

Welcome to the 27th Annual NMSG Scientific Meeting!

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Dear Colleagues,

On behalf of the Neuromuscular Study Group (NMSG), we are delighted to welcome you to San Antonio, Texas, for our 27th Annual Scientific Meeting.

For nearly three decades, the NMSG has united researchers from around the world to collaborate on advancing neuromuscular science. This meeting in particular has become a unique opportunity for our community to come together for a vibrant exchange of ideas that reinforces our commitment to progressing innovation in our field. Whether you are presenting a poster or discussing trials between sessions, we encourage you to engage fully with your colleagues and our industry partners, as your active participation will greatly strengthen the value of our time together.

A few meeting highlights for this year.

- Emerging Investigators: We welcome back this valuable session where emerging talent can connect with and learn from established leaders in the field. Join us at 3:40 pm on Friday.

- Abstract Poster Presentations: We had 138 submissions this year. Please stop by to see their work at 5 pm on Friday in the Minuet and Patio Rooms.
- Industry Partners: We appreciate the immense industry involvement. Please join us for their presentations starting at 2:00 pm on Saturday and visit their tables daily in the Grand Ballroom.
- Shark Tank: In its seventh year, the Shark Tank session will feature four exciting proposals, with the winner receiving a \$10,000 grant. New this year: Everyone who attends the session will be able to score the presentations. Join us at 9:00 am on Sunday.

Outside of the scientific program, take time to enjoy the history and charm of the Alamo here in San Antonio. Starting at the historic Alamo, with its cypress-shaded River Walk and tucked-away patios just steps away, San Antonio offers a truly welcoming setting. We hope you will soak in the rich heritage, savor South Texas hospitality and cuisine, and make the most of this charming location during your visit.

We are excited for the continuing opportunity to share breakthroughs, clinical insights, and new ideas that can improve the treatment and care of our patients. Let us continue to embrace the spirit of collaboration as we explore the latest research and inspire one another with our findings.

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2026 NMSG Scientific Meeting Platform Presentations

33 - Multilevel Neurophysiologic Assessment of Cortical and Peripheral Motor System Dysfunction in Amyotrophic Lateral Sclerosis

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Introduction:

Amyotrophic lateral sclerosis (ALS) is characterized by progressive upper and lower motor neuron degeneration. While cortical hyperexcitability has been implicated in ALS pathogenesis, most transcranial magnetic stimulation (TMS) studies have focused on upper limb muscles. Relationships between cortical dysfunction, peripheral motor unit remodeling, and muscle impairment within the same lower limb motor system remain incompletely understood.

Objectives:

To characterize cortical excitability abnormalities in ALS using single- and paired-pulse TMS and determine their relationships with peripheral motor unit integrity and muscle performance within the same lower limb muscle, the vastus lateralis (VL).

Methods:

This prospective pilot study included 10 ALS patients and 10 matched controls. Participants underwent strength testing, single- and paired-pulse TMS over the VL motor cortex representation, and peripheral motor unit assessment using motor unit number index (MUNIX), and motor unit size index (MUSIX). TMS measures included resting motor threshold (RMT), cortical silent period (CSP), short-interval intracortical inhibition (SICI), short-interval intracortical facilitation (SICF), intracortical facilitation (ICF), and long-interval intracortical inhibition (LICI).

Results:

ALS demonstrated increased RMT (57.96vs45.08%, $p=0.045$) and markedly reduced CSP duration (67.57vs164.4ms, $p<0.0001$). SICF and ICF were significantly enhanced (both $p<0.0001$), while SICI and LICI were preserved. Reduced CSP correlated with lower muscle torque ($p<0.01$). Greater SICF responses and inhibitory dysfunction correlated with MUSIX ($p<0.05$), linking cortical dysfunction to peripheral motor unit remodeling.

Conclusions:

ALS is associated with impaired corticospinal conduction, reduced sustained cortical inhibition, and enhanced facilitatory intracortical responses. Cortical excitability abnormalities within the VL motor system were strongly associated with muscle weakness and peripheral motor unit remodeling, supporting integrated cortical-peripheral motor system degeneration in ALS.

114 - Clinical Outcomes and Safety of Nucleoside Therapy for Thymidine Kinase 2 Deficiency in a Brazilian Cohort

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Introduction: Thymidine Kinase 2 deficiency (TK2d) is a rare mitochondrial DNA (mtDNA) depletion syndrome leading to a severe and progressive myopathic disorder. Nucleoside supplementation (deoxythymidine and deoxycytidine) has been shown to favorably alter the disease's course, particularly in severe infantile-onset cases. However, long-term data on efficacy and safety remain limited.

