

2020 Muscle Study Group Annual Scientific Meeting

The MSG meeting is scheduled for Sept 25, 26, and 27 and we published Issue 4 of the *RRNMF Neuromuscular Journal* which contains the abstracts from the meetings prior to the first day of the meeting.

This year due to COVID-19 the MSG meeting has gone 100% virtual. While this will be a challenge it has some opportunities. Typically, about 175 neuromuscular specialists sign up for the meeting which for several years has been in Snowbird, Utah, but this year was scheduled to be in Georgetown, Washington DC. We have also had meetings in Oxford, England and the early years of MSG were held in upstate New York, in Beaver Hollow, outside of Buffalo.

But this year it is being held in your own home/office! And as a result, we have over 500 individuals registered not only from the US, UK and Europe but from 17 other countries! The planning committee had to be creative in organizing the conference. First, we decided to begin early in the morning and end around noon or 1, because we have many attendees from the UK and Europe, and now as it turns out from all over the world. Most of our speakers we had invited agreed to do their talk virtually. Some were pre-recorded. The challenge was the scientific “platform” presentations from MSG members and posters from attendees. We have a few 15-minute scientific platform presentations from MSG members, especially from prior, current and future MSG funded neuromuscular fellows. But most were in the “poster” category. We debated on having a virtual “poster room”. But we opted to give each “poster” instead a 5-minute FLASH presentation followed by 5 minutes of Q and A. At the end of the morning sessions we plan to have “rooms” with the FLASH presenters from that day that any conference attendee can visit and ask more questions. Welcome to the virtual era. I am anxious to see how this year’s conference works out.

We are indebted to the Planning Committee who was able to be nimble and adjust to the COVID pandemic for this meeting; to the executive committee, and especially to our administrative director, Liz (Elizabeth) Paulk who has worked very, very hard to make this a successful meeting for us all. Thank you Liz! In addition, we would like to thank all of the sponsors who continued to support this meeting even when the decision was made to go virtual. Their generous support was appreciated even more because of that. And thank you to all the invited speakers, the FLASH presenters, and attendees. MSG hired Amardeep Gill, a virtual event producer in New York City to put this all together and “Gill” has been a pleasure to work with. Next year we tentatively plan to have the meeting take place in Georgetown on September 24-26, 2021.

But who knows.. we may prefer to keep this virtual! Let us know how you like this one.

Thanks,
Rick

2020 Planning Committee

Carolina Barnett-Tapia, M.D., Ph.D. // Chair University of Toronto
Chafic Karam, M.D. // Oregon Health and Science Hospital
Gita Ramdharry, Ph.D. // Queen Square MRC Centre for Neuromuscular Disease
James B. Lilleker, MBChB, Ph.D. // The University of Manchester
Kimberly A. Hart, M.A. // University of Rochester Medical Center
Lindsay Alfano, DPT // Nationwide Children's Hospital
Richard Barohn, M.D. // MSG Chair University of Missouri
Prof Michael Hanna, M.D. // MSG Co-Chair University College London

MSG Executive Committee

Richard Barohn, M.D. // Chair University of Missouri
Prof Michael Hanna, M.D. // Co-Chair University College London
Robert Griggs, M.D. // Former Chair University of Rochester Medical Center
Mazen Dimachkie, M.D. // Investigator Member, Treasurer University of Kansas Medical Center
Valeria Sansone, M.D. // Investigator Member NEMO Clinical Center
Michael McDermott, Ph.D. // Biostatistician University of Rochester Medical Center
Rabi Tawil, M.D. // Director, MSG Coordination Center, University of Rochester Medical Center
William David, M.D., Ph.D. // Massachusetts General Hospital
Melissa McIntyre, DPT, DPT // Evaluator Member University of Utah
Marie Wencel, CCRP // Coordinator Member University of California, Irvine

Elizabeth Paulk, MSG Administrative Manager, epaulk@kumc.edu. 913.945.6939
Amardeep Gill, ZOOM Event Producer, customerservice@streamguru.net

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AGENDA //

Friday, September 25

Carolina Barnett-Tapia, M.D., Ph.D. & Chafic Karam, M.D. // *Moderators*

MUSCLE STUDY GROUP

- 8-8:15 A.M.** **WELCOME** Richard J. Barohn, M.D., Prof Michael G. Hanna, M.D.
- 8:20-8:30 A.M.** **UPDATE ON THE PHASE 2/3 STUDY OF ARIMOCLOMOL IN IBM ***
Mazen Dimachkie, M.D. // *University of Kansas Medical Center*
- 8:32-8:42 A.M.** **MSG INTERNATIONAL INCLUSION BODY MYOSITIS (IBM)
GENETICS CONSORTIUM UPDATE *** Alaa Khan, Ph.D. // *UCL Queen's Square*
- 8:45-8:55 A.M.** **INFLUENCE OF NT5c1A ANTIBODIES ON DISEASE PROGRESSION, CLINICAL PHENOTYPE
AND BLOOD AND MUSCLE BIOMARKERS IN SPORADIC INCLUSION BODY MYOSITIS:
A PROSPECTIVE EVALUATION *** Tahseen Mozaffar, M.D. // *University of California, Irvine*
- 9:00-9:20 A.M.** **DEVELOPMENT WORK FOR AN APP-BASED INTERVENTION TO PROMOTE PHYSICAL
ACTIVITY IN PEOPLE LIVING WITH AND BEYOND CANCER**
Dr. Abi Fisher // *Associate Professor, UCL School of Behaviour Change*
- 9:25-9:55 A.M.** **CHALLENGES OF HEALTH ECONOMIC ASSESSMENT FOR SPINRAZA AND ZOLGENSMA**
Rick Chapman, Ph.D. // *Institute for Clinical & Economic Review*
- 10-10:20 A.M.** **INCORPORATING IMPLEMENTATION SCIENCE QUESTIONS INTO CLINICAL
EFFECTIVENESS TRIALS**
Geoff Curran, Ph.D. // *Professor, University of Arkansas for Medical Sciences*
- 10:25-10:50 A.M.** **THE HEALEY ALS PLATFORM TRIAL: INNOVATIVE TRIAL DESIGN AND COLLABORATION
TO ACCELERATE DRUG DEVELOPMENT**
Sabrina Paganoni, M.D., Ph.D. // *Healey Center for ALS, Massachusetts General Hospital*
- 10:55-11:10 A.M.** **BREAK**

**Not for CME Credit*

- 11:10-11:25 A.M.** **PROXIMAL NERVE IMAGING IN CMT1A**
Reza Sadjadi, M.D. // *MSG Fellow, Massachusetts General Hospital*
- 10:27-11:37 A.M.** **LONG-TERM SAFETY AND EFFICACY OF GOLODIRSEN IN MALE PATIENTS WITH
DUCHENNE MUSCULAR DYSTROPHY AMENABLE TO EXON 53 SKIPPING**
Francesco Mutoni, M.D. // *Chair of Paediatric Neurology, UCL GOS Institute of Child Health*
- 11:39-11:49 A.M.** **SATISFACTION WITH ANKLE FOOT ORTHOSES IN INDIVIDUALS WITH CHARCOT-MARIE-TOOTH**
Riccardo Zuccarino, M.D., PMR // *Fondazione Serena Onlus, Centro Clinico Nemo*
- 11:50 A.M.-12 P.M.** **EXPLORING MUSCLE STRUCTURE, FUNCTION AND GAIT PATTERNS IN PEOPLE WITH
DISTAL HEREDITARY MOTOR NEUROPATHY: NATURAL HISTORY AND THE EFFECT OF
REHABILITATION INTERVENTIONS, STUDY PROTOCOL**
Aljwhara Alangary, PT // *Ph.D. Student, UCL institute of Neurology, UK*
- 12-12:20 P.M.** **EXPANDING POSSIBILITIES IN THE TREATMENT OF SPINAL MUSCULAR ATROPHY**
Perry Shieh, M.D., Ph.D. // *Representative, Genentech*
- 12:25-12:45 P.M.** **SAREPTA PIPELINE OVERVIEW AND THE EVOLUTION OF REMOTE ASSESSMENT
AND STRATEGIES FOR IMPLEMENTATION IN THE COVID-19 ERA AND BEYOND**
Linda P. Lowes, PT, Ph.D. // *Associate Professor, The Ohio State University of College of Medicine*
Louise Rodino-Klapac, Ph.D. // *Senior Vice President, Gene Therapy, Sarepta Therapeutics, Inc.*
- 12:45 P.M.** **CLOSING** Richard J. Barohn, M.D., Prof Michael G. Hanna, M.D.
- 12:45-1:30 P.M.** **FLASH PRESENTER AND SPONSOR NETWORKING
ZOOM BREAKOUT ROOMS (OPTIONAL)**

