, Octapharma, Orphazyme, Ra Pharma/UCB, Sanofi Genzyme, Sarepta Therapeutics, Shire Takeda, Spark Therapeutics, The Myositis Association, and UCB Biopharma/RaPharma.

Jacqueline Palace - Received support for scientific meetings and honoraria for advisory work from Merck Serono, Novartis, Chugai, Alexion, Roche, Medimmune, argenx, Vitaccess, UCB, Mitsubishi, Amplo, Janssen. Grants from Alexion, argenx, Clene, Roche, Medimmune, Amplo biotechnology. Patent ref P37347WO and licence agreement Numares multimarker MS diagnostics. Professor Palace has shares in AstraZeneca. Her group has been awarded an ECTRIMS fellowship and a Sumaira Foundation grant to start later this year. Professor Palace is a Charcot fellow, who worked in Oxford 2019–2021. She acknowledges partial funding to the university hospitals trust for highly specialised services by NHS England. She is on the medical advisory boards of the Sumaira Foundation and MOG project charities, is a member of the Guthy Jackson Charitable Foundation and MAGNIMS, is on the Board of the European Charcot Foundation and the steering committee of the UK NHSE IVIG Committee, was chairman of the NHSE neuroimmunology patient pathway, and is an ECTRIMS Council member, on the educational committee, since June 2023. She is on the ABN advisory groups for MS and neuroinflammation and was for neuromuscular diseases.

Andreas Meisel - Received speaker or consultancy honoraria or financial research support (paid to his institution) from Alexion Pharmaceuticals, argenx, Axunio, Desitin, Grifols, Hormosan Pharma, Janssen, Merck, Novartis, Octapharma, and UCB.

Renato Mantegazza - Received funding for travel, meeting attendance or advisory board participation from Alexion, argenx, Biomarin, Catalyst, Sanofi, Regeneron, and UCB.

Axel Nolting - Employee of Merck Healthcare KGaA, Darmstadt, Germany.

IMBALANCED PRO-INFLAMMATORY IMMUNE RESPONSES IN SEROPOSITIVE AND SERONEGATIVE MG

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INTRODUCTION: Imbalance of innate and adaptive immune cell subsets has been reported as an important feature of MG immunopathogenesis. Single-cell RNA sequencing (scRNA-seq) provides an opportunity to assess the roles of innate and adaptive immunity in an unbiased, comprehensive and parallel fashion.

METHODS: To validate our hypothesis that pro-inflammatory immune responses are imbalanced in MG, we utilized scRNA-seq to evaluate immune cell subsets in peripheral blood mononuclear cells (PBMCs) in four treatment-naïve MG patients (2 AChR + and 2 AChR-/MuSK-) and 24 healthy controls.

RESULTS: Our scRNA-seq analysis demonstrated high resolution for subgroup analysis in PBMCs and identified 30 cell subsets, including CD4, CD8, NK, γδT cells, monocytes, dendritic cells and B cells. In innate immune cell subsets, intermediate monocytes (CD14+ + CD16+), known for producing pro-inflammatory cytokines, were significantly expanded in MG patients compared to healthy controls. Conversely, regulatory NK cells and DCs were significantly decreased in MG patients. In adaptive immune cell subsets, pro-inflammatory B cells were significantly expanded, while regulatory CD4 and CD8 cells were decreased in MG patients. Pathway analysis further validated that PTPRC-MRC1, PTPRC-CD22, and SELPLG-SELL were significantly increased, whereas self-control HLA-CD8a was decreased in MG patients.

SUMMARY/CONCLUSION: Our results indicate that pro-inflammatory innate and adaptive immune cell subsets are imbalanced in both seropositive and seronegative MG patients. Pathway analysis suggests enhanced pro-inflammatory responses linking innate and adaptive immune cell subsets. This study demonstrates that scRNA-seq is a powerful tool for unbiased evaluation of immune cell subsets and provides insight into MG immunopathogenesis.

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DISTRIBUTION AND TEMPORAL CHANGES OF AUTOANTIBODY-MEDIATED PATHOGENIC MECHANISMS AMONG ACHR-POSITIVE MG PATIENTS

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INTRODUCTION: AChR-specific autoantibodies (AChR-Ab) mediate MG pathology through three molecular mechanisms: antibody-dependent complement deposition (ADCD), acetylcholine blocking, and receptor modulation. ADCD inhibition and FcRn-mediated IgG reduction are therapeutic approaches targeting AChR-Ab-mediated pathology. Given that AChR-Ab isotypes (IgG, IgM and IgA) and the four IgG subclasses mediate pathology with different efficiencies, the emergence of these new therapeutics underscores the importance of investigating the distribution of AChR-Ab isotype/subclass and the pathogenic mechanisms they mediate.

OBJECTIVE: To address this knowledge gap by measuring AChR-Ab isotypes, IgG subclasses, the three pathogenic mechanisms, and how they changed over two years.

METHODS: Longitudinally collected samples from 50 AChR-Ab+ MG patients were studied using a set of cell-based assays.

RESULTS: In cross-sectional samples, AChR-IgG was found in 92% of patients; the coexistence of IgM or IgA with IgG was observed in 6% and 8%, respectively, and 4% had all three isotypes. AChR-IgG1 was found in 67%, followed by IgG3 (21%), and IgG2 (17%). ADCD was active in 78%, followed by modulation (58%), and blocking (28%). ADCD and modulation were simultaneously active in 42%, ADCD and blocking were active in 10%, and all three were active in 16%. Blocking alone was active in 2%; modulation alone was not found. Temporal fluctuations of AChR-Ab isotypes/subclasses and associated pathogenic mechanisms were observed.

SUMMARY/CONCLUSION: These results demonstrate that a subset of patients can mediate pathogenic mechanisms and include isotypes/subclasses that current therapeutics may not effectively target. Accordingly, defining individual patient AChR-Ab profiles may afford more accurate

application of therapeutics designed to target specific autoantibody-mediated mechanisms.

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Kevin C O'Connor - Received research support from AstraZeneca-Alexion Rare Disease, Amgen, Cabaletta Bio, UCB, Seismic and argenx. K.C.O. is an equity shareholder of Cabaletta Bio. KCO has served as a paid advisor for Roche and Merck.

PROTEOMIC ANALYSIS REVEALS A DISTINCT IMMUNOLOGICAL SIGNATURE FOR LATE-ONSET MYASTHENIA GRAVIS

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INTRODUCTION: Myasthenia gravis (MG) is a heterogeneous autoimmune disease with autoantibodies against postsynaptic neuromuscular junction antigens (80% of patients with autoantibodies against acetylcholine receptor (AChR)). AChR+ MG patients may have varied clinical presentation, age of onset, and treatment response.

OBJECTIVE: This exploratory proteomics analysis examined the differences in the immunopathogenesis of AChR+ve early onset (symptom onset < 50 years of age) and late-onset MG (EOMG and LOMG) patients from the B-Cell Targeted Treatment in MG (BeatMG, NCT02110706) study utilizing a comprehensive panel of inflammatory markers.

METHODS: We used the Proximity Extension Assay (PEA) (provided by the Olink platform) to examine 768 inflammatory proteins in the baseline serum samples collected for the BeatMG study. We performed enrichment analysis to assess the pathways associated with proteins of interest.

RESULTS: Baseline samples from 47 patients [age: 54.9 ± 17.7, 22 women (47%)] out of 52 patients from the BeatMG study with all necessary data points were included. Twenty patients were categorized as EOMG [38.4 ± 12.4, 15 women (75%)], and 27 patients were in the LOMG [67.1 ± 8.7, 7 women (25.9%)] group. The EOMG group had a higher percentage of thymectomy (55% vs. 0%, p-value <0.001). Several proteins were more abundant in the LOMG group, including CXCL17, JCHAIN, CD83, and TNFRSF11A. These proteins are involved in regulating leucocyte differentiation, interleukin-10 production, and myeloid leukocyte differentiation and migration pathways. TNFRSF11A SNP has been previously reported to be associated with LOMG.

SUMMARY/CONCLUSION: LOMG is potentially mediated by distinct immunopathogenic mechanisms. Further validation of these findings is ongoing.

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Bhaskar Roy - Consultant for argenx, Takeda Pharmaceuticals. I have stocks in Caballeta Bio and Pfizer.

Fatemeh Khani-Habibabadi - Received a postdoctoral fellowship from the MGFA. (2022 MGFA Jackie McSpadden Post-Doctoral Fellow)

Kevin OConnor - Received research support from AstraZeneca-Alexion Rare Disease, Amgen, Cabaletta Bio, UCB, Seismic and argenx. K.C.O. is an equity shareholder of Cabaletta Bio. KCO has served as a paid advisor for Roche and Merck.

Richard Nowak – Received research support from the National Institutes of Health, Genentech, Inc., Alexion Pharmaceuticals, Inc., argenx, Annexon Biosciences, Inc., Ra Pharmaceuticals, Inc. (now UCB S.A.), the Myasthenia Gravis Foundation of America, Inc., Momenta Pharmaceuticals, Inc. (now Janssen), Immunovant, Inc., Grifols, S.A., and Viela Bio, Inc. (Horizon Therapeutics, now Amgen Inc.). Served as a consultant and advisor for Alexion Pharmaceuticals, Inc., argenx, Cabaletta Bio, Inc., Cour Pharmaceuticals, Ra Pharmaceuticals, Inc. (now UCB S.A.), Immunovant, Inc., Momenta Pharmaceuticals, Inc. (now Janssen), and Viela Bio, Inc. (Horizon Therapeutics, now Amgen Inc.).