Objectives: To demonstrate treatment efficacy and safety among patients with TK2d treated with nucleosides.

Methods: This is a retrospective, long-term follow-up study of 14 patients with TK2d (5 children and 9 adults) who were receiving nucleoside supplementation through a compassionate use program. Patients were systematically evaluated over a period ranging from 18 to 36 months, with assessments conducted every 3 months during the first year of treatment and every 6 months thereafter. Comprehensive functional assessments of motor, respiratory, and bulbar function were performed in addition to periodic measurements of liver and pancreatic function.

Results: All 14 TK2d patients showed beneficial effects across motor, respiratory, and bulbar function domains. Milestones were regained/gained in all children and 3 out of 9 adults. Adults reported severe gastrointestinal symptoms. Liver and pancreatic enzyme abnormalities were noticed in most of the adults.

Conclusions: Deoxythymidine and deoxycytidine were found to be safe and beneficial in this long-term cohort of pediatric and adult TK2d patients, though elevations in liver and pancreatic enzymes were observed and require regular monitoring. This study provides valuable evidence supporting this therapy as an effective, safe, long-term, disease-modifying treatment option for both pediatric and adult patients.

43 - Longitudinal assessment of motor function in Duchenne Muscular Dystrophy in a pediatric cohort: development of Italian centile curves for the North Star Ambulatory Assessment, 10-Meter Walk/Run Velocity and Rise from Floor Velocity

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Introduction: Individuals with Duchenne Muscular Dystrophy (DMD) show highly heterogeneous motor function progression, complicating clinical monitoring.

Objective: To develop Italian centile curves for the North Star Ambulatory Assessment (NSAA), 10-meter walk/run velocity (10MWRV), and rise from floor velocity (TRFV), and to compare them with UK centiles.

Methods: Subjects were selected from the Italian DMD Registry; patients enrolled in clinical trials were excluded. NSAA scores and timed test measures were rescaled to the [0,1] interval and analyzed using GAMLSS models with beta inflated distributions, modelling age effects on mean, dispersion, and skewness.

Results: A total of 7201 assessments from 720 participants were analyzed, including 430 individuals who lost function during follow-up. The 10th, 25th, 50th, 75th, and 90th centiles were evaluated. Comparison with UK centiles in individuals aged 5-16 years showed only partial overlap: NSAA curves differed mainly at the extreme centiles, whereas age at loss of function was similar between cohorts. Italian patients were initially slower in TRFV but remained more stable over time, while decline in 10MWRV occurred earlier compared with the UK cohort. Longitudinal centile monitoring showed variability over time: for NSAA, 206/586 patients remained within the same centile, while 380 changed centiles; for rise from floor, 270/578 remained stable and 308 changed centiles; for 10MWRV, 235/575 remained stable and 340 changed centiles.

Conclusions: Italian centiles for NSAA, 10MWRV, and RFFV are useful tools for longitudinal monitoring of motor function in DMD, particularly during advanced stages of disease progression.

5 - Neuromuscular junction failure in sarcopenia is linked to NaV1.4 loss and reversed by CIC-1 inhibition

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Introduction: Sarcopenia is the age-related loss of muscle strength and size that leads to mobility limitations and loss of independence in older adults. The underlying cellular mechanisms remain unclear, and treatments are limited.

Objectives: We examined the reliability of neuromuscular junction (NMJ) synaptic transmission for force production in older humans and rodents as the critical interface between the nervous system and muscle.

Methods: Ten older adults with complaints of physical limitations (85.9±4.4 years; 40% female) and eight control adults (29.5±8.7 years; 38% female) were measured for isokinetic leg extensor strength and single fiber electromyography for their quadriceps muscles. Adult and old C57BL/6N mice and Wistar rats were analyzed using electrophysiological and immunofluorescent methods to evaluate neuromuscular transmission, muscle excitability, NMJ morphology, and protein expression levels.

Results: Older individuals exhibit NMJ transmission failure that correlates with muscle weakness. Pre-clinical experiments showed similar NMJ transmission failure in aged mice and rats that was associated with localized loss of muscle fiber excitability at NMJs. This excitability defect highlights a novel mechanism of sarcopenia. Across species, immunohistochemistry revealed a reduction in the voltage-gated sodium channel specific for skeletal muscle (NaV1.4) at the post-synaptic NMJ membrane. Acute NaV1.4 inhibition with μ -conotoxin GIIIB in adult rats reproduced findings of NMJ transmission failure observed in aged rodents and humans. Finally, CIC-1 chloride channel inhibition enhanced muscle excitability and muscle function in old rodents.