All times US Central Time

AGENDA //

Saturday, September 26

Lindsay Alfano, DPT & James B. Lilleker, MBChB, Ph.D. // *Moderators*

MUSCLE STUDY GROUP

- 8-8:10 A.M.** **OPENING** Richard J. Barohn, M.D., Prof Michael G. Hanna, M.D.
- 8:10-9:05 A.M.** **ROBERT C. GRIGGS, M.D. ANNUAL MSG LECTURE: HOW THE FSHD PUZZLE WAS SOLVED**
Rabi Tawil, M.D. // *Fields Endowed Professor of Neurology, University of Rochester Medical Center*
- 9:07-9:27 A.M.** **RARE DISEASES: WHY CONSIDER ECONOMICS?** Karen Lee // *CADTH*
- 9:30-9:50 A.M.** **A NOVEL APPROACH TO OPTIMIZING MOVEMENT IN TREATED CHILDREN WITH SPINAL MUSCULAR ATROPHY** Megan Iammarino, PT, DPT // *Nationwide Children's Hospital*
- 9:55-10:10 A.M.** **BREAK**
- 10:10-10:25 A.M.** **MOLECULAR BIOMARKERS IN MYOTONIC DYSTROPHY TYPE 2**
Paloma Gonzalez Perez, M.D., Ph.D. // *MSG Fellow, Massachusetts General Hospital*
- 10:27-10:37 A.M.** **RESULTS FROM A NATIONAL CROSS-SECTIONAL STUDY OF DISEASE-BURDEN IN AMYOTROPHIC LATERAL SCLEROSIS (ALS): RESULTS FROM A NATIONAL CROSS-SECTIONAL STUDY** Jennifer Weinstein, MS // *University of Rochester*
- 10:39-10:49 A.M.** **EXOME SEQUENCING IDENTIFIES NOVEL CANDIDATE GENES AND PHENOTYPIC EXPANSION IN A NEUROMUSCULAR COHORT**
Daniel Calame, M.D., Ph.D. // *Baylor Medical College*
- 10:51-11:01 A.M.** **A SAFETY STUDY OF WEEKLY STEROIDS IN MUSCULAR DYSTROPHY (WSMD)**
Senda Ajroud-Driss, M.D. // *Associate Professor of Neurology, Northwestern University Feinberg School of Medicine*
- 11:03-11:13 A.M.** **AAV GENE THERAPY FOR TNNT1-ASSOCIATED NEMALINE MYOPATHY**
Eleonora D'Ambrosio, M.D. // *University of Massachusetts*
- 11:15-11:25 A.M.** **FOLLOW-UP CARE IN MYASTHENIA GRAVIS DURING COVID-19: COMPARISON OF TELEMEDICINE AND IN-PERSON ENCOUNTERS**
Constantine Farmakidis, M.D. // *Assistant Professor, University of Kansas Medical Center*
- 11:28-11:38 A.M.** **POST-COVID GUILLAIN-BARRE SYNDROME MIMICKING MYOSITIS**
Sai Si Thu, M.D. // *SUNY Downstate Medical Center, USA*
- 11:38-11:45 A.M.** **BREAK**
- 11:45 A.M.-12:05 P.M.** **TOTALITY OF EVIDENCE: CONTROLLING DYSTROPHIN AS AN ANTIGEN IN DUCHENNE MUSCULAR DYSTROPHY (DMD)**
Brian E. Pfister, Ph.D., MBA // *Executive Director, US Medical Head-Neurology, PTC Therapeutics*
- 12:10-12:30 P.M.** **THE FUTURE OF MYASTHENIA GRAVIS TREATMENT, SPECIFICALLY THINKING ABOUT WHEN AND WHERE COMPLEMENT AND FCN INHIBITORS MIGHT BE USED MOST EFFECTIVELY BASED ON AVAILABLE DATA** James Howard, M.D. // *Representative, UCB*
- 12:30 P.M.** **CLOSING** Richard J. Barohn, M.D., Prof Michael G. Hanna, M.D.
- 12:30-1:30 P.M.** **FLASH PRESENTER AND SPONSOR NETWORKING
ZOOM BREAKOUT ROOMS (OPTIONAL)**

All times US Central Time

AGENDA //

Sunday, September 27

Kimberly A. Hart, M.A & Gita Ramdharry, Ph.D. // Moderators

MUSCLE STUDY GROUP

- 8-8:15 A.M.** **OPENING** Richard J. Barohn, M.D. Prof Michael G. Hanna, M.D.
- 8:20-9:45 A.M.** **SHARK TANK SESSION (\$10K GRANT AWARDED TO BEST PRESENTATION)**
Vera Bril, BSc, M.D., FRCPC, Laurie Gutmann, M.D., James Lilleker, MBChB, Ph.D.,
William David, M.D., Ph.D. // *Sharks*
Will Meurer, M.D. // *Moderator*
- HEAD TO HEAD** Dr. Vino Vivekanandam // *UCL Institute of Neurology*
- CLASH OF THE TITINS** Jennifer Roggenbuck, MS, LGC // *The Ohio State University College of Medicine*
- PROJECT NMD MUSE: INSPIRING A DEEPER UNDERSTANDING OF MOTOR UNIT BEHAVIOR IN NEUROMUSCULAR DISEASE** Kristina M. Kelly, PT, DPT, EdM, NCS, CPT, PES // *The Ohio State University*
- EXPLORING CSF BIOMARKERS IN PREPARATION FOR CLINICAL TRIALS TARGETING CNS IN DM1**
Carola Rita Ferrari-Aggradi // *Medical Student, University of Milan*
- 9:45-10 A.M.** **BREAK**
- 10-10:10 A.M.** **RESPIRATORY FUNCTION AND THE ROLE OF NON-INVASIVE VENTILATION IN MYOTONIC DYSTROPHY TYPE 1: A RETROSPECTIVE STUDY**
Carola Rita Ferrari-Aggradi // *Medical Student, University of Milan*
- 10:13-10:23 A.M.** **MAGNETIC RESONANCE IMAGING (MRI) IN PERIODIC PARALYSIS**
Dr. Vinojini Vivekanandam // *UCL Institute of Neurology*
- 10:25-10:35 A.M.** **INCIDENCE AND RISK FACTORS FOR PATELLOFEMORAL DISLOCATION IN ADULTS WITH CHARCOT-MARIE-TOOTH DISEASE: AN OBSERVATIONAL STUDY**
Enza Leone, PT, MSc // *UCL Great Ormond Street Institute of Child Health*
- 10:35-10:45 A.M.** **ANNOUNCEMENT OF SHARK TANK AWARD**
- 10:45-10:55 A.M.** **REFRACTORY CIDP: CHARACTERISTICS, ANTIBODIES AND RESPONSE TO ALTERNATIVE TREATMENT**
Jamila Godil // *Medical Student, Oregon Health and Science University*

- 10:57-11:07 A.M.** **TIMED MOTOR FUNCTION TESTS IN BOYS WITH NONSENSE DMD MUTATIONS**
Darina Dinov, DO // *PGY-2 Child Neurology Resident, Virginia Commonwealth University*
- 11:09-11:19 A.M.** **PATIENT ACCEPTABLE SYMPTOM STATES (PASS) IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY (CIDP)** Meg Mendoza, Ph.D. // *Research Analyst I, UHN*
- 11:21-11:31 A.M.** **SCREENING FOR GENETIC MUTATIONS IN PATIENTS WITH NEUROPATHY WITHOUT DEFINITE ETIOLOGY IS USEFUL** Braden Vogt // *Medical Student, Brown University*
- 11:33-11:43 A.M.** **OPTIMIZING HAND-FUNCTION PATIENT OUTCOME MEASURES FOR INCLUSION BODY MYOSITIS**
Ava Lin, M.D., Ph.D. // *Clinical Assistant Professor, University of Michigan*
- 11:45-11:55 A.M.** **FURTHER INSIGHT INTO DYSPHAGIA USING MBS-IMP IN ADULT PATIENTS WITH NEPHROPATHIC CYSTINOSIS AND MYOPATHY**
Stacey Sullivan MS, CCC-SLP // *Massachusetts General Hospital*
- 11:57 A.M.-12:07 P.M.** **LIVE CELL-BASED ASSAY FOR ANTIBODIES TO CLUSTERED ACETYLCHOLINE RECEPTOR IN MYASTHENIA GRAVIS, CROSS VALIDATION, INTER-ASSAY STABILITY AND UTILITY IN A PAEDIATRIC COHORT SUSPECTED FOR MG** Hans Frykman, M.D., Ph.D., FRCPC // *Clinical Assistant Professor, The University of British Columbia*
- 12:09-12:19 P.M.** **DIAGNOSTIC OUTCOME OF GENETIC TESTING ON NEUROMUSCULAR DISORDERS IN A TERTIARY CENTER** Husam Al Sultani, M.D. // *Nerve and Muscle Center of Texas*
- 12:20-12:30 P.M.** **PATIENT PREFERENCE IN VIRTUAL VERSUS IN-PERSON VISITS IN NEUROMUSCULAR CLINICAL PRACTICE** Komal Naeem // *Neurology Resident (3rd Year), Baylor College of Medicine*
- 12:30 P.M.** **CLOSING** Richard J. Barohn, M.D., Prof Michael G. Hanna, M.D.
- 12:35-1:35 P.M.** **FLASH PRESENTER AND SPONSOR NETWORKING ZOOM BREAKOUT ROOMS (OPTIONAL)**

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ABSTRACTS FROM THE 2020 MUSCLE STUDY GROUP
ANNUAL SCIENTIFIC MEETING

Title: **Timed motor function tests in boys with nonsense DMD mutations**

Author: *Darina Dinov, Heather Gordish-Dressman, Mathula Thangarajh; CINRG investigators.*

Abstract: **Introduction:** Boys with nonsense DMD mutations have worse motor outcomes but the natural history of timed motor function tests are not known.

Objective: To learn the natural history of decline in motor function from boys with confirmed nonsense DMD mutations using the DMD Natural History data.