Henry Kaminski - Principal investigator for the Rare Disease Network (MGNet supported by NIH grant U54NS115054) is a consultant for R43NS12432, Roche, Takeda, Cabaletta Bio, UCB Pharmaceuticals, Canopy EMD Serono, Ono Pharmaceuticals, ECoR1, Gilde Healthcare, and Admirix, Inc., has received research support from argenex (paid to institution), and has equity interest in Mimivax, LLC, and serves as a consultant for GRO Biotechnology, CSL Behring, Amplo Biotechnology, and Sanofi.

SAFETY AND EFFICACY OF BCMA-DIRECTED MRNA CAR T-CELL THERAPY IN GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: Descartes-08 is an autologous, BCMA-directed mRNA chimeric antigen receptor (CAR) T-cell therapy administered in an outpatient setting and without lymphodepletion chemotherapy. In a phase 1/2 study in generalized myasthenia gravis (MG), six once-weekly infusions of 52.5x106 CAR+ cells/kg per infusion led to deep and durable improvements in MG severity scales.

OBJECTIVE: We present the primary results of a phase 2b double-blind randomized controlled trial comparing this dose and schedule of Descartes-08 against placebo (NCT04146051).

METHODS: Patients ≥18 years of age with non-MuSK+ MG who required immunosuppressive therapy and had MG-ADL ≥6 were eligible. After leukapheresis and manufacturing of autologous product, participants were randomized 1:1 to receive Descartes-08 or placebo. Blinded follow-up was at Day 57 and Day 85, after which placebo group could cross over to Descartes-08 under open label. Primary endpoint was the proportion of participants achieving ≥5-point improvement in MG Composite score at Day 85. Key secondary endpoints included type and frequency of adverse events, proportion of MG-ADL and QMG responders in Descartes-08 versus placebo, and change from baseline severity scores in patients who received placebo and crossed over to Descartes-08.

RESULTS: 36 patients across 21 academic medical centers and community clinics in North America and Turkey received median 6 doses (range 2-6) of Descartes-08 or placebo over six weeks.

SUMMARY/CONCLUSION: The first double-blind randomized controlled trial of an engineered cell therapy in autoimmune disease has completed enrollment. The primary and key secondary efficacy and safety endpoints will be reported.

Disclosures:

Tuan Vu - USF Site Principal Investigator for MG clinical trials sponsored by Alexion/AstraZeneca Rare Disease, Amgen, argenx, Cartesian Therapeutics, Dianthus Therapeutics, Immunovant, Johnson & Johnson, Regeneron Pharmaceuticals, and UCB Pharma, and has served as a speaker for Alexion/AstraZeneca Rare Disease, argenx, and CSL Behring. He served on advisory boards and/or performed consulting work for Alexion/AstraZeneca Rare Disease, argenx, Amgen, Dianthus Therapeutics, Johnson & Johnson, ImmunAbs, and UCB Pharma.

Michael Rivner - Consultant and received research support from Alexion, Argenx, UCB and Allergan and received research support from Momenta, Shire Takeda, Orion, Biohaven, Catalyst, Apellis Pharmaceuticals and Cartesian Therapeutics.dited

Thomas Ragole - Research grants from Alexion/AstraZeneca Rare Disease and Argenx; Consulting and/or Scientific Advisory Boards for Alexion/AstraZeneca Rare Disease and UCB

DISMANTLING OF NEUROMUSCULAR JUNCTION IN MYASTHENIA GRAVIS - A POINT OF NO RETURN

Dubravka Dodig (Toronto, Canada)

INTRODUCTION: AChR-MG is a T-cell dependent- B-cell mediated neuromuscular junction (NMJ) disease. A major effector mechanism is a complement-mediated attack resulting in AChR loss thereby functionally denervating the muscle endplate. 10%-15% of patients have incomplete disease control, are treatment-refractory, or have become intolerant to immunosuppressive therapy. In the ultimate stage of "burned-out" disease, untreated weakness may become fixed in association with muscle atrophy-”myasthenic neuromyopathy.”

OBJECTIVE: Help in understanding whether myasthenic muscle atrophy hampers the therapeutic response.

METHODS: We report 2 patients with long standing gMG resistant to treatment and fixed muscle weakness. Both patients have not been treated with any immunosuppressive or immunomodulatory therapies for over one decade. Both developed fixed muscle weakness which was unresponsive to re-initiation of standard therapy with steroids and immunosuppressive therapies.

RESULTS: Treatment with C5 complement inhibitor, eculizumab, resulted in restoration of normal function at the level of neuromuscular junction based on clinical evidence of reversal of atrophy and weakness of the bilateral triceps muscles (the patient 1), and fixed bifacial and bilateral hip flexor weakness (patient 2). Both patients reported remarkable improvement of quality of life.

SUMMARY/CONCLUSION: Restoration of muscle bulk and power in these patients supports the notion that chronic advanced dismantling of NMJ in gMG is a reversible process. NMJ is likely a dynamic structure capable of restoration in the absence of autoimmune assault. The limitations include observational retrospective analysis, small number of patients, and patients’ uniform gender and race.

OBSERVED EFFICACY OF EFGARTIGIMOD IN GENERALIZED MYASTHENIA GRAVIS ACROSS PATIENT SUBGROUPS IN THE ADAPT-SC+ STUDY

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INTRODUCTION: Efgartigimod is a human IgG1 antibody Fc-fragment that reduces total IgG levels (including pathogenic autoantibodies) through neonatal Fc receptor blockade. In the ADAPT-SC study, subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20) showed non-inferior total IgG reduction to efgartigimod IV in participants with generalized myasthenia gravis (gMG). Participants completing ADAPT-SC or enrolled in ADAPT+ (efgartigimod IV open-label extension) were eligible for the ADAPT-SC+ open label extension.

OBJECTIVE: Assess efficacy through post hoc analyses of efgartigimod PH20 SC in AChR-Ab+ participants in ADAPT-SC+ stratified by disease duration, thymectomy status, and MG therapies.

METHODS: Efgartigimod PH20 SC 1000 mg was administered in cycles of 4 once-weekly injections. Subsequent cycles were initiated based on clinical evaluation. MG-ADL scores assessed clinical efficacy.

RESULTS: In AChR-Ab+ participants (n=141), clinically meaningful improvements (CMI) from cycle baseline (≥2 point mean change in MG-ADL total score [SE]) were observed at week 4 of Cycle 1 across multiple subgroups. This is demonstrated in participants with disease duration of <3 years (-3.4 [0.62]), 3-<6 years (-4.6 [0.48]), and >6 years (-4.1 [0.39]). Thymectomized (-4.5 [0.40]) and nonthymectomized (-3.8 [0.37]) participants showed similar improvements. Participants receiving only concomitant acetylcholinesterase inhibitors (AChEis) (-5.5 [0.77]), any nonsteroidal immunosuppressive treatments (-3.8 [0.38]), or any steroids (-3.8 [0.31]) also achieved CMI.

SUMMARY/CONCLUSION: Efgartigimod PH20 SC resulted in consistent improvements in AChR-Ab+ participants across subgroups, including those only receiving AChEis. Clinical improvements across subgroups were similar to those seen during ADAPT, reinforcing efgartigimod's efficacy across a broad gMG population.

Disclosures:

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

Tuan Vu - Served as a speaker for Alexion, argenx, and CSL Behring; performed consulting work for argenx, Alexion/Astra Zeneca, Dianthus, ImmunAbs, and UCB; and participated in trials in MG sponsored by Alexion/Astra Zeneca, argenx, UCB, Amgen, Immunovant, Regeneron, Johnson & Johnson, Dianthus, and Cartesians Therapeutics.

Ratna Bhavaraju-Sanka - Served on advisory boards for argenx and is a consultant to Sanofi.

Eddie Brauer - Employee of argenx.

René Kerstens - Employee of argenx.

Kimiaki Utsugisawa - Consultant for UCB Pharma, Janssen Pharma, Horizon Therpeutics (Viela Bio), Chugai Pharma, Hanall BioPharma, Merck, and Mitsubishi Tanabe Pharma, and has received speaker honoraria from argenx, Alexion Pharmaceuticals, UCB Pharma, and the Japan Blood Products Organization.

Andreas Meisel - Received speaker honoraria from Alexion Pharmaceuticals, Inc, argenx BV, Grifols, SA, Hormosan Pharma GmbH, Novartis, and UCB; honoraria from Alexion Pharmaceuticals, Inc, argenx, Janssen, Merck, and UCB for consulting services; and financial research support (paid to his institution) from Octapharma, argenx, and Alexion Pharmaceuticals, Inc. He is chairperson of the medical advisory board of the German Myasthenia Gravis Society.

COMORBIDITIES IN SEROPOSITIVE AND SERONEGATIVE MYASTHENIA GRAVIS: A SINGLE CENTER EXPERIENCE

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INTRODUCTION: Medical comorbidities may influence myasthenia gravis (MG) disease course. Some studies suggest a higher prevalence of comorbidities in seropositive MG compared to the general population. Relatively little is known about comorbidities in seronegative MG.