Conclusions: NMJ transmission deficits are a key, reversible driver of sarcopenia and reveal a novel therapeutic target for addressing muscle weakness in aging.

92 - Real-World Givinostat Tolerability and Dose Modification in Nonambulatory Males with Duchenne Muscular Dystrophy

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Introduction:

Givinostat is approved for Duchenne muscular dystrophy (DMD) with weight-based dosing up to a target of 6 mL (53.2 mg) twice daily. In the EPIDYS clinical trial, participants included were fully ambulatory, which differs from real-world populations that include nonambulatory individuals. Data describing givinostat tolerability in this broader population remains limited.

Objectives:

To describe dosing patterns and tolerability of givinostat among nonambulatory males with DMD in a real-world neuromuscular clinic.

Methods:

This retrospective study included nonambulatory males with DMD treated with givinostat at a single center. Data collected included dose modifications and adverse effects. Descriptive analyses were performed.

Results:

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118 - Lysosome Remodeling in CMT1A Neuropathy: Pathogenic Mechanism or Compensatory Response?

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Introduction: Charcot-Marie-Tooth disease type 1A (CMT1A), caused by *PMP22* gene duplication, is the most common inherited peripheral neuropathy and currently lacks disease-modifying therapies. Although *PMP22* overexpression is central to disease pathogenesis, the downstream cellular mechanisms that drive myelin dysfunction remain poorly understood. Emerging evidence implicates lysosomal pathways in *PMP22*-associated neuropathies, primarily from cellular models and studies of protein quality control. However, whether lysosomal abnormalities occur within intact myelin from physiologically relevant models of CMT1A has not been established and their functional significance remains unclear.

Objectives: To determine whether *PMP22* overexpression in a genetically relevant mouse model of CMT1A is associated with lysosomal remodeling in peripheral nerve myelin and to explore the potential pathogenic or compensatory nature of these changes.

Methods: Teased peripheral nerve fibers from CMT1A and control mice were analyzed by confocal immunofluorescence. Lysosomal abundance, morphology and degradative potential were assessed using LAMP1 and Cathepsin D. Three-dimensional quantitative imaging was used to measure lysosome number, volume, intensity and spatial distribution within peripheral nerve myelin.

Results: Quantitative analyses revealed accumulation of LAMP1-positive lysosomes within CMT1A myelin, accompanied by altered lysosome abundance and morphology. Studies assessing lysosomal proteolytic capacity through Cathepsin D localization and expression are ongoing.

Conclusions: Lysosomal remodeling is a prominent feature of peripheral nerve pathology in CMT1A. Ongoing studies integrating lysosomal morphology, function, ultrastructure, trafficking dynamics and pharmacologic manipulation will determine whether lysosome accumulation contributes to disease pathogenesis or represents a compensatory response to *PMP22* overexpression. Defining the role of lysosomes in CMT1A may reveal new therapeutic opportunities.

117 - Manifesting dystrophinopathy in a girl with Williams-Beuren syndrome: a dual molecular diagnosis supported by skewed X-inactivation

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Introduction: Duchenne muscular dystrophy (DMD) is an X-linked neuromuscular disorder predominantly affecting males. Manifesting dystrophinopathy in females is very rare, typically reflecting mechanisms favoring expression of the pathogenic *DMD* allele, particularly skewed X-chromosome inactivation. Williams-Beuren syndrome (WBS) is a 7q11.23 microdeletion syndrome associated with neurodevelopmental delay, growth restriction, dysmorphic features, and multisystem involvement.

Methods: Case report.

Results: A preschool-aged girl presented with developmental delay, growth restriction, dysmorphic features, motor clumsiness, and a family history of dystrophinopathy in male relatives. On examination, axial hypotonia and a broad-based gait were observed, while laboratory testing showed hyperCKemia with mild transaminase elevation. Chromosomal microarray identified a heterozygous 1.57-Mb deletion at 7q11.23, confirming WBS. Persistent hyperCKemia and family history of dystrophinopathy prompted targeted molecular testing, which identified a heterozygous familial *DMD* nonsense variant (c.1966C>T). Karyotyping excluded structural X-chromosome abnormalities, whereas X