Method: A total of 27 boys with 144 observations over 10 years were studied. The three timed function tests evaluated were time to run/walk 10 m velocity, time to climb 4 stairs and time to stand from supine. Data was analyzed using mixed linear model.

Result: All three timed function tests declined over time. Walk velocity declined by 0.2 m/sec each year. Corticosteroid treatment was protective with current steroid user having a walk velocity of 0.4 units greater than those not on steroids.

Conclusion: Increased knowledge of motor outcomes in nonsense DMD mutations can help with clinical trial design in this subset of patients.

- Title: **Patient Preference in Virtual Versus In-Person Visits in Neuromuscular Clinical Practice**
- Author: *H. Al Sultani, K. Hafeez, A. Shaibani, A. Habib*, H. Kushlaf**, K. Johnson***, N. Robbins****, Z. Siddiqi ***** (Houston, Tx, Irvin, CA*; Cincinnati, OH**; Jefferson, LA***; Hanover, NH****; Edmonton, AB*****)*
- Abstract: The COVID-19 pandemic has led to increased utilization of tele-health services. To inform future decisions on the subject, we phone surveyed patient preference of virtual vs in-person visits in 12 neuromuscular centers in the USA and Canada. The survey consisted of 11 questions. The Data from the first 278 collected surveys revealed that 24.82% preferred virtual visits and 53.96% preferred in-person visits. 67.99% reported physical face-to-face interaction as “very important”. For receiving a new diagnosis, 58.99% preferred in-person vs 30.58% reported no preference. Fewer patients were worried about not having physical examination or routine vitals recording (38.49% and 21.22% respectively). 82.73% believed virtual visits were sufficiently private. 68.35% didn’t consider expenses a factor in their decision. While 91.73% were comfortable with communication technology. 52.16% preferred video communications, and 23.74% preferred phone calls. **Conclusion:** Although neither technology, privacy or finance burdened patients in our study, more patients preferred physical interaction over virtual communication especially to receive a new diagnosis. This emphasizes the importance of the healing effect of the physician’s touch.

Title: Diagnostic Outcome Of Genetic Testing on Neuromuscular Disorders in a Tertiary Center

Author: *H. AlSultani, K. Naeem*, A. Mendez-Zaidi**, A. Shaibani* (Houston, Tx)*

Abstract: Utilization of diagnostic genetic testing in neuromuscular disorders has been expanding and the methods have been progressively improving. To illustrate this trend, we collected genetic testing data in a tertiary neuromuscular clinic from 2014-2020. A total of 514 tests were ordered. 64.57% were neuromuscular panels, 25% single gene tests and 9.84% WES. Results: 28.6% of the total were positive for a pathogenic variant (PV). Per method, positive testing was 43% for single gene testing, 23.17% for panels and 30% for WES. For specific disorders positive outcome was; 18% for MND, 38% for myopathy, and 19% for neuropathy. Diagnostic predictability of panels after negative single gene testing was 44% and that of WES after negative panels was 38%. Conclusions: genetic testing has improved diagnosis of neuromuscular disorders. Compared to other studies, our data showed higher diagnostic yield, reflecting the progressive improvement in the diagnostic outcome of genetic testing.

Title: **Live Cell-Based Assay For Antibodies To Clustered Acetylcholine Receptor In Myasthenia Gravis, Cross Validation, Inter-Assay Stability And Utility In A Paediatric Cohort Suspected For MG**

Authors: *H. Frykman and A. Cruz (Vancouver, CA)*

Abstract: **Introduction:** A live cell-based assay (CBA) expressing clustered acetylcholine receptor (AChR) on the cell surface through co-expression of rapsyn has been shown to detect AChR antibodies (Ab) in 16%-60% of myasthenia gravis (MG) patients that do not have measurable AChR Ab or muscle-specific tyrosine kinase antibodies by radioimmunoprecipitation assay (RIPA).

Objective: To validate the CBA for testing of clustered AChR Ab in the diagnosis of MG

Methods: 49 AChR Ab RIPA positive and 50 healthy control sera were blinded and assayed three times by CBA. Additionally, a cohort of RIPA negative sera from 45 Canadian children age 16 years and younger with suspect MG were assayed.

Results: In all three assays, 48 tested CBA positive and 51 negative. 7 children samples were CBA positive. Follow-up showed 3 have ocular MG and 4 have generalized MG.

Conclusion: The clustered AChR CBA is highly sensitive and replicable and improves diagnostic sensitivity of MG in children.

- Title: **Respiratory Function and the Role of Non-Invasive Ventilation in Myotonic Dystrophy Type 1: a Retrospective Study**
- Author: *C.R. Ferrari Aggradi, A. Lizio, E. Falcier, E. Roma, F. Rao, A. Zanolini, A. Barp, J. Casiraghi, S. Pozzi, E. Carraro, A. Pirola, V.A. Sansone (The NEMO Clinical Center, Neurorehabilitation Unit, University of Milan, Italy)*
- Abstract: **Introduction:** The factors that influence respiratory function decline, one of the main causes of death in myotonic dystrophy type 1, need to be further explored.
Objectives: To analyze respiratory function and the role played by NIV initiation over time.
Methods: 152 adult patients with DM1 were subjected to: arterial blood gas analysis, spirometry, cough efficacy, nocturnal oximetry and respiratory muscle strength.
Results: 75 of 152 had normal respiratory function (49,34%, mean age: 37 years, mean BMI: 23,51, mean disease duration: 10 years), 77 received NIV indication (50,66%, mean age: 48 years, mean BMI: 25,88, mean disease duration: 14 years) but only ¼ were NIV compliant (19/77, 24,68%, mean follow-up: 4,95 years). 5 were lost to follow up.
Conclusions: Compliance is a limiting factor in respiratory care in DM1. Ongoing analysis of longitudinal respiratory, neuromotor and psychological assessments will provide insights into respiratory function decline including the role of NIV.

- Title:** Perceptions of current myasthenia gravis (MG) therapies and unmet needs of neurologists and patients in the USA: a blinded retrospective survey with patient chart review
- Authors:** C. Karam¹, D. Gelinis², M. Jefferson², G. Buckland³, N. Silvestri⁴
Affiliations: 1Oregon Health & Science University, Portland, OR, USA; 2argenx, Boston, MA, USA; 3Collective Acumen, Greenwich, CT, USA; 4 University at Buffalo, Buffalo, NY, USA
- Abstract:** **Introduction:** Perceived satisfaction with MG therapy may influence treatment decision-making by physicians.
Objectives: To categorize the spectrum of disease control perceived by patients and neurologists to gain insight on unmet need and to optimize potential treatment selection.
Methods: This blinded survey of 60 neurologists included retrospective chart review of 180 patient charts identified as three target populations: “controlled but dissatisfied,” “controlled but at-risk,” and “uncontrolled, unstable.” Descriptive statistics were performed.
Results: Neurologists reported only 25% of patients had “uncontrolled, unstable” disease but 34% lacked satisfactory outcome, suggesting >50% of patients may have unmet needs. Despite the perception of disease control, dissatisfaction was high among “controlled” patients and neurologists. “At-risk” patients were more likely to have moderate disease with more comorbidities and more complex treatment regimens, including novel agents.
Conclusions: While MG is considered a treatable disease, this study supports the need for novel, more effective therapies with fewer side effects.
Disclosures: Author contributions: All authors critically interpreted the results, reviewed and/or revised drafts of this abstract, and approved the final version for publication. Funding disclosure: This study was funded by argenx US, Inc., manufacturer of efgartigimod. Collective Acumen conducted the study and analyzed the data. C. Karam served as a deputy editor for Neurology and as a consultant for Acceleron Pharma, Inc; Akcea Therapeutics; Alnylam Pharmaceuticals, Inc; Argenx; Biogen; CSL Behring; and Sanofi Genzyme. Dr Karam has received personal compensation for speaking engagements from Akcea Therapeutics; Alnylam Pharmaceuticals, Inc; CSL Behring; and Sanofi Genzyme and research/grant support from Akcea Therapeutics and Sanofi Genzyme. D. Gelinis and M. Jefferson are employees of argenx. G. Buckland is an employee of Collective Acumen. N. Silvestri has served as a consultant for argenx and Alexion Pharmaceuticals.

- Title: **A case of hemiplegic migraine (HM) in a girl with initial diagnosis of congenital muscular dystrophy: a challenging diagnosis.**
- Author: *E. Albamonte, A. Barp, F. Salmin, E. Carraro, M. Moscardi, S. Bergamoni*, V.A. Sansone Neurorehabilitation Unit, the NEMO Clinical Center in Milan, University of Milan, Milan, Italy *Pediatrics Division, Niguarda Ca' Granda Hospital, Milan, Italy.*
- Abstract: **Introduction:** Hemiplegic migraine (HM) is a rare form of migraine in which attacks are accompanied by aura manifestations such as unilateral/bilateral weakness and sometimes with chronic ataxia; it usually starts in the first or second decade of life.
Case Report: we describe an eight-years old girl with hypotonia at birth, absent tendon reflexes and psychomotor delay with an initial diagnosis of a congenital muscular dystrophy, due to a muscle biopsy which was consistent with a dystrophic process. At seven years-old, the patient started having recurrent episodes of loss of consciousness and falls, often associated with transitory limb paresis and drowsiness. Brain MRI revealed mild cerebellar atrophy and vermian hypoplasia. Genetic test for HM revealed the presence of a heterozygous mutation c.4503_4505 del in CACNA1A gene. A therapy with acetazolamide was started with a marked reduction of the attacks.
Conclusions: Early onset, hypotonia and recurrent falls in hemiplegic migraine may mimic a neuromuscular disease.