OBJECTIVE: The purpose of this study was to evaluate epidemiology and disease course in both seropositive and seronegative MG patients with comorbidities.

METHODS: This is single center, observational, retrospective cohort study evaluating demographic, clinical outcomes and comorbidities in seropositive and seronegative MG via chart review at the University of Rochester Neuromuscular clinic. Categorical variables were analyzed via chi-squared test, and continuous variables were analyzed via two-sample t-test.

RESULTS: 39 seropositive and 25 seronegative subjects were analyzed. The average age was higher in the seropositive than seronegative group (64.3 versus 54.3 years, p=0.04), with average MG disease duration of 7 years and 10.2 years, respectively. More women were seen in the seronegative group (80% versus 66.7%, p=0.04).

Patients with seronegative MG had a higher prevalence of psychiatric comorbidities (48% versus 25.6%, p=0.004) and higher MG-ADL scores that were not statistically significant (4.6 versus 3.7, p=0.19). The prevalence of vascular and autoimmune comorbidities was similar in both groups (71.8% and 68%, p=0.18) and (15.3% and 16%, p=0.33).

SUMMARY/CONCLUSION: A high prevalence of psychiatric comorbidities was found in the seronegative MG population. The most common comorbidity in both groups was vascular disease. Further study is needed to clarify longitudinal clinical outcomes and to use this data to inform tailored treatment approaches in patients living with MG with comorbidities.

Disclosures:

Emma Ciafaloni - Consultant for Argenx, Alexion, Sarepta, UCB, Hoffman-LaRoche, Biogen. Dr. Ciafaloni has received personal compensation serving on a Scientific Advisory or Data Safety Monitoring board for Novartis, AnnJi Pharmaceutical, ML-BIO, Avidity. The institution of Dr. Ciafaloni has received research support from CDC, CureSMA, FDA, Orphazyme, Sarepta, PCORI, Neurogene. Dr. Ciafaloni has received publishing royalties from a publication relating to health care.

DOSE SELECTION AND CLINICAL DEVELOPMENT OF EFGARTIGIMOD PH20 SUBCUTANEOUS IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS

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INTRODUCTION: Efgartigimod intravenous (IV) was evaluated for treatment of generalized myasthenia gravis (gMG) in the phase 3 ADAPT study, in which it demonstrated efficacy and was well tolerated. Based on observed association between efgartigimod treatment and reductions in total IgG levels (including pathogenic autoantibodies), a population PK/PD approach was used for selection of a subcutaneous (SC) efgartigimod PH20 dose that would result in similar PD effect as efgartigimod IV (10 mg/kg).

OBJECTIVE: Confirm dose selection and consistency of effect for efgartigimod PH20 SC (coformulated with recombinant human hyaluronidase PH20).

METHODS: PK and PD data from a phase 1 study, in which healthy participants (n=32) received a single efgartigimod PH20 SC injection at various fixed doses or 10 mg/kg, were used for the PK/PD analysis. The selected dose was subsequently evaluated in healthy participants and patients with gMG (ADAPT-SC/SC+ studies) as treatment cycles of 4 once-weekly injections.

RESULTS: 1000-mg dose of efgartigimod PH20 SC was predicted to result in comparable reduction in total IgG on Day 29, 1 week after the fourth injection, and was selected for evaluation in the ADAPT-SC/SC+ studies. Patients ranging in weight from 42.0 to 150.2 kg (median=78.3) achieved similar total IgG reductions as those treated with efgartigimod IV. These reductions were associated with improvements in MG-ADL clinical outcome measure. Additional analyses in patients of varying body weights from ADAPT-SC+ will be presented.

SUMMARY/CONCLUSION: The ADAPT-SC study demonstrated that SC dose selection was appropriate, as treatment with efgartigimod PH20 SC 1000 mg resulted in noninferior reduction in total IgG to efgartigimod IV.

Disclosures:

Jeffrey Guptill - Employee of argenx; (2010 MGFA and ABF Clinician-Scientist Development Award in Myasthenia Gravis Recipient)

Jan Noukens - Partner in Curare Consulting BV and consultant for argenx.

Tonke Van Bragt - Partner in Curare Consulting BV and consultant for argenx.

Kimiaki Utsugisawa - Consultant for UCB Pharma, Janssen Pharma, Horizon Therapeutics (Viela Bio), Chugai Pharma, Hanall BioPharma, Merck, and Mitsubishi Tanabe Pharma, and has received speaker honoraria from argenx BV, Alexion Pharmaceuticals, UCB Pharma, and the Japan Blood Products Organization.

Jan L. De Bleecker - Consultant for argenx, Alexion Pharmaceuticals, Inc, CSL, UCB Pharma, Alnylam Pharmaceuticals Inc, Janssen, and Sanofi Genzyme.

James Howard - Received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, and UCB Pharma; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biohaven Ltd, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc (now Amgen), Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, UCB Pharma, and Zai Labs; non-financial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Pharma and Zai Labs.

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Tuan Vu - Speaker for Alexion, argenx, and CSL Behring; performed consulting work for argenx, Alexion/Astra Zeneca, Dianthus, ImmunAbs, and UCB; and participated in trials in MG sponsored by Alexion/Astra Zeneca, argenx, UCB, Amgen, Immunovant, Regeneron, Johnson & Johnson, Dianthus, and Cartesians Therapeutics.

Denis Korobko - Received speaker honoraria from Roche, Novartis Russia, Sanofi, Merck, Janssen (Johnson & Johnson company); research grants from Novartis, UCB, argenx, Viela Bio Inc. (now Horizon Therapeutics), Bristol Myers Squibb; and for consulting/serving on scientific advisory boards for Novartis Russia, Janssen (Johnson & Johnson company) and BIOCAD.

Li Liu - Employee of argenx.

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ALTERATIONS IN PERIPHERAL B AND T CELL SUBSETS IN MUSK-MG SUBJECTS AFTER RITUXIMAB TREATMENT

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INTRODUCTION: The anti-CD20 B cell depleting therapy rituximab is an effective treatment for muscle-specific kinase myasthenia gravis (MuSK-MG), however the mechanisms of B cell depletion on specific B cell and T cell compartments are unknown.

OBJECTIVE: To evaluate the immunological effects of rituximab on B and T cell populations in MuSK-MG subjects.

METHODS: PBMCs from MuSK-MG subjects (n=5) before and 4-15 months after rituximab treatment were analyzed by spectral flow cytometry.

RESULTS: Analysis of peripheral CD20+CD19+ B cells showed switched and unswitched memory B cells were downregulated after treatment, whereas IgD-CD27- double negative (DN) B cells increased. Within the DN B cell compartment, rituximab reduced CXCR5 +CD11c- DN1 B cells and increased in CXCR5-CD11c + DN2 and CXCR5-CD11c- DN3 populations, demonstrating an enrichment of extrafollicular B cells. Treatment resulted in increased expression of CD95, T-bet, and CD11c and reduced expression of CD21 and CXCR5 in CD20+CD19+ B cells. Analysis of T cell populations demonstrated increases in total CD4+ T cells and naïve CD8+ T cells following treatment.

SUMMARY/CONCLUSION: Our results suggest that DN B cells are persistent after treatment and are skewed towards an extrafollicular response, a pathway which leads to differentiation of short-lived plasmablasts. The impact of B-cell depleting therapy on CD4+ and CD8+ T cells in MuSK-MG indicates that B cells also influence T cell responses. Future longitudinal studies will determine if these alterations are associated with clinical response and will shed light on the relationship between B cells and T cells that regulate the autoimmune response in MuSK-MG.

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Patricia Sikorski - 2022 MGFA and ABF Clinician-Scientist Development Award in Myasthenia Gravis Recipient

Henry Kaminski - Consultant for Roche, Takeda, Cabaletta Bio, UCB Pharmaceuticals, Canopy Immunotherapeutics, EMD Serono, Ono Pharmaceuticals, ECoR1, Gilde Healthcare, and Admirix, Inc. Argenix provides an unrestricted educational grant to George Washington University. He is an unpaid consultant for Care Constitution. Dr. Kaminski has equity interest in Mimivax, LLC

Linda Kusner - Contracts with the following companies: Alexion, Alnylam, CSL Behring, and Gro Biosciences. Dr. Kusner has equity interest in Mimivax, LLC

NIPOCALIMAB, A NEW NEONATAL FRAGMENT CRYSTALLIZABLE BLOCKER, LEADS TO RAPID, SUBSTANTIAL AND SUSTAINED GENERALIZED MYASTHENIA GRAVIS DISEASE CONTROL

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INTRODUCTION: In gMG, there remains an unmet need for treatments providing meaningful symptom control. Nipocalimab has demonstrated positive results in a 24-week double-blind Ph3 study with rapid, substantial, and sustained efficacy.

METHODS: Mean changes in MG-ADL were compared between nipocalimab + standard of care (SOC) and placebo+SOC. The proportion of patients achieving Minimal Symptom Expression (MSE), MG-ADL total score 0/1 and percentage of time with MSE were compared. The proportion of patients with sustained within person meaningful change (WPMC)[≥2-point improvement], starting from Week 4 and percentage of time spent with WPMC.