Title: **Post-COVID GBS Mimicking Myositis**
Author: *S.S. Thu, Z. Charmchi, Y. Anziska*

Abstract: **Introduction:** Cases of Guillain-Barre syndrome (GBS) have been reported in patients infected with SARS-coronavirus-19 (COVID-19). However, all cases occurred in acute infection. We describe GBS occurring in a patient 3.5 weeks after his first COVID-symptoms, from which he had fully recovered weeks earlier, and whose repeated SARS-CoV-2-RNA was negative. This case was atypical in that patient complained of severe bilateral thighs pain and tenderness preceding weakness. Unlike most reported cases, we utilized plasma exchange as treatment to avoid thrombotic complications common in COVID.
Objectives: To report a case with atypical post-COVID GBS, diagnosed on nerve conduction studies.
Methods: Data was extracted from the hospital's electronic medical record.
Results: The patient improved considerably after 5 rounds of plasma exchange and was discharged to inpatient rehabilitation.
Conclusions: GBS can occur both in acute and post-COVID infection, sometimes with unusual presentations. Neurologists should be alert to this complication occurring even weeks after recovery.

Title: **Further insight into dysphagia using MBS-ImP in adult patients with nephropathic cystinosis and myopathy**

Authors: *S. Sullivan, N. Grant, F. Eichler, R. Sadjadi (Boston, MA)*

Abstract: **Introduction:** Nephropathic cystinosis is a lysosomal storage disorder with known myopathic features such as dysphagia which has significant implications for social eating and overall quality of life. Dysphagia is not well characterized in this patient population and there is no guidance towards potential treatment targets.

Objectives: We applied advanced MBS-ImP analysis for more granular description of swallowing impairments with aim to capture deficit that correlated with patient symptom description, not adequately demonstrated with previous examinations.

Methods: We retrospectively evaluated 10 video fluoroscopic swallowing studies from patients with nephropathic cystinosis with various levels of oral and pharyngeal stage dysphagia.

Results: We demonstrated significant oral stage involvement related to lingual strength and control that impacts bolus hold, transport and clearance.

Conclusions: This study provides better insight to dysphagia in this patient population and paves the path for future studies of treatment targets and outcome measures.

- Title:** Exome sequencing identifies novel candidate genes and phenotypic expansion in a neuromuscular cohort
- Author:** *D. Calame, D. Marafi, J. Fatih, T.E. Lotze, P. Mancias, S. Biliciler, F. Abid, K. Sheikh, O. Yesilbas*, H. Erdem**, N. Elcioglu***, B. Tuysuz***, J.E. Posey, D. Pehlivan, J.R. Lupski (Houston, TX; Van, TR*; Ankara, TR**; Instabul, TR***)*
- Abstract:** **Introduction:** Recent advances in exome sequencing (ES) have revolutionized the approach to neuromuscular disorders (NMDs). Significant challenges remain due to overlapping phenotypes, genetic heterogeneity, and the rarity of individual conditions. Around 40-75% of NMD patients lack a molecular diagnosis, a critical step to inform expectant management and guide development of precision therapy.
Objectives: To identify novel NMD genes.
Methods: Family-based ES analysis was applied to a cohort of 43 NMD families.
Results: Preliminary analysis identified two novel candidate genes, DHX9 (autosomal dominant axonal CMT) and COL19A1 (autosomal recessive arthrogyriosis multiplex congenita), a 4.6% novel gene discovery rate. Other novel discoveries include biallelic PNPT1 variants causing CMT, heterozygous ATP7A variants causing distal arthrogyriosis and axonal neuropathy, congenital muscular dystrophy due to biallelic TNNT3 splice-site variants, and biallelic EPG5 variants causing congenital myopathy and intellectual disability.
Conclusion: ES is a powerful tool to identify novel NMD genes and reveal new genotype-phenotype relationships not predicted by current knowledge.

Title: **Results from a National Cross-Sectional Study of Disease-Burden in Amyotrophic Lateral Sclerosis (ALS): Results from a National Cross-Sectional Study**

Author: *Christine Zizzi, BA¹; Ellen Wagner, MS¹; Jennifer Weinstein, MS¹, Jamison Seabury, BS¹, Nuran Dilek, MS²; Michael McDermott, PhD²; Sumaira Hussain, BSc³; Joanne Wu, ScM³; James Caress, MD⁴; Richard Bedlack, MD, PhD⁵; Volkan Granit, MD, MSc³; Jeffrey Statland, MD⁶; Paul Mehta, MD⁷; Michael Benatar, MD, PhD³; Chad Heatwole, MD, MS-CI²*

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Abstract: **Introduction:** Patients with ALS experience a wide range of clinical symptoms that affect how they feel and function.

Objectives: To identify the most common and important disease manifestations in ALS.

Methods: We conducted a cross-sectional study of 532 patients from the Centers for Disease Control and Prevention National ALS Registry to identify the relative importance of 189 individual symptoms.

Results: ALS participants provided over 89,000 symptom rating responses. The symptomatic themes with the highest prevalence in ALS were inability to do activities (93.8%), fatigue (92.6%), problems with hand and finger function (87.7%), and limitations with mobility or walking (86.7%). Symptomatic theme prevalence was widely associated with assistive ventilation reliance, impaired speech, and unemployment.

Conclusions: ALS symptoms, some under-recognized, vary based on disease characteristics and demographic features. These symptoms represent potential targets for future therapeutic interventions.

Study Supported By: Funding for this project was provided by the ALS Association. Research activities were conducted in collaboration with the Center for Disease Control and Prevention and the CReATe Consortium (U54 [NS092091](#)).

Title: **Satisfaction with Ankle Foot Orthoses in Individuals with Charcot-Marie-Tooth**
Author: *Riccardo Zuccarino MD^{***}, Kirsten M. Anderson^{**}, Michael E. Shy MD^{*}, Jason M. Wilken^{**}*
Department of Neurology, The University of Iowa Carver College of Medicine, Iowa City, IA; **Department of Physical Therapy and Rehab Science, The University of Iowa Carver College of Medicine, Iowa City, IA *Neuromuscular Omnicentre (NEMO)- Fondazione Serena Onlus, Via del Giappone 3, Arezano, GE, Italy*

Abstract: **Introduction:** Ankle foot orthoses (AFOs) are commonly prescribed to individuals with Charcot Marie Tooth (CMT). The aim of this study was to evaluate patient reported satisfaction with orthotic devices and services in individuals with CMT to provide baseline knowledge prior to advance AFO care for individuals with CMT.
Methods: A survey including the Orthotics and Prosthetics Users Survey (OPUS) was emailed to individuals with CMT using the INC Contact Registry. The OPUS includes 11 device specific questions and 10 service related questions.
Results: 314 individuals completed the survey. Over one third of participants provided negative responses, including dislike of AFOs appearance, discomfort, experience with abrasions or irritations and pain. Ratings of orthotic services were generally positive.
Conclusions: Lower scores related to comfort, abrasions and pain identified clear areas for AFO improvement. Continued research in these areas will be beneficial to informing and advancing AFO development and improving clinical care.

Title: **Systemic Gene Transfer of Adeno-Associated Alpha-Sarcoglycan for Limb-Girdle Muscular Dystrophy in Young and Aged Mice**

Author: *Eric R. Pozsgai, Danielle A. Griffin, Ellyn L. Peterson, Amber Kempton, Oliver Rogers, Young-Eun Seo, Louise R. Rodino-Klapac*
Sarepta Therapeutics, Inc., Cambridge, MA, USA

Abstract **Introduction:** LGMD2D, due to an SGCA gene mutation, is progressive and debilitating. **Objectives:** Report findings of SGCA gene transfer in mice. **Methods:** Single systemic delivery of 1.0×10^{12} , 3.0×10^{12} , and 6.0×10^{12} vg of scAAVrh74.tMCK.hSGCA was administered in 4-to-5-week-old mouse model of LGMD2D (sgca^{-/-}). The same vector was delivered to 12-month-old sgca^{-/-} mice to assess effects on older, more severely affected muscle. **Results:** All three doses showed robust protein expression of α -SG at the sarcolemma, improved histopathology, increased locomotor activity and specific-force generation, protection against eccentric force loss, and reduced serum CK compared with controls. No vector toxicity was detected. In aged mice, treatment resulted in widespread, high-level protein expression in muscles analyzed, reduced fibrosis, and increased resistance to contraction-induced injury in tibialis anterior muscle. **Conclusions:** Systemically delivered scAAVrh74.tMCK.hSGCA may offer clinical treatment for LGMD2D, and may be efficacious when delivered in older subjects with more severely diseased muscle. **Disclosures:** This study was funded by Sarepta Therapeutics, Inc. All authors are employees of Sarepta Therapeutics and may have stock options.

Title: **Follow-up care in myasthenia gravis during COVID-19: comparison of telemedicine and in-person encounters**

Author: *C. Farmakidis, S. Hunt, M. Pasnoor, O. Jawdat, D. Jabari, R. Barohn*, M.M. Dimachkie (Kansas City, KS; Columbia, MO*)*

Abstract: **Introduction:** Telemedicine may have a role in myasthenia gravis.
Objective: Compare videoconferencing (ZM), telephone (TEL) and in-person (PER) follow-up encounters.

Methods: Retrospective analysis of follow-up encounters March through June 2020.

Results: N=94 encounters. Differences in patient age and distance from clinic were not statistically significant while median MG-ADL scores appeared to differ [ZM 3.6, TEL 2.8, PER 5, $p=0.02$]. Mean encounter duration [ZM 24.3, TEL 22.8, PER 31.5, minutes, $p<0.01$] and MG-specific physical exam regions mean [ZM 2.4, TEL 1.1, PER 3, $p<0.01$] differences appeared to be significant. However, the median number of medical actions after each encounter type did not appear to differ [ZM 3, TEL 2.5, PER 3, $p=0.34$].

Conclusion: Telehealth encounters occurred without respect to age/distance. Patients with higher MG-ADL scores were more likely to be evaluated in person. While duration and exam content appear to differ between ZM, TEL and PER encounters, clinical decision-making remained similar.

Title: **Deflazacort Or Prednisone Treatment For Duchenne Muscular Dystrophy (DMD): Real-World Outcomes At Cincinnati Children's Hospital Medical Center (CCHMC)**

Author: *Jessica Marden¹, Jonathan Freimark¹, Zhiwen Yao¹, James Signorovitch¹, Cuixia Tian², Brenda Wong³*

¹Analysis Group, Inc., Boston, Massachusetts

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Abstract: **Introduction:** Corticosteroids are the standard of care for Duchenne muscular dystrophy. **Objective:** This study assessed real-world deflazacort and prednisone treatment, and ambulatory, pulmonary, and growth outcomes. **Methods:** Among 200 boys, ~75% received deflazacort, ~13% prednisone, and ~12% were prednisone-to-deflazacort switchers. **Results:** From adjusted regressions, deflazacort patients compared with prednisone had: 0.59 stairs/second greater 4-stair climb velocity, 4.6 points higher NSAA score, and 9.9% higher FVC %-predicted ($P < 0.05$ each). Total body mass was 6.9kg lower, height was 6.2cm lower, and % lean body mass was 4.4% higher. In Kaplan-Meier analyses, by age 15 (age 20), 56.4% (85.1%) of prednisone-initiated patients were wheelchair-bound, compared to 43.7% (78.7%) of deflazacort-initiated patients ($P < 0.01$). By age 15 (20), 13.7% (64.8%) of prednisone-initiated patients had scoliosis compared to 8.9% (33.7%) of deflazacort-initiated patients ($P = 0.05$). **Conclusions:** This study adds evidence associating deflazacort with greater functional and lean body mass preservation, and delay of scoliosis vis-à-vis prednisone.

Title: **Pulmonary function in non-ambulatory patients with nmDMD from the STRIDE Registry and CINRG Duchenne Natural History Study: a matched cohort analysis.**

Author: *Andrés Nascimento Osorio,¹ Már Tulinius,² Filippo Buccella,³ Isabelle Desguerre,⁴ Janbernd Kirschner,⁵ Eugenio Mercuri,⁶ Francesco Muntoni,⁷ Joel Jiang,⁸ Allan Kristensen,⁸ Panayiota Trifillis,⁸ Claudio L. Santos,⁸ and Craig M. McDonald⁹ on behalf of the STRIDE and CINRG DNHS investigators*

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Abstract: **Introduction:** The STRIDE registry provides observational data on ataluren use in patients with nmDMD.

Objective: Decline in pulmonary function was compared between non-ambulatory nmDMD patients receiving ataluren+ standard of care (SoC; corticosteroid/palliative therapies) and DMD patients receiving SoC [CINRG DNHS].

Methods: Propensity score matching identified comparable non-ambulatory patients from STRIDE and CINRG DNHS using predictors of disease progression. Kaplan–Meier analyses estimated age at loss of ambulation (LOA) and pulmonary function decline. Results: Median age at LOA for STRIDE vs CINRG DNHS cohorts (each n=22) was 12.4y vs 11.1y. Mean Ataluren exposure for patients in STRIDE up to LOA was 302d. Median Age at %-predicted forced vital capacity (FVC) <60% was delayed for patients from STRIDE vs the CINRG DNHS (18.7y vs 15.6y). Mean Ataluren exposure for patients in STRIDE up to %-predicted FVC <60% was 661d.

Conclusion: Aaluren+SoC treatment may slow pulmonary disease progression in non-ambulatory nmDMD patients.

Title: **Demographics and safety data from patients with nonsense mutation Duchenne muscular dystrophy receiving ataluren in the STRIDE Registry.**

Author: *Francesco Muntoni,^{1,2} Filippo Buccella,³ Isabelle Desguerre,⁴ Janbernd Kirschner,⁵ Andrés Nascimento Osorio,⁶ Már Tulinius,⁷ Joel Jiang,⁸ Allan Kristensen,⁸ Panayiota Trifillis,⁸ and Claudio L. Santos⁸*

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Abstract: **Introduction:** Ataluren promotes the production of a functional dystrophin and is indicated for the treatment of patients with nonsense mutation Duchenne muscular dystrophy (nmDMD). STRIDE is an ongoing registry providing real-world data on ataluren use in nmDMD patients.

Objectives: Describe the demographics of the STRIDE population and interim safety results as of January 2019.

Method: Patients' data are collected at the consent date; Patients are followed for ≥ 5 years.

Results: As of January 2019, 220 boys (210 confirmed nmDMD) were enrolled in STRIDE in 11 countries and received ≥ 1 ataluren dose. Mean ataluren exposure (SD) was 822 ± 368 days. Safety outcomes were consistent with the known ataluren profile. Mean age at consent date (SD) was 10.6 ± 3.6 years. Mean age at first symptoms and nmDMD confirmation was 2.8 ± 1.8 years, and 5.2 ± 2.9 years, respectively.

Conclusions: STRIDE constitutes the first drug registry for nmDMD. STRIDE data analyses provide insights into the real-world ataluren effectiveness/safety.

Title: **A safety study of Weekly Steroids in Muscular Dystrophy (WSiMD)**
 Author: *Senda Ajroud-Driss, Aaron Zelikovich, Glenn Walter, Abhinandan Batra, Benjamin Josselin, Patricia Casey, Robert Sufit, Elizabeth McNally*
Dept of Neurology, Center for Genetic Medicine, Department of Medicine (Cardiology) Northwestern University Feinberg School of Medicine. Department of Physiology and Functional Genomics, University of Florida.

Abstract: **Introduction:** Corticosteroids are known to improve strength and prolong ambulation in Duchenne Muscular Dystrophy, where common dosing strategies include daily or high dose weekend steroids. Steroid use in Becker Muscular Dystrophy or Limb Girdle Muscle Dystrophy (LGMD) has been less well studied, with at least one study showing adverse outcomes in dysferlin-related LGMD. Recently, once weekly steroid dosing was found to promote strength and lean muscle in preclinical models including the mdx mouse and two mouse models of LGMD.

Objective: To report the results of an open label safety and efficacy clinical trial of oral weekly corticosteroids in adults with BMD and LGMD subtypes.

Methods: Participants received prednisone at 0.75-1g/kg orally on Mondays after the evening meal. Participants completed strength and functional assessments, a quality of life questionnaire, safety laboratory testing, DEXA scans, exploratory biomarkers as well as muscle MRI imaging before starting steroid treatment and at the end of the 6-month period.

Results: Twenty patients completed 6 months of once weekly prednisone (1 BMD and 19 with different LGMD subtypes, 13 male, 7 female.) 12 of 20 (60%) were ambulatory. Once weekly prednisone was overall well tolerated. We observed no significant negative impact on body weight, blood pressure, forced vital capacity, bone density or safety labs. There was a significant decrease in serum CK, accompanied by an increase in lean mass without an increase in fat mass on DEXA that was significant in the upper and lower extremities. For ambulatory patients we noted an improvement in 6min walk and 10 m run test. MRI analysis revealed a reduction in water T2 in at least one muscle in 80% of the subjects and in all except for one of the ambulatory patients.

Conclusions: Once weekly steroids, given as 0.75-1gm/Kg was well tolerated in LGMD. Although underpowered for efficacy, this study suggests improved lean mass and function in the study cohort and warrants additional investigation of once weekly steroids. This study was funded by Kurt & Peter Foundation.

- Title:** Oral Suspension Formulation of Edaravone for Amyotrophic Lateral Sclerosis: Human Pharmacokinetics and Development Plan
- Author:** *Koji Takei, Tomoyuki Omura, Tomohiro Takahashi, Munetomo Matsuda, Yoshinobu Nakamaru, Hidetoshi Shimizu, Manabu Hirai, Steven Toler*, Joseph Palumbo*, Stephen Apple***
*Mitsubishi Tanabe Pharma Corporation, Tokyo, Japan; *Mitsubishi Tanabe Pharma Development America, Inc., Jersey City, New Jersey, USA; **Mitsubishi Tanabe Pharma America, Inc., Jersey City, New Jersey, USA*
- Abstract:** **Introduction:** An investigational oral formulation of edaravone is being developed as a potential alternative option to the current intravenous (IV) formulation.
Objectives: To describe progress in the clinical development plan for an oral suspension formulation of edaravone.
Methods: A pharmacokinetic (PK) bridging study with long-term safety data and a dosing optimization study were conducted. A Phase 3 safety study in patients with amyotrophic lateral sclerosis (ALS) is ongoing.
Results: The oral formulation was shown to have similar PK to the IV formulation. Safety will be investigated in a 48-week safety study in adult ALS patients (N=150). The efficacy and safety of daily dosing will be assessed in a 48-week, Phase 3b study (N≈400). PK data and study designs will be presented.
Conclusions: The clinical development plan for oral edaravone is intended to help establish the data needed to seek registration for marketing authorization pending further discussion with health authorities.
Acknowledgments: Funded and conducted by Mitsubishi Tanabe Pharma Corporation, Tokyo, Japan (MTPC). ST is an employee of Mitsubishi Tanabe Pharma Development America, Inc (MTDA). TO and JP are former employees of MTPC and MTDA. SA is an employee of Mitsubishi Tanabe Pharma America, Inc (MTPA). All other authors are employees of MTPC.