RESULTS: Nipocalimab+SOC demonstrated statistically significant improvement in MG-ADL (over weeks 22,23, and 24) vs placebo+SOC, LS-mean change[SE] −4.7 [0.329] vs −3.25 [0.335]; difference in means[SE]= −1.45 [0.470], p=0.002). The mean difference, in favor of nipocalimab+SOC, was significant as early as week 1: LS mean change[SE]:

−2.72 [2.979] vs −1.77 [2.426]; difference in means[SE]−0.82 [0.410], p=0.046. Nipocalimab+SOC patients were 3X more likely to achieve MSE at any point during the study vs placebo; Odds Ratio [95% CI]: 3.0 [1.3, 6.8]; 31.2% vs. 13.2%. For the 25 patients reaching MSE, 18 nipocalimab, 7 placebo, the time sustaining MSE [percent time with MSE] was 101.5 days, (60.4%, nipocalimab+SOC) vs 55 days, (32.7%, placebo+SOC). Similarly, the proportion of patients with sustained WPMC favored nipocalimab+SOC, 55.8% vs 26.3%, placebo+SOC, p<0.001. The median percent time spent with WPMC was 84.5% nipocalimab+SOC vs 39.9% placebo+SOC, p=0.007.

CONCLUSION: Based on MG-ADL data from Phase 3 study, nipocalimab a new FcRn demonstrates rapid, substantial and sustained symptom control.

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Richard Nowak - Research support: Alexion Pharmaceuticals, Genentech, Grifols Momenta, Myasthenia Gravis Foundation of America, NIH, Ra Pharmaceuticals; consultant/advisor: Alexion Pharmaceuticals, CSL Behring, Grifols, Ra Pharmaceuticals, Roivant Sciences, Momenta.

Maria Ait-Tihyaty - Employee, contractor or consultant for Janssen Pharmaceuticals and may hold stock or stock option in Johnson & Johnson.

Ibrahim Turkoz - Employee, contractor or consultant for Janssen Pharmaceuticals and may hold stock or stock option in Johnson & Johnson.

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Sheryl Pease - Employee, contractor or consultant for Janssen Pharmaceuticals and may hold stock or stock option in Johnson & Johnson.

Sarah Gingerich - Employees, contractor or consultant for Janssen and may hold stock or stock option in Johnson & Johnson.

Hans Katzberg - Consultant to Octapharma,UCB, Alnylam, CSL Behring, Alexion, ArgenX, Dyne, Roche, Takaeda, Dianthus, Merz; he has been on the DSMB for Alexion, UCB, Abcuro, Octapharma and ArgenX and has received clinical trial support from Takaeda, CSL Behring, Roche and ArgenX

EVALUATION OF THE INDIRECT AND NONMEDICAL IMPACTS OF GENERALIZED MYASTHENIA GRAVIS ON PATIENTS AND CAREGIVERS

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INTRODUCTION: Generalized myasthenia gravis (gMG) is a rare, chronic autoimmune disorder. Indirect gMG-associated economic impacts on patients and caregivers are poorly studied.

OBJECTIVE: Assess indirect and nonmedical costs for US patients with gMG and caregivers.

METHODS: Data from independently recruited patients and caregivers were collected for 2022 via web-based survey (August-December 2023). Total indirect costs using survey data and nationally representative earnings data were stratified by age/sex/payer and weighted by gMG prevalence yielding weighted averages.

RESULTS: Respondents included 239 patients with gMG and 81 caregivers (63% and 58% aged 18-49 years, respectively; 69% and 42% female). Time since gMG diagnosis/caring began was <10 years for most (83%/91%). Most patients (61%) had commercial insurance. Many caregivers were parents (26%) or spouses/partners (37%). On average, patients received formal/paid (9 hours/week) and informal (75 hours/week) care. The primary nonmedical gMG-related patient cost was equipment ($1201/year). The primary out-of-pocket caregiver cost was non-gMG household member care ($3103/year). Lost social productivity was 46% of patient productivity costs ($11,949/year). Caregiver productivity costs were lost earnings from early retirement (30%; $6414/year), absenteeism (26%; $5544/year), lost social productivity (26%; $5532/year), and reduced work productivity (18%; $3973/year). Indirect costs for patients ($33,388/year [weighted]) were driven by lost productivity and for caregivers ($92,101/year) by informal caregiving. Indirect patient costs increased with Myasthenia Gravis Activities of Daily Living score (0-6 [n=68], $30,698/year; 7-12 [n=115], $51,300/year; 13-18 [n=51], $71,534; 19-24 [n=5], $93,253).

SUMMARY/CONCLUSION: Both patients with gMG and caregivers report high annual indirect and nonmedical costs. This contributes substantially to the total economic impact of gMG.

Disclosures:

Kelly G. Gwathmey - Received compensation from Alexion for speaking/consulting honoraria, and argenx and UCB for consulting honoraria.

Olivia Hunt - Employee of Avalere, which received funding to conduct this research and consults with life sciences organizations.

Mayvis Rebeira - Employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.

Pushpa Narayanaswami - Received research support from Alexion/AstraZeneca Rare Disease and Momenta/Janssen; served on advisory boards and/or consulted for Alexion/AstraZeneca Rare Disease, Amgen, argenx, CVS, Dianthus, GSK, ImmuneAbs, Janssen, Novartis, and UCB; serves as Data Monitoring Committee Chair for argenx and Sanofi; and receives royalties from Springer Nature.

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Allison Foss - Employee of the Myasthenia Gravis Association, a member of the argenx Leadership Council, Rare Disease Connect in Neurology Steering Committee for UCB and has received consulting honoraria.

Christina Ramirez - Cofounder and board treasurer for Own MG.

Jamie Sullivan - Employee of EveryLife Foundation, which receives funding from the research sponsor for work unrelated to this research.

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Taylor T. Schwartz - Employee of Avalere, which received funding to conduct this research and consults with life sciences organizations.

Nicole Betor - Employee of Avalere, which received funding to conduct this research and consults with life sciences organizations.

THE PHASE 3 PREVAIL STUDY ASSESSING THE EFFICACY AND SAFETY OF SUBCUTANEOUS GEFURULIMAB IN ADULTS WITH GENERALIZED MYASTHENIA GRAVIS: TRIAL IN PROGRESS

James F. Howard Jr. (Chapel Hill, NC), Kelly G. Gwathmey (Charlottesville, VA), Chongbo Zhao (Shanghai, China), Sanjay Rakhade (Winchester, MA), Joachim Scholz (Boston, MA), Alexandra Peláez-Rivas (Boston, MA), Annie M. Racine (Natick, MA), Alanna McEneny (Boston, MA), Shulian Shang (Boston, MA), Tuan Vu (Tampa, FL)

INTRODUCTION: Complement component 5 (C5) inhibitors are effective treatments for anti-acetylcholine receptor antibody-positive generalized myasthenia gravis (AChR-Ab+ gMG). Gefurulimab is a new bispecific nanoantibody that binds C5, blocks its enzymatic cleavage, and thus, inhibits the terminal complement pathway. Gefurulimab is suitable for subcutaneous (SC) self-administration. Its extended half-life allows for once-weekly injection. Gefurulimab is currently under investigation for treatment of AChR-Ab+ gMG in a phase 3, multicenter, randomized, double-blind, placebo-controlled study (PREVAIL; NCT05556096).

OBJECTIVE: Provide an overview of PREVAIL, which will evaluate the efficacy and safety of gefurulimab in adults with AChR-Ab+ gMG.

METHODS: PREVAIL will enroll ≤254 adults with AChR-Ab+ gMG, including those with mild disease. Patients may continue taking previously prescribed therapies, including immunoglobulins. Patients are randomized 1:1 to weekly SC self-injection of gefurulimab or placebo. The primary endpoint is change from baseline in Myasthenia Gravis Activities of Daily Living (MG-ADL) total score at week 26. Secondary endpoints include change from baseline in Quantitative Myasthenia Gravis (QMG) total score and Myasthenia Gravis Composite (MGC) total score. Safety, pharmacokinetics, pharmacodynamics, immunogenicity, and quality of life will also be assessed. PREVAIL includes an open-label extension.

RESULTS: PREVAIL is currently active and recruiting patients at ~160 sites in North America, South America, Europe, Asia, and the Pacific region.

SUMMARY/CONCLUSION: Gefurulimab has the potential to offer patients with gMG a new, effective, safe, and convenient (once-weekly SC) treatment option that can be self-administered. Results from PREVAIL will inform the clinical development program of gefurulimab.

Disclosures:

James F. Howard Jr. - Received research support (paid to institution) from Ad Scientiam, Alexion, AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention (Atlanta, GA, USA), the Muscular Dystrophy Association, the Myasthenia Gravis Foundation of America, the National Institutes of Health (including the National Institute of Neurological Disorders and Stroke and the National Institute of Arthritis and Musculoskeletal and Skin Diseases), PCORI, Ra Pharmaceuticals (now UCB Pharma), and Takeda Pharmaceuticals; honoraria from AcademicCME, Alexion, AstraZeneca Rare Disease, argenx, Biologix Pharma, F. Hoffmann-La Roche Ltd, Horizon Therapeutics, Immunovant, Medscape CME, Merck EMB Serono, Novartis Pharmaceuticals, PeerView CME, Ra Pharmaceuticals (now UCB), Regeneron Pharmaceuticals, Sanofi US, and Zai Laboratories; and nonfinancial support from Alexion, AstraZeneca Rare Disease, argenx, Biohaven Ltd, Ra Pharmaceuticals (now UCB), and Toleranzia AB.