Title: **Magnetic Resonance Imaging (MRI) in Periodic Paralysis**
 Authors: *Vinojini Vivekanandam^{*1}, Sachit Shah², Emma Matthews¹, Karen Suetterlin¹, Iwona Skorupinska¹, Jasper Morrow¹, Tarek Yousry², Michael G Hanna¹.*
Affiliations: 1. MRC Centre for Neuromuscular Diseases, QS Institute of Neurology, UCL. 2. Neuromuscular MRI Research Group, UCL Institute of Neurology.

Abstract: **Introduction:** The primary periodic paralyses (PP) include hypokalaemic periodic paralysis (HypoPP), hyperkalaemic periodic paralysis (HyperPP) and Andersen Tawil Syndrome (ATS). To date, very few studies have reported neuromuscular MRI changes in these groups.
Objectives: 1. Define the presence, frequency and pattern of lower limb neuromuscular MRI abnormalities in PP.
Methods: Ethics approval was attained (Joint National Hospital for Neurology and Institute of Neurology Research Ethics Committee.) Lower limb MRI scans of patients with genetically proven PP and 10 controls were attained. 38 muscles were scored using the Modified Mercuri semi-qualitative scale. Clinical data was retrospectively collated.
Results: A total of 77 scans were identified. Distinct changes exist in patients with periodic paralysis which consists predominantly of fatty infiltration. Changes are more marked in the thighs, and are most severe in the subset of patients with hypoPP.
Conclusions: This will be the largest review of neuromuscular MRI in patients with PP. Despite the episodic nature of symptoms, there are definite fatty infiltration changes suggesting the disease course is not benign. Differences between subsets also exist.

- Title: **Patient and Treatment Characteristics of a Large US Sample of Patients With Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) Initiating Intravenous Immunoglobulin (IVIG) Therapy**
- Author: *C. Anderson-Smits**, *J.B. Layton***, *M.E. Ritchey***, *V. Hayden**, *S. Chavan**, *N. Souayah****
(*Shire US Inc., a Takeda company, Cambridge, MA, USA**; *RTI Health Solutions, Research Triangle Park, NC***; *Department of Neurology, Rutgers University, Newark, NJ****)
- Abstract: **Introduction:** CIDP is a rare immune-mediated neuropathy with significant burdens. Per guidelines, IVIG is first-line therapy.
Objectives: Describe characteristics of US patients with CIDP initiating IVIG treatment.
Methods: Adult immunoglobulin-naïve patients with CIDP from 2008–2018 were identified via diagnosis coding using the IBM® Watson Health™ MarketScan® Research Databases.
Results: Demographics were similar between new IVIG users (n=3975) and the full cohort (n=32 090). IVIG users, compared with the full cohort, had greater comorbidity and symptom burden (eg, weakness and/or difficulty walking, neuropathic pain, diabetes, hypertension, leukemia/lymphoma, hypothyroidism, rheumatoid arthritis, other auto-immunity disorders). Patient characteristics were similar by initial IVIG product, except for index treatment year.
Conclusions: There was a trend to initiate IVIG in patients with CIDP who had greater comorbidity and symptom burden. Patient characteristics were not correlated with initial IVIG selection; rather, difference in selection varied by year.

- Title: **Phase 3 Study of HyQvia for Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP): ADVANCE-CIDP 1 Infusion Protocol**
- Author: *S. Hasan**, *K. Duff***, *A. Nagy****, *L. Yel*** (*Shire US Inc., a Takeda company, Cambridge, MA, USA**; *Baxalta US Inc., a Takeda company, Cambridge, MA, USA***; *Baxalta Innovations GmbH, a Takeda company, Vienna, Austria****)
- Abstract: **Introduction:** HYQVIA® (Immune Globulin Infusion [Human] 10% with recombinant human hyaluronidase [rHuPH20]; fSCIG) allows for dispersion and absorption of large-dose subcutaneous immunoglobulin.
Objectives: Describe infusion protocol for fSCIG in ADVANCE-CIDP1 (NCT02549170).
Methods: Planned enrollment is 174 adults. The primary outcome is relapse rate (proportion of patients with increase ≥ 1 point in adjusted Inflammatory Neuropathy Cause and Treatment disability scale score from baseline). Recommended sites for infusion are upper to middle abdomen and thighs with 24G needle(s). Number of infusion sites can be 1, 2, or 3, and a needle set can be single, bifurcated, or trifurcated. Maximum infusion volume per site is 600 mL for patients ≥ 40 kg and 300 mL for patients < 40 kg.
Results: This study is ongoing and blinded.
Conclusion: fSCIG is being evaluated as a novel maintenance therapy for CIDP. Baxalta (a Takeda company) funded this study; Shire (a Takeda company) provided medical writing support.

Title: **Infusion Parameters And Demographics Of Patients With Chronic Inflammatory Demyelinating Polyneuropathy During Scig Self-Administration Training**

Author: *Robert McNeill¹, Elyse Murphy¹, Chris Vannam², Melody Bullock², Ayman Kafal¹*
¹CSL Behring LLC, King of Prussia, ²Specialty Pharmacy Nursing Network (SPNN) Inc.

Abstract: **Introduction:** Subcutaneous immunoglobulin (SCIg) was approved for maintenance therapy in adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP) in 2018.

Objectives: Here, we analyzed training data from patients with CIDP as they transitioned to SCIg (Hizentra[®]).

Methods: This was a retrospective, observational study utilizing data collected by specialty pharmacy nurses on self-administration training, discontinuations, and infusion parameters between 3/2018–12/2019 in patients with CIDP.

Results: Overall, 310 adult patients completed 1–7 training visits. SCIg discontinuations due to side effects occurred in 5.8%. Of successfully-trained patients, 54.5% required ≤ 3 training visits. By their final visit, most patients (92.8%) had increased their infusion rate, mL/hr/site (mean increase of 43.37% [standard deviation 66.91%]) and over half (53.8%) were able to reduce their infusion sites by ≥ 1 .

Conclusions: Ongoing training after completion of formal training can improve patients' ability to optimize and individualize their SCIg self-administration technique. Training techniques may need to differ depending on individual patient need.

Funding: CSL Behring

Title: **Patient Acceptable Symptom States (PASS) in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)**

Author: *M. Mendoza, C. Tran, C. Barnett (Toronto, ON)*

Abstract: **Background:** At present, we do not have a patient-anchored definition of what constitutes as a “good” outcome during CIDP treatment.

Objective: We aim to understand how CIDP patients value their current health; by estimating patient acceptable symptom state (PASS) thresholds for common CIDP outcome measures.

Methods: We conducted an online-survey asking North American CIDP patients questions on symptom satisfaction, general demographic and clinical characteristics.

Results: In total, 128 individuals were satisfied with their disease burden (PASS-positive) while 190 participants were not (PASS-negative). In comparison to PASS-negative, PASS-positive patients had better average outcome scores with no differences in age, sex or disease duration. We estimated PASS thresholds for EQ5D (0.57), RODS (32), ONLS (3), INCAT (2) and CAPPRI (14).

Conclusions: Our PASS thresholds represent a global state of “being well” and can be applied as secondary endpoints for CIDP research and aid in clinical decision-making.

Title: **Refractory CIDP: characteristics, antibodies and response to alternative treatment**
 Author: *Jamila Godil**, *Nizar Chahin**, *Alan Pestronk***, *Erik Ensrud**, *Matthew J. Barrett**** and *Chafic Karam** (**Department of Neurology, Oregon Health & Science University, Portland, OR, USA.*
***Department of Neurology, Washington University School of Medicine*
****Department of Neurology, Virginia Commonwealth University, Richmond, VA, USA.*

Abstract: **Introduction:** CIDP is the most common immune mediated neuropathy. Patients usually respond well to high doses of immunoglobulins (intravenous (IV) or subcutaneous), steroids, or plasmapheresis. However, approximately 20-30% of patients with CIDP do not respond well to these therapies, which are considered first-line treatments, and approximately 15% of patients remain refractory to all treatment modalities.
Objective: To review the characteristics, antibodies, and response to alternative treatments in a cohort of patients with refractory CIDP.
Methods: We performed a retrospective chart review of all CIDP patients seen at Oregon Health & Science University Neuromuscular clinic between 2017-2019. We extracted information regarding demographics, clinical characteristics, antibodies, and response to alternative treatments. During this time period it was routine clinical practice of our group to test all CIDP patients for neurofascin (NF) and contactin antibodies.
Results: Among 45 CIDP patients studied, 34 (76%) showed improvement with first-line therapy (steroids, IVIG and/or plasmapheresis) and 11 (24%) were considered refractory to first line therapy. Of the latter, seven (64%) responded to alternative treatment (cyclophosphamide or rituximab). Three were refractory to all treatment. One patient was not prescribed alternative treatment. At the end of study, 39 patients (87%) were ambulatory without aid and 5 (11%) were in remission. One patient died from complications of alcoholic liver cirrhosis. Thrombosis was seen in three patients receiving IVIG. Six patients (13%) tested positive for NF antibodies. Four tested positive for NF155 IgM antibodies only and of those, one responded to IVIG, two partially responded to IVIG and one was refractory. One patient tested positive for NF155 IgG4. Another tested positive for NF155 IgG4 and NF155 IgM. Both patients with IgG4 antibodies were refractory to IVIG, but one responded to rituximab and one was refractory to all treatment.
Conclusion: Less than a quarter of patients did not respond to steroids, IVIG, and/or plasmapheresis. Most of the refractory patients responded to rituximab or cyclophosphamide. Patients with NF antibodies tended to be more resistant to IVIG. The majority of refractory CIDP patients were seronegative and disease management relied on clinical judgment.