Tuan Vu - Received research support from Alexion/AstraZeneca Rare Disease, Amgen, Amylyx, argenx, Cartesians, CSL Behring, Dianthus, Healy Platform Trials, Immunovant, Ipsen, Johnson & Johnson, PTC Therapeutics, Regeneron, Sanofi, UCB, and Woolsey Pharma; served on speakers bureaus for Alexion, AstraZeneca Rare Disease, argenx, and CSL Behring; served on ad boards or as consultant for Alexion/AstraZeneca Rare Disease, Amgen, argenx, ImmunAbs, Johnson & Johnson, and UCB.

Kelly G. Gwathmey - Received honoraria from AcademicCME, Alexion, AstraZeneca Rare Disease, Amgen, argenx, and UCB.

Chongbo Zhao - Received advisory board/consultant fees from Nona Biosciences, Roche, Sanofi, and Zailab.

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MEDIASTINAL RADIOTHERAPY FOR NON-OPERABLE THYMOMA WITH MYASTHENIA GRAVIS

Cathy Meng Fei Li (London, Canada), Stephen Chrzanowski (Needham, MA), Amanda Guidon (Boston, MA)

INTRODUCTION: Thymectomy is standard of care for nearly all patients with thymomatous generalized myasthenia gravis (gMG). However, optimal management of thymoma in poor surgical candidates with medically refractory gMG is unknown.

OBJECTIVE: To report an illustrative case and literature review of primary radiotherapy in patients with thymomatous gMG when surgical management of thymoma is not advised.

METHODS: Case report and literature review of primary radiation to the thymus or mediastinum in thymomatous gMG using PubMed. Adjuvant radiotherapy and/or patients with invasive thymic carcinoma were excluded.

RESULTS: An 84-year-old male with atrial fibrillation and acetylcholine receptor antibody-positive gMG presented with moderately-severe bulbar-predominant myasthenic flare (MGFA Severity Class IIIb), and CT thorax demonstrated a thymoma. His gMG was medically refractory to prednisone, mycophenolate mofetil, and efgartigimod. IVIg was not tolerated due to exacerbation of congestive heart failure. Radiotherapy with 60Gray (Gy) to the anterior mediastinum over 4 weeks (3Gy/fraction, 5 days/week) led to symptomatic improvement and regression of thymoma. His MG remains under control (Class IIA) with reduction of pharmacotherapy after 1-year follow-up.

Literature review reveals 3 other patients with thymomatous gMG who underwent mediastinal radiation without thymectomy. One patient received 39Gy of radiation resulting in complete thymoma regression and MG remission for over 4 years. Another patient received 40Gy with improved MG control for over 1 year. The last patient died from acute heart failure during radiation.

SUMMARY/CONCLUSION: This report adds to the limited literature that primary radiation to the thymus may provide tumor and MG control in selected patients who are poor thymectomy candidates.

Disclosures:

Amanda Guidon - Reports serving on advisory boards for Argenx, Alexion and UCB. Research funding from MGNET, NINDS, Project Data Sphere, the Dysimmune Disease Foundation and the MGFA. Publishing royalties from Oakstone Publishing.

SAFETY OUTCOMES IN PREGNANT PATIENTS TREATED WITH THE COMPLEMENT 5 INHIBITOR THERAPY (C5IT) ECULIZUMAB

Pushpa Narayanaswami (Boston, MA), Chloe Sader (New York, NY), Min Yee (Newton Centre, MA), Frederic Honore (Boston, MA), Tuan Vu (Lutz, FL)

INTRODUCTION: Pregnancy can induce protective immunological changes including complement amplification, which may unmask or worsen complement-mediated conditions such as generalized myasthenia gravis (gMG), neuromyelitis optica spectrum disorder (NMOSD), paroxysmal nocturnal hemoglobinuria (PNH), and atypical hemolytic uremic syndrome (aHUS). To date, eculizumab exposures during pregnancy have not suggested safety concerns, but with limited reported exposures since FDA approval (PNH, 2007; aHUS, 2011; gMG, 2017; NMOSD, 2019), further investigation is needed. Available pregnancy-related safety data for C5ITs will provide further information for clinical decision-making.

OBJECTIVE: To report pregnancy-related safety outcomes for eculizumab-treated patients.

METHODS: A cumulative analysis of pregnancy outcomes in patients treated with eculizumab (March 16, 2007–April 1, 2024) from the Alexion pharmacovigilance safety database was conducted across approved indications, unknown indications, and off-label use from all sources (clinical trials, postmarketing data, literature, and registries).

RESULTS: Overall, 2043 eculizumab maternal exposures during pregnancy included patients with PNH (n=1095, 54%), aHUS (n=387, 19%), gMG (n=92, 5%), NMOSD (n=32, 2%), and unknown indications/off-label use (n=437, 21%). Among all exposures, 628/2043 (31%) had known outcomes; of these, 382/628 (61%) resulted in live birth and 140/628 (22%) ended in spontaneous abortion.

SUMMARY/CONCLUSION: Regardless of indication, live birth was the most common outcome with eculizumab exposure; spontaneous abortion rates were aligned with the general US population (15%–20%). Limitations include small proportion of exposures with known outcomes, limited disease-specific data, and selective reporting bias. To address the limitations of pharmacovigilance data, further investigations include exploring pregnancy outcomes with ravulizumab, a long-acting C5IT, in an observational study (currently recruiting; NCT06312644).

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Pushpa Narayanaswami - Received research support from Alexion, AstraZeneca Rare Disease, Janssen, and has served on advisory boards for Janssen, Alexion/AstraZeneca Rare Disease, argenx, UCB S.A, Janssen, Dianthus. as a Data Monitoring Committee Chair for Sanofi, and argenx.

Chloe Sader - Employee of Alexion, AstraZeneca Rare Disease and may own stocks in Alexion, AstraZeneca Rare Disease.

Min Yee - Employee of Alexion, AstraZeneca Rare Disease and may own stocks in Alexion, AstraZeneca Rare Disease.

Frederic Honore - Employee of Alexion, AstraZeneca Rare Disease and may own stocks in Alexion, AstraZeneca Rare Disease.

Tuan Vu - Received research or grant support from Alexion/AstraZeneca Rare Disease; Amylyx Pharma; argenx; CSL Behring; Dianthus; Amgen; Healey Platform Trials; Immunovant, Johnson & Johnson; Regeneron, UCB; Sanofi; PTC and Woolsey Pharma; and is a consultant and/or serves on speaker bureau for Alexion/AstraZeneca Rare Disease; argenx; CSL Behring; and Dianthus.

DESIGN OF A PHASE 3 RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED STUDY EVALUATING THE EFFICACY AND SAFETY OF SUBCUTANEOUS EFGARTIGIMOD PH20 ADMINISTERED BY PREFILLED SYRINGE IN ADULTS WITH OCULAR MG

James Howard (Chapel Hill, NC), Carolina Barnett-Tapia (Toronto, Canada), Jeffrey Guptill (Ghent, Belgium), Rosa Jimenez (Ghent, Belgium), Fien Gistelinck (Ghent, Belgium), Sophie Steeland (Ghent, Belgium), Fien M. Verhamme (Ghent, Belgium), Sui Wong (London, United Kingdom)

INTRODUCTION: An unmet need exists for approved, effective treatments for patients with ocular myasthenia gravis (oMG). Retrospective analysis of data supporting the approval of efgartigimod for treatment of adults with generalized myasthenia gravis (gMG) indicated a benefit in ocular symptoms in this population.

OBJECTIVE: To report the design of a phase 3, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of subcutaneous (SC) efgartigimod coformulated with recombinant human hyaluronidase PH20 in oMG.

METHODS: Adults with confirmed oMG and a Myasthenia Gravis Impairment Index (MGII) patient-reported outcome (PRO) subcomponent ocular score ≥6 who are on stable MG therapy will be randomized 1:1 to receive 4 once-weekly efgartigimod PH20 SC 1000 mg or placebo injections followed by 4 weeks of follow-up. The primary endpoint is change in MGII PRO ocular score from baseline to Week 4. Key secondary endpoints include changes from baseline to Week 4 in MGII ocular score (PRO plus physical examination), Myasthenia Gravis Activities of Daily Living ocular domain score, and MGII total score. Statistical analyses for efficacy endpoints will be conducted in hierarchical order at a 1-sided significance level of α=.025. Safety assessments include adverse event incidence and severity. Participants may continue in the up-to-2-year open-label extension part of the study evaluating long-term efgartigimod PH20 SC efficacy and safety in oMG.

RESULTS: Further study details will be presented.

SUMMARY/CONCLUSION: This is the first phase 3 clinical trial evaluating the safety and efficacy of efgartigimod PH20 SC in patients with oMG that may address the unmet need for treatment in oMG.

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James Howard - Received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx,

Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, and UCB Pharma; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biohaven Ltd, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc (now Amgen), Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, UCB Pharma, and Zai Labs; and nonfinancial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Pharma, and Zai Labs.