- Title: **Incidence and risk factors for patellofemoral dislocation in adults with Charcot-Marie-Tooth disease: an observational study**
- Author: *E. Leone, S. Davenport, C. J. Robertson, M. Laurà, G. Ramdharry (London, UK)*
- Abstract: **Introduction:** Patellofemoral dislocation is frequently reported by people with Charcot-Marie-Tooth disease (CMT). To date, the frequency and the risk factors for patellofemoral dislocation in adults with CMT are unknown.
Objectives: To determine the incidence and the risk factors for patellofemoral dislocation in adults with CMT.
Methods: A cross-sectional, observational study was conducted among adults with different CMT subtypes attending a specialist neuromuscular centre. Participants were invited to undergo a knee examination.
Results: The incidence of patellofemoral dislocation was 32.3% (10/31). Patellar dislocation was associated with CMT-1A ($p=0.013$) and younger age at disease onset ($p=0.004$). Patella alta ($p=0.001$), J-sign ($p=0.017$), lateral patellar glide ($p=0.001$), generalised hypermobility ($p=0.012$) and hamstring weakness ($p=0.012$) were associated with higher risk of patellofemoral dislocation.
Conclusions: Patellofemoral dislocation was common among adults with CMT and was associated with multiple risk factors. The identified predictors may be addressed by clinicians through preventive, supportive and corrective measures.

- Title:** Exploring muscle structure, function and gait patterns in people with Distal Hereditary Motor Neuropathy: natural history and the effect of rehabilitation interventions, Study Protocol.
- Authors:** A. Alangary, J. Morrow, M. Laura, A. Rossor, M. M. Reilly, G. Ramdharry* (London, UK*)
- Abstract:** **Background:** Distal Hereditary Motor Neuropathy (dHMN) is a rare inherited neuromuscular disorder. It is characterised by distal weakness. Though patients usually have a normal lifespan it is a disabling condition and most eventually need aids to walk. In order to improve walking quality in patient with dHMN, research is needed to understand the impairments that lead to altered gait patterns, and to develop interventions to correct walking gait conservatively.
- Aims:** Primary: (1) To explore the natural history of muscle structure and function in dHMN over one year. Secondary: (2) To ascertain relationships between intramuscular fat fraction, muscle volume, isokinetic muscle strength and moments/power generation. (3) To explore the effect of bilateral carbon fibre ankle foot orthoses (AFO) on the kinetics and kinematics of gait of people with dHMN. (4) To explore the effect of resistance training of the ankle muscles in people with ankle muscle strength over grade 4 MRC scale on muscle structure, function, and gait patterns.
- Methods:** Objective1&2: dHMN participants aged over 18 will undergo the following measures: MRI scans of the calves and thighs muscles, isokinetic strength and power measures of the lower limb using the HUMAC Norm dynamometer, 3D motion analysis to capture kinetic and kinematic data of complete gait cycles. For direct comparison of gait deviations, twenty age and gender matched health controls will also be recruited to undergo the same measures. Scans, dynamometry and clinical measures will be repeated after one year to explore the natural history of the disease. Objective3: dHMN participants will undergo additional gait analysis: wearing just shoes (control condition), wearing their own prescribed orthoses (where appropriate), and wearing bilateral carbon fiber AFOs. Objective4: up to 15 dHMN participants will be prescribed a home based, resistance training program for 16 weeks, supervised through weekly phone calls, monthly visits and an exercises diary. Response to training will be analysed by: MRI scans, myometry, and 3D motion analysis.

Title: **Screening for genetic mutations in patients with neuropathy without definite etiology is useful**

Author: *B. Vogt, N. Chahin, W. Wiszniewski, T. Ragole, C. Karam (Portland, OR)*

Abstract: **Introduction:** Many genetic neuropathies are misdiagnosed. Recently, the first therapeutic for a genetic neuropathy, namely hATTR Amyloidosis, has been approved. The two companies who created these therapeutics are currently sponsoring free genetic neuropathy panels.

Objective: To determine the clinical usefulness of systemic genetic testing in neuropathies without definite etiology.

Methods: We systematically performed genetic testing in all patients with neuropathy who did not have a definite etiology, seen between 2017 and 2020. The testing consisted of an inherited neuropathy panel (72 to 81 genes).

Results: Pathogenic mutations were found in 30/200 (15%). The management was altered in 4/200 (2%) overall, and 4/108 (5.6%) of patients not suspected to have an inherited neuropathy.

Conclusion: Screening for genetic mutations in patients with neuropathy without a definite etiology is useful. While only a minority of patients with unsuspected inherited neuropathy tested positive, the findings altered management in some, improving morbidity and, perhaps, mortality.

Title: **Optimizing hand-function patient outcome measures for inclusion body myositis**
Author: *Ava Y Lin, Catherine S Siener, Anna Faino, Michelle Seiffert, Conrad C Wehl, Leo H Wang*

Abstract: Inclusion body myositis (IBM) is the most common acquired myopathy after the age of 45. The slowly progressive and heterogeneous disorder is a challenge for measuring clinical trial efficacy. One current method for measuring progression utilizes the IBM Functional Rating Scale (FRS). We have found that the hand domain scores in the IBM-FRS do not consistently change until there is extreme loss of grip and finger flexor strength. Therefore, we performed a cross-sectional observational study of 83 IBM and 38 control patients recruited at the 2019 Annual Patient Conference of The Myositis Association. We evaluated new hand function patient-reported outcome measures modified from the NIH Patient-Reported Outcomes Measurement Information System (PROMIS). We find that hand-function PROs have a higher correlation with pinch and grip strength than the IBM-FRS.

- Title:** Top 10 research priorities for patients with primary mitochondrial disease and their carers
- Author:** *T. D. Graves^{1,2}, L. Butterworth³, C. Feeney⁴, S. Holmes¹, A. Hunter⁵, J. Lowndes⁶, S. Rahman⁷, J. Sharpe⁸, R. H. Thomas⁹, S. Upadhyaya¹⁰, M. Votruba¹¹, L. Weaver¹², R. Wheeler¹³ (The Rare Mitochondrial Diseases Priority Setting Partnership Steering Committee)*
- Abstract:** Primary mitochondrial diseases encompass a number of clinical presentations with a spectrum of severity, lack effective disease-modifying therapies and have high mortality. It is therefore vital to know that research meets the needs of people with mitochondrial disease. Priority setting partnerships are an established collaborative methodology bringing patients, charity representatives and clinicians together to establish the most pressing and unanswered research priorities. We developed a web-based questionnaire, asking patients affected by primary mitochondrial disease, their carers and clinicians to pose their research questions.
- Results:** 709 questions were received (from 50 patients, 47 carers and 50 clinicians). Unanswerable questions were excluded, this left 42 answerable questions. Individuals were invited to prioritise these questions from ‘important’ to ‘less important’ using a web-platform. The top 24 questions were then discussed at a face-to-face workshop where a definitive top 10 of unanswered research questions for primary mitochondrial disease was decided.
- Conclusions:** These questions will be presented and should be taken forward by researchers to ensure that their research is relevant to those affected by primary mitochondrial disease.

Title: **AAV gene therapy for TNNT1-associated nemaline myopathy**
Author: *E.S. D'Ambrosio, M. Sena-Esteves, H.L. Gray-Edwards, M. Otero, H. Grimason, L. Labdi (Worcester, MA, University of Massachusetts)*

Abstract: Nemaline myopathy is one of the most common congenital myopathies. It is characterized by early onset muscular weakness and rod-like inclusions in myocytes. A non-sense mutation in exon 11 of the TNNT1 gene (encoding for the slow skeletal muscle isoform of troponin T) results in selective atrophy of slow-twitch myofibers and in a unique form of nemaline myopathy, named Amish Nemaline Myopathy (ANM). Currently there is no treatment for ANM. The development of an AAV gene therapy is viable, but requires the expression of TNNT1 to slow-twitch fibers only. We designed AAV8 vectors carrying a muscle-specific promoter (MHCK7) and incorporated both TNNT1 and suppressive microRNAs (miR208a and miR-133, characteristic of cardiac and fast-twitch myofibers respectively). This approach enabled the expression of TNNT1 in slow-twitch myofibers, while preventing its ectopic expression in other tissues or myofibers. We will then test the designed vector in *Tnnt1*^{-/-} mice and quantify its transduction efficiency.

Title: Systemic Gene Transfer with AAVrh74.MHCK7.SGCB Increased β -Sarcoglycan Expression in Patients with Limb Girdle Muscular Dystrophy Type 2E

Author: *Louise R. Rodino-Klapac,^{1,3} Eric R. Pozsgai,^{1,3} Sarah Lewis,^{1,3} Danielle A. Griffin,^{1,3} Aaron S. Meadows,^{1,3} Amanda Nicholl,¹ Carrie Nease,¹ Kelly J. Lehman,¹ Kathleen Church,¹ Natalie F. Miller,¹ Megan A. Iammarino,¹ Linda P. Lowes,¹ Jerry R. Mendell^{1,2}*
¹Center for Gene Therapy, The Research Institute at Nationwide Children's Hospital, Columbus, Ohio, USA; ²Department of Pediatrics and Neurology, The Ohio State University, Columbus, OH, USA; ³Sarepta Therapeutics, Inc., Cambridge, MA, USA

Abstract: **Introduction:** LGMD2E is progressive and debilitating.
Objectives: Report findings of AAVrh74.MHCK7.SGCB gene transfer (NCT03652259).
Methods: Patients: 4-15y, SGCB mutation, >40% on 100-meter walk test. Cohort 1 (n=3) and Cohort 2 (n=3) received single IV infusion of 5×10^{13} vg/kg AAVrh74.MHCK7.SGCB and 2×10^{14} vg/kg, respectively. Prednisone 1 mg/kg/day initiated 1d before (30d-[Cohort 1] and 60d-[Cohort 2] taper). Endpoints: Primary—safety. Secondary—SGCB expression 8w posttreatment. Other—CK decrease, function.
Results: Immunohistochemistry Cohort 1: mean 51% SGCB-positive fibers expressing mean 47% intensity; mean 36.1% SGCB expression vs normal (western blot). Cohort 2: mean 72% SGCB-positive fibers expressing mean 73% intensity; mean 62.1% SGCB expression vs normal. Functional improvements in all Cohort 1 patients (Table 1). Mean CK decreased from baseline by 72% at 1y in Cohort 1, 89% at 90d in Cohort 2. Two Cohort 1 patients had elevated liver enzymes (returned to baseline); one Cohort 2 patient had vomiting/dehydration (resolved).
Conclusions: The results of this study reflect optimized rAAVrh74.MHCK7.SGCB construct design. We observed increased β -sarcoglycan expression across all patients at a systemic dose of 2×10^{14} vg/kg compared to the dose of 5×10^{13} vg/kg, substantial reduction in CK in both cohorts, sustained improvement in all functional measures in patients in Cohort 1, and similar safety and tolerability profiles in both Cohorts.

Table 1. Summary of Functional Data at 1 Year

Patient	Assessment	NSAD	Time to Rise (sec)	4-Stair Climb (sec)	100MWR (sec)	10MWR (sec)
1	Baseline	40	5.0	2.4	52.0	5.0
	1-year	44	3.8	2.2	48.4	4.5
	Δ from Baseline	4	1.2	0.2	3.6	0.5
2	Baseline	48	1.5	1.6	35.1	3.4
	1-year	54	1.0	1.1	31.8	2.9
	Δ from Baseline	6	0.5	0.5	3.3	0.5
3	Baseline	41	3.5	2.8	48.8	5.2
	1-year	48	2.9	2.0	39.9	4.3
	Δ from Baseline	7	0.6	0.8	8.9	0.9

NSAD, North Star Assessment for Dysferlinopathy; 100MWR, 100-Meter Walk/Run; 10MWR, 10-Meter Walk/Run

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Title: **Long-Term Safety and Efficacy of Golodirsén in Male Patients with Duchenne Muscular Dystrophy Amenable to Exon 53 Skipping**

Author: *Francesco Muntoni;¹⁻³ Laurent Servais;^{4,5} Volker Straub;⁶ Michela Guglieri;⁶ Ashish Dugar;⁷ Meaghan Whalen-Kielback;⁷ Deb Steiner;⁷ Erica Koenig;⁷ Tao Feng;⁷ Baoguang Han;⁷ Xiaodong Wang;⁷ Eugenio Mercuri;⁸ on behalf of the SKIP-NMD study group*
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Abstract: **Introduction:** Golodirsén restores mRNA reading frame in patients with Duchenne muscular dystrophy (DMD) mutations amenable to exon 53 skipping.

Objectives: To report golodirsén long-term safety and efficacy in this first-in-human, phase 1/2, multicenter trial.

Methods: Patients (n=25) received open-label golodirsén 30 mg/kg/week IV until week 168. Safety (up to 189 weeks) and pulmonary/motor/muscle function (144 weeks) were assessed.

Results: Majority of reported AEs were mild, nonserious, and assessed as unrelated to golodirsén, with no discontinuations due to safety. Ambulation benefits of golodirsén were suggested by post hoc comparisons vs matched natural history controls (Table). Cumulative percent predicted forced vital capacity decline of 8.4% over 3 years (144 weeks) in golodirsén-treated patients compares favorably with published DMD natural history decline of ~5% annually.

Conclusions: Long-term golodirsén treatment had acceptable safety and was well tolerated. These data support golodirsén as a treatment option in patients with DMD amenable to exon 53 skipping.

Table. Functional Outcomes in Golodirsén-Treated Patients Compared with Matched Exon 53 Skipping-Amenable Natural History External Controls Identified from a Longitudinal Multicenter Cohort Study¹

	Golodirsén (N=25)	Matched Natural History Controls (N=19)
6-minute walk test mean (SE) change from baseline to Year 3, m	-99.0 ^a	-181.4
Loss of ambulation at Year 3, %	9	26

^aP=0.067 vs controls

1. Brogna C, et al. PLoS ONE 2019; 14: e0218683.

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Title: Combined Prospective and Retrospective Analysis of Duchenne Muscular Dystrophy Patient Outcomes Following 7 Years of Eteplirsen Treatment Compared With Natural History External Control Cohorts

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Abstract: **Introduction:** Study 201/202 (n=12) evaluated eteplirsen over 4 years in patients with Duchenne muscular dystrophy and confirmed genetic mutations amenable to exon 51 skipping.

Objective: To describe long-term clinical outcomes of patients from Study 201/202 by retrospective chart review (Study 4658-405).

Methods: Total follow-up time was 7 years of eteplirsen treatment. Functional outcomes included loss of ambulation (LOA) and annual change in forced vital capacity percent predicted (FVC %p). Outcomes were compared with natural history external control cohorts treated with standard-of-care with adjustment for baseline characteristics.

Results: Data from 10 participants were available for chart review. Median age at LOA was 15.2 years. Comparison with natural history controls showed that median time to LOA was 2.09 years longer in eteplirsen-treated patients (P=0.01), and eteplirsen-treated patients had a significant attenuation in pulmonary decline (P<0.0001; Table).

Conclusion: Study 4658-405 highlights the functional benefits of eteplirsen up to 7 years.

Table. Functional Outcomes Over 7 Years in Eteplirsen-Treated Patients and External Natural History Controls		
	Study 201/202/405 (n=12)	Natural History Comparators
Median age at LOA ^a	15.2	12.0 ^b , 13.0 ^c
Time to LOA, years, KM estimate (95% CI)	5.09 (4.87, -)	3.00 (2.29, -) ^d
P value vs comparator	0.01	
FVC%p annual rate of change	-3.3	-6.0 ^e
P value vs comparator	<0.0001	
^a Descriptive analysis based on published data ^b DuchenneConnect, untreated exon 51 skipping-amenable patients receiving steroids (n=106) ^c Cooperative International Neuromuscular Research Group Duchenne Natural History Study (CINRG DHNS) untreated exon 51 skipping-amenable patients receiving steroids (n=30) ^d Standard of care treated, exon 51 skipping-amenable patients from the Fondazione Telethon NMD Italian Network Registry (n=8), the Leuven NMRC Registry (n=3), and the placebo arm of the DEMAND III trial (n=60) ^e CINRG DHNS exon 51 skipping-amenable untreated male patients (n=20)		

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Disclosures: OM, AD, SS, and KT: Employees of Sarepta Therapeutics, Inc. HZA-H: Served on advisory boards for Avexis, Audentes, Biogen, and Sarepta. BJB: Is the co-founder Aavanti Bio, Inc AMC: Served on advisory boards for Acceleron, Avexis, Genentech, and Sarepta, and on DMSB for Catabasis. PH: Has no conflict of interest to declare. CP: Served on advisory boards for AveXis, Biogen, Sarepta, is a speaker for AveXis, Biogen, has or is conducting research for AveXis, Astellas, Biogen, Catabasis, CSL Behring, PTC, Pfizer, Sarepta, Scholar Rock. PBS: Consultant (AveXis, Biogen, PTC Therapeutics, and Sarepta Therapeutics, Inc.), and speakers' bureaus (Alexion, Biogen, and Grifols). KRW: Consultant (AskBio, Dynacure, PTC Therapeutics, Roche, and Sarepta Therapeutics, Inc.), and serves on the DSMB for Fibrogen and on a dose escalation committee for Wave. JS: Employee of Analysis Group Inc., Boston, MA, USA. JRM: Has received Grants from the Parent Project Muscular Dystrophy and has received personnel fees from Sarepta and National Children's Hospital