Carolina Barnett-Tapia - Served as an advisory board member for argenx, Alexion, UCB and Janssen; been a consultant for argenx, Janssen, and UCB; received research support from US Department of Defense, Muscular Dystrophy Canada, MGNet, Grifols and Octapharma; and is the primary developer of the MGII and may receive royalties.

Jeffrey Guptill - Employee of argenx. (2010 MGFA and ABF Clinician-Scientist Development Award in Myasthenia Gravis Recipient)

Rosa Jimenez - Employee of argenx.

Fien Gistelinck - Employee of argenx.

Sophie Steeland - Employee of argenx.

Fien M. Verhamme - Employee of argenx.

Sui Wong - Received research support (paid to her institution) from Visual Snow Initiative, myaware and MGFA; honoraria/consulting fees from argenx and Immunovant.

SYMPTOM SEVERITY ASSESSMENT USING MG-ADL ITEMS AND DOMAINS IN A 24-WEEK, PHASE 3 STUDY (VIVACITY) OF NIPOCALIMAB IN GENERALIZED MYASTHENIA GRAVIS.

Constantine Farmakidis (Kansas city, KS), Kavita Gandhi (Raritan, NJ), Maria Ait-Tihyaty (Titusville, NJ), Ibrahim Turkoz (Titusville, NJ), Sheryl Pease (Raritan, NJ), Zia Choudhry (Titusville, NJ), Charlotte Gary (Issy-les-Moulineaux, France), Antoine El Khoury (Raritan, USA), Sindhu Ramchandren (Titusville, NJ)

INTRODUCTION: Nipocalimab as an add-on to standard-of-care (SOC) demonstrated statistically significant improvement in MG-ADL compared to placebo+SOC in a 24-week double-blind phase 3 study in generalized myasthenia gravis. Post-hoc analyses evaluated improvements in distinct muscle function groups using MG-ADL items and domains for nipocalimab+SOC (nipocalimab) versus placebo+SOC (placebo).

METHODS: Baseline floor effects (score=0) distribution was evaluated with median/mean item and domain scores. Mean change from baseline (CFB) for four domains (bulbar, respiratory, limb, and ocular) were evaluated at 24-weeks and analysis of variance tested treatment differences with nipocalimab versus placebo. Based on items/domains score distributions, responders were defined using within-person change threshold of 1-point for items and 2-points for domains except for the 1-item respiratory domain with 1-point threshold. Generalized- estimating-equations evaluated improvement likelihood in items/domains over 24-weeks.

RESULTS: In 153 patients, median baseline MG-ADL item scores were 1.0-2.0 (range 0-3). Mean (range) domain scores in nipocalimab and placebo were bulbar [2.7 (0-7), both arms], limb [2.4 (0-5); 2.5 (0-5)], ocular [3.5 (0-6); 2.8 (0-6)] and respiratory [1.1 (0-2); 1.0 (0-2), item], respectively. Mean CFB for MG-ADL domains were significantly higher in nipocalimab versus placebo ($p<0.05$). Proportion achieving MG-ADL item response ranged from 42.7% (swallowing) to 97.6% (respiratory) over 24-weeks favoring nipocalimab. The odds-ratio (95%CI) of MG-ADL domain responder over 24-weeks were: bulbar 1.6
(0.9-2.7), respiratory 2.0 (1.0-3.6), limb 1.8 (1.0-3.1) and ocular 2.9 (1.5-5.4), all favoring nipocalimab.

SUMMARY/CONCLUSION: MG-ADL total score changes were driven by item and domain-level symptom improvements in all muscle function groups favoring nipocalimab.

Disclosures:

Constantine Farmakidis - Consulting for the Muscular Dystrophy Association and medical advisory board participation for Argenx, UCB and Janssen.

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

Maria Ait-Tihyaty - Employee of Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

Ibrahim Turkoz - Employee of Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

Sheryl Pease - Employee of Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

Zia Choudhry - Employee of Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

Charlotte Gary - Employee of Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

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Sindhu Ramchandren - Employee of Janssen Pharmaceuticals and may hold stock or stock options in Johnson & Johnson.

FEASIBILITY OF 12 WEEKS OF REMOTE MONITORING IN GENERALIZED MYASTHENIA GRAVIS

Hannah Dimmick (Denver, CO), Tefani Perera (Calgary, Canada), Gordon Jewett (Calgary, Canada), Lawrence Korngut (Calgary, Canada), Reed Ferber (Calgary, Canada)

INTRODUCTION: Remote monitoring represents a possible strategy to gain greater insight into daily symptom fluctuations in myasthenia gravis (MG). However, remote monitoring tools have not yet been established as feasible in MG, particularly for time periods >1 week.

OBJECTIVE: Therefore, this study aimed to investigate whether prolonged remote monitoring with a wearable device and daily surveys represents a realistic data collection method in MG.

METHODS: All participants had a diagnosis of generalized MG. Participants were asked to wear a wrist-worn accelerometer (watch) continuously and complete a 3-question daily questionnaire (DQ) about their symptoms each evening for 84 days. Sufficient watch wear time was defined as ≥16 hours per day.

RESULTS: Thirty participants were included in the analysis, totaling 2327 participant days. Adherence for watch usage and DQ completion declined somewhat linearly throughout the study period. Mean participant days with sufficient watch wear time declined from 83.0% on study days 1-42 to 66.9% on days 43-84. Mean DQ completion rate declined from 84.8% on days 1-42 to 72.8% on days 43-84. Combined watch and DQ compliance for the entire study duration was

>80% in 53% of participants. We observed >60% sufficient watch wear time and DQ compliance nearly every day of the study (76/84 days; 84/84 days, respectively).

SUMMARY/CONCLUSION: These results indicate that daily remote monitoring via wearable device and survey is feasible in MG patients over a multi-week period, but compliance is likely to decline with increasing study duration. This may represent a helpful method for tracking MG patients' behavior and symptoms between clinical visits.

REVIEW OF EFFICACY OF NEW COMPLEMENT INHIBITING MONOCLONAL ANTIBODIES IN MYASTHENIA GRAVIS: A REAL WORLD EXPERIENCE FROM A TERTIARY NEUROLOGY CENTER.

Priyanshu Bansal (Pittsburgh, PA), Jason Gandhi (Pittsburgh, PA), Gurleen Kaur (Pittsburgh, PA), Rohan Desai (Pittsburgh, PA), George Small (Pittsburgh, PA), Sandeep Rana (Sewickley, PA)

INTRODUCTION: Complement component 5 (C5) targeting monoclonal antibodies have shown efficacy and safety in treating acetylcholine receptor antibody-positive Myasthenia Gravis (AChR+ gMG). Eculizumab and Ravulizumab are C5 monoclonal antibody inhibitors used for AChR+ gMG, with Ravulizumab being longer-acting and potentially faster acting, now increasingly used in patients with or without prior Eculizumab treatment.

OBJECTIVE: To evaluate outcomes for AChR+ gMG patients treated with Ravulizumab, with or without prior eculizumab therapy.

METHODS: Data from the AHN EMR system for 11 AChR+ gMG patients on Eculizumab and Ravulizumab were analyzed. Outcomes included Vital Capacity (VC), Myasthenia Gravis - Activities of Daily Living scores (MG-ADL), MG exacerbations - acute worsening of symptoms, and reduction of other therapies.

RESULTS: Median patient age 58 years (23-70). Median disease duration 8 years (2-16). Median VC at diagnosis 2 L (2-4). Median prior immunotherapies 4 (0-4). Median MG-ADL score prior to therapy 11 (6-13). Outcome medians were: VC before Eculizumab/Ravulizumab 2.53 (1.53-3.8), VC with Eculizumab 3.51 (1.86-3.8), VC with Ravulizumab 1.7 (1.53-3.2); Median MG-ADL at the most recent visit 3 (0-9) and change from baseline 5.5 (3-13); Median total lifetime exacerbations 2 (0-9), after eculizumab 1 (0-4), after Ravulizumab 0 (0-2). Elimination/reduction of other therapies (n): prednisone 5 (45.45%), pyridostigmine 3 (27.27%), death 1 (9.09%).

SUMMARY/CONCLUSION: Within the study's small size, there is a trend of fewer exacerbations with Ravulizumab superior to eculizumab. MG-ADL scores improved post-therapy with median change from baseline of 5.5 with reduction of prednisone and pyridostigmine. We also noted very well tolerability of these therapies with minimal side-effects.

Disclosures:

George Small - Panel of speakers for Alexion.

A TEXT MESSAGING-BASED PATIENT EDUCATION PROGRAM AIMED AT IMPROVING OUTCOMES IN MYASTHENIA GRAVIS.

Samreen Ahmed (Glen Ellyn, IL), Diana Mnatsakanova (Chicago, IL), Pritikanta Paul (San Francisco, CA)

INTRODUCTION: Most Myasthenia Gravis patients can function normally with optimal treatment but require close monitoring and personalized treatments due to its fluctuating nature. However, many patients face a rough journey due to limited disease education and inadequate access to healthcare providers.

OBJECTIVE: A pilot project to test the hypothesis that one way text-based educational messaging improves disease literacy and treatment adherence improving outcomes.

METHODS: We developed 35 educational messages to systematically deliver disease-specific information to MG patients to improve their disease knowledge. We utilized existing HIPAA-compliant text messaging systems to target newly diagnosed MG patients, regularly sending messages (n=8 messages per week for 24 weeks) that provided (i) information on the disease (ii) tips for managing symptoms in daily life (iii) details about treatment medications and potential side effects, and (iv) guidance on preventive health.

RESULTS: We have already recruited eight patients (6 seropositive, 4 females, age 21-69 yrs), all newly diagnosed in the last six months, with one lost to follow-up. All patients when offered agreed to join the study. Based on survey responses received from 7 patients, the intervention was “very helpful” in improving perceptions of disease knowledge (N=6), self-confidence (N=6) and better medication compliance (N=4).

SUMMARY/CONCLUSION: Our ongoing study demonstrates that educational messages to MG patients can serve as a comprehensive source of disease information. This easily scalable approach can bridge gaps by providing reliable information addressing patients' most common concerns quickly, and alleviating provider burden. This message-based intervention potentially fills the care gap for patients in underserved communities.

DEVELOPING MUSK L-CBA TO DETECT ANTI-MUSK ANTIBODY

Sazan Ismael (Vancouver, Canada), Pankaj Kumar (Vancouver, Canada), Ali Mousavi (Vancouver, Canada), Hans Frykman (Vancouver, Canada)

INTRODUCTION: Myasthenia gravis (MG) is an autoimmune disorder that causes weakness of voluntary muscles by autoantibodies. These antibodies form against acetylcholine receptor (AChR), muscle-specific kinase (MuSK), or other AChR-related proteins in the postsynaptic muscle membrane. While RIPA is the current method to detect anti-MuSK antibody, a different approach with higher sensitivity is needed.

OBJECTIVE: To find a better method to detect anti-MuSK antibody.

METHODS: Sera from 19 identified MuSK MG patients and 20 healthy controls were tested for anti-MuSK antibody with L-CBA and MuSK RIPA at UBC laboratory. Furthermore, 21 samples that are clinically identified as MG but MuSK seronegative by RIPA and SPR were tested for MuSK Ab L-CBA. Moreover, 20 samples that are clinically identified as non-MG were tested for MuSK Ab L-CBA. All of samples were tested at 1:20 and 1:100 dilution.

RESULTS: By L-CBA method, 0 out of 20 healthy controls and 12 out of 19 clinically identified MuSK MG patients were detected as positive for anti-MuSK antibody. In addition, MuSK Ab L-CBA detected 0 out of 21 MG cases, but 2 out of 20 samples that are identified as non-MG. It is noteworthy that both of these MuSK Ab L-CBA positive cases were identified as myopathy.

SUMMARY/CONCLUSION: While the sensitivity of MuSK RIPA has been reported as 58%, MuSK L-CBA has shown higher sensitivity (73%) according to our MuSK MG identified samples. Nevertheless, MuSK L-CBA showed 100% specificity with the healthy controls which is also higher than MuSK RIPA specificity, 92%.

CLINICAL OUTCOMES OF ADULT MYASTHENIA GRAVIS PATIENTS ON EFGARTIGIMOD: A RETROSPECTIVE CHART REVIEW

Tyler Krall (Phoenix, AZ), James Kelbert (Phoenix, AZ), Samuel Byrne (Phoenix, AZ), Christina Chrisman (Phoenix, AZ)

INTRODUCTION: Efgartigimod (Vyvgart) is an Fc receptor antagonist that received FDA approval in 2021 for the treatment of myasthenia gravis. There is limited data on its effects outside of clinical trial scenarios and therefore some uncertainty on the ideal dosing frequency.

OBJECTIVE: This project aims to analyze the objective clinical short and long-term outcomes for adult myasthenia gravis patients on efgartigimod through multiple dosing cycles.

METHODS: Myasthenia gravis patients at a single academic neuromuscular center, receiving efgartigimod were retrospectively identified. Patients not being actively seen by the principal investigator were excluded. Demographics, treatment dates, dosing intervals, and Myasthenia Gravis Activities of Daily Living (MG-ADL) scores were collected.

RESULTS: Nine patients were included. Five patients were male and four patients were female with the average age being 64. The average time between cycles was 47 days (SD = 46.5, CI = 34.98 - 59.01). The average baseline MG-ADL was 8.56. Upon initiation of treatment the average decrease in MG-ADL was 4.44 at 60 days (SD = 3.43), 4.71 at 6 months (SD = 3.64), and 5.29 at 12 months (SD = 5.06). There was a statistically significant reduction in the MG-ADL score at all time intervals (p-value = <0.0046 at 60 days, <0.014 at 6 months, <0.0326 at 12 months).

SUMMARY/CONCLUSION: This data shows efgartigimod may be used at individualized dosing schedules and is an effective treatment for myasthenia gravis. Further studies of what may lead to fluctuations in dosing as well as better tracking of dosing schedules is needed.

Disclosures:

Christina Chrisman - Consulting and speaking.

EXPLORING OUTCOMES AND CHARACTERISTICS OF MYASTHENIA GRAVIS 2 (EXPLORE-MG2): DESIGN, RATIONALE, AND BASELINE RESULTS

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INTRODUCTION: Though much information exists about the diagnosis, treatment, and epidemiology of myasthenia gravis (MG), a comprehensive data registry linked with biospecimens is critical to better understand disease mechanisms, outcomes, and the impact of treatment strategies. The MG Rare Disease Clinical Research Network (MGNet) was funded by the National Institutes of Health (NIH) and as part of that initiative a prospective, multicenter natural history study and biorepository was developed: Exploring Outcomes and Characteristics of Myasthenia Gravis 2 (EXPLORE-MG2).

OBJECTIVE: To define clinical features and disease course as well as establish the largest paired longitudinal biospecimen repository for discovery.

METHODS: EXPLORE-MG2 is a web-based observational registry that incorporates NIH recommended common data elements for MG. Key eligibility criteria include: ≥18 years old; diagnosed with MG within 2-years of enrollment. Participants are followed for at least 2-years with study visits occurring approximately every 6-months in the context of usual clinical care.

RESULTS: A total of 302 participants (43% female) were enrolled from 1/2021 through 5/2024 across 10 US sites. Of those 17% have completed minimum 2-year follow-up period. The mean age at enrollment and diagnosis was 59.2 and 56.7 years, respectively. Mean MG-ADL and MGC scores were 3.8 and 6.2 at enrollment along with the following autoantibody status: 72.2% AChR, 14.2%, MuSK, 0.3% LRP4, 13.3% seronegative. We will present additional baseline characteristics/demographics at the meeting.

SUMMARY/CONCLUSION: EXPLORE-MG2 will improve clinical trial readiness and facilitate development of treatment-responsive biomarkers. Samples and clinical data will be available to researchers for current and future investigation.

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Inmaculada Aban - Reports serving on a steering committee for Roche.

Henry Kaminski - Reports serving as a consultant for Roche, Takeda, Cabaletta Bio, UCB Pharmaceuticals, Canopy Immunotherapeutics, EMD Serono, Ono Pharmaceuticals, ECoR1, Gilde Healthcare, and Admirix, Inc. Argenx provides an unrestricted educational grant to George Washington University. He is an unpaid consultant for Care Constitution. Dr. Kaminski has equity interest in Mimivax, LLC.

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Jeffrey Guptill - Study was designed and initiated while at Duke University. JG is currently an employee at argenx. (2010 MGFA and ABF Clinician-Scientist Development Award in Myasthenia Gravis Recipient).heh

Betty Soliven - Reports serving in an Advisory Board for argenx, and as a consultant for CVS Pharmacy. She has served as the site PI for Alexion and Genentech/Roche, and site co-I for UCB in MG clinical trials.

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Katherine Ruzhansky - Reports serving on advisory boards for Alexion, argenx, Immunovant, and UCB/Ra, and has served as a site PI for Alexion, Argenx, UCB, and Janssen.

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IDENTIFYING HEALTHCARE DISPARITIES IN MYASTHENIA GRAVIS: A POST-COVID-19 PANDEMIC BRONX TALE

Eleni Drakou (New York, NY), Gautham Upadrasta (Avenel, NJ), Leslie Delfiner (Chappaqua, NY), Daniel José Correa (Bronx, NY)

INTRODUCTION: Race and ethnic healthcare disparities have been observed within neuromuscular disorders, including Myasthenia Gravis (MG), with higher rates of complications and healthcare utilization among non-Whites and Hispanics. We serve a diverse Bronx population, heavily impacted during the COVID-19 pandemic. We describe an MG disparities study design and cohort.

OBJECTIVE: Evaluate health inequities in critical MG adult and pediatric outcomes in a diverse population as a function of race, ethnicity, primary language preference, adjusting for COVID-19 history.

METHODS: We include adult and pediatric MG patients at Montefiore (1/1/2022-2/28/2024). Sociodemographics include race, ethnicity, primary language preference, insurance status. Outcomes include 1o) intubation and non-invasive ventilation, 2o) ER visits, hospitalizations, ICU admissions, missed-care-opportunities, time-to-diagnosis / -therapy / -thymectomy, worst MGFA classification. With multivariable logistic regression we will assess the association of 1o and 2o outcomes with race, ethnicity, primary language, and adjust for COVID-19 history.

RESULTS: In descriptive analysis, the cohort includes 255 patients with a mean age 51 years (SD 23, 2-96). Race was self-identified, with 79 Black (31%), 50 White (20%), 7 Asian (3%), and 2 Pacific Islander (1%). Unknown race reported by 117 (46%), of which 69 (59%) identified as Hispanic/Latino ethnicity. Ethnically, there were 82 (32%) Hispanic/Latinos, 126 (49%) non-Hispanic/Latinos, and 47 (18%) with no documented ethnicity.

SUMMARY/CONCLUSION: We aim to develop a model to evaluate healthcare inequities in MG within a diverse urban population to address barriers and promote health equity. Demographic analysis suggests continued historical discordances in race conceptualization among Hispanic/Latinos vs. US Census categories and researchers. We invite multi-center collaborators.

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EXPEDITING MYASTHENIA GRAVIS DIAGNOSTIC EVALUATION: A NOVEL, PROOF-OF-CONCEPT TOOL FOR UNDIAGNOSED, SYMPTOMATIC PATIENTS THAT USES SOCIAL MEDIA TARGETING AND SELF-ASSESSMENT

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INTRODUCTION: Myasthenia gravis (MG) patients often encounter diagnostic delays, and undiagnosed patients lack tools for self-advocacy. We developed a novel, peer-reviewed, literature-supported self-assessment tool and logic to gauge MG likelihood for undiagnosed patients with MG-like symptoms. This group was targeted via social media and enrolled in our clinical trial to expediate their path to a neurologist.

OBJECTIVE: We tested the feasibility of a direct-to-patient social media campaign in engaging undiagnosed individuals with MG-like symptoms. The ongoing trial will validate the MG-likelihood-logic and time to potential MG diagnosis.

METHODS: Adults with undiagnosed MG-like symptoms were targeted using social media advertising and recruited to an observational clinical trial (NCT06381284). Users were directed to the study landing-page and completed eligibility. A remote neurologist reviewed trial results: a symptom survey, self-moderated physical tests, and MG-likelihood-logic. Participants received a report indicating their likelihood of MG and will be followed for one-year to self-report their final diagnosis.

RESULTS: The ad campaign cost $3,477. Engagement metrics included: 252,520 impressions, 21,625 ad clicks (8.56% click-through rate), 2,095 unique landing-page visitors, and 146 enrolled and eligible. The study target of 104 patients (45.5 ± 15.1 years, 74% female) completing the physical tests was reached in 78 days. Of these, 66 were deemed high-likelihood for MG, 36 medium-likelihood, and 2 low-likelihood.

SUMMARY/CONCLUSION: With high engagement at a low cost, social media effectively targeted undiagnosed patients with MG-like symptoms. Further analysis is needed to validate the MG-likelihood-logic. Our proof-of-concept study suggests a social media campaign with a self-assessment tool can create pathways for earlier MG diagnosis.

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Archit Gupta - Salaried employee for ZS Associates (sponsor of research).

Michelle Townshend - Salaried employee of ZS Associates (sponsor of research).

Vidya Viswanathan - Salaried employee of ZS Associates (sponsor of research).

Kevin Neal - Paid sub-contractor of ZS Associates (sponsor of research).

Hari Jayaraman - Salaried employee of ZS Associates (sponsor of research).

Anand Trivedi - Salaried employee of ZS Associates (sponsor of research).

Vijesh Unnikrishnan - Salaried employee of ZS Associates (sponsor of research),

Pritikanta Paul - Paid sub-contractor of ZS Associates (sponsor of research),

ALTERNATIVE DOSING OF EFGARTIGIMOD IN MYASTHENIA GRAVIS

Lindsay Malatesta (Nashville, TN), Kyoko Kohno (Nashville, TN), Rachel Renwick (Nashville, TN), Christopher Lee (Nashville, TN)

INTRODUCTION: Efgartigimod is a human IgG1 antibody Fc-fragment that competes with endogenous IgG binding, which reduces IgG recycling and increases IgG degradation. The efficacy of efgartigimod for myasthenia gravis (MG) was proven in the ADAPT trial. The FDA approval mirrored the dosing protocol studied in the trial; one infusion weekly for 4 weeks with subsequent cycles administered based on clinical evaluation, but no sooner than 50 days from the start of the previous treatment cycle. This is a novel dosing strategy was based on patients' responses. Applicability of medications from clinical trials into clinical practice is of interest, especially with this unique study design.

OBJECTIVE: Describe potential alternative efgartigimod dosing in the clinical setting that varies from product labeling.

METHODS: 65 MG patients who received at least one cycle of efgartigimod were included in analysis. Baseline demographics, dosing strategies, MG-ADL scores, and continuation versus discontinuation of treatment were assessed.

RESULTS: Of the 65 patients enrolled, 55 patients received efgartigimod cycles on every 50-day cycles and 10 patients received doses outside of current product labeling. Alternative dosing strategies ranged from receiving the infusions in a 2 weeks on, 2 weeks off repeating schedule, or starting subsequent dosing cycles sooner than 50 days. Of the patients who received efgartigimod on alternative dosing strategies, 7 of 10 patients have remained on therapy. No significant safety concerns were reported with patients on alternative dosing compared to traditional dosing.

SUMMARY/CONCLUSION: The results of this data support alternative dosing strategies of efgartigimod in MG.

Disclosures:

Lindsay Malatesta - AD Board for Alexion

ACETYLCHOLINE RECEPTOR ANTIBODIES AS A BIOMARKER OF TREATMENT STRATEGY WITH RITUXIMAB IN MYASTHENIA GRAVIS

Li Zhang (Chicago, IL), Arjun Seth (Chicago, IL)

INTRODUCTION: Myasthenia Gravis (MG) is an autoimmune disorder caused by autoantibodies directed against the postsynaptic nicotinic acetylcholine receptor (AChR) in the neuromuscular junction. Rituximab is an anti-CD20 monoclonal antibody used to treat myasthenia through B cell depletion. Studies have shown that AChR titers do not correlate with disease activity and that AChR titers can vary in those on complement inhibitors or oral immunosuppressants.

OBJECTIVE: Our hypothesis is that AChR titers can be used as a biomarker of disease treatment strategy with rituximab in correlation with MG severity by the Myasthenia Gravis Activities of Daily Living (MG-ADL).

METHODS: This is a retrospective case series of 12 AChR MG patients comparing AChR titers and MG-ADL scores before and after 1 to 3 in cycles of rituximab.

RESULTS: There was a 58% average reduction in AChR titers in 11 out of 12 patients post-rituximab infusions. These 11 patients had an average decrease in their MG-ADL scores of 7.5. MG-ADL scores improved greatly in 9 out of these 11 patients, from an initial score ranging from 7-20 to a post rituximab score ranging from 0-2. One patient did not have a change in their AChR titers after 1 cycle of rituximab but did have a decrease in their MG-ADL by 5.

SUMMARY/CONCLUSION: This data suggests a correlation between AChR titer reduction and improvement of MG-ADL scores after rituximab infusion in MG. This supports our hypothesis that AChR titers could be used as a surrogate biomarker for longer term treatment strategy of rituximab in MG.

SAFETY AND TOLERABILITY OF WHOLE-BODY ELECTRICAL MUSCLE STIMULATION EXERCISE IN ADULTS WITH MYASTHENIA GRAVIS: A PRELIMINARY ANALYSIS

Mamatha Pasnoor (Kansas City, KS), Melissa Currence (Kansas City, KS), Sandhya Sasidharan (Fairway, KS), Arsh Ketabforoush (Columbia, MO), Abby Davis (Kansas City, KS), W. David Arnold (Columbia, MO), Kristina Kelly (Columbia, MO)

INTRODUCTION: Fatigable muscle weakness affects patients with Myasthenia Gravis (MG), impacting daily activities. Exercise can improve physical function in MG but may be difficult to tolerate. For this population to fully realize the benefits of exercise, improved approaches are needed.

OBJECTIVE: To assess safety and tolerability of whole-body electrical muscle stimulation (WB-EMS) exercise in adults with myasthenia gravis.

METHODS: Participants complete supervised WB-EMS Exercise sessions (10-12 exercises performed in 20 minutes, 2x/week for 4 weeks, stimulation levels are customized). Before and immediately after each session, vital signs and numeric pain rating scale (NPRS) are captured. Rate of perceived exertion (RPE-10) is assessed after each exercise. Tolerability for each session is rated on a Likert scale of 0-9 (0=very tolerable, 9=very intolerable). Participants report worst pain/soreness between sessions via NPRS. Adverse events (AEs) are reviewed at each visit. Descriptive statistics are calculated.

RESULTS: Two participants have finished the study. They attended 100% of scheduled visits and completed 93.8% (15/16). One visit was stopped due to dysautonomia; this was the only AE (Grade 2, unlikely related). Vital signs showed appropriate responses to exercise at 15/16 sessions. NPRS exhibited clinically insignificant changes in 15/16 sessions. RPE-10 was maintained at mild/moderate intensity 91.1% of the time. Average RPE-10, tolerability, and worst pain/soreness between sessions were 3.11, 3.91, and 3.06, respectively.

SUMMARY/CONCLUSION: Preliminary analysis suggests that WB-EMS Exercise is safe and tolerable for adults with MG and could be an avenue for alternative exercise participation. Recruitment is ongoing. Updated results will be presented.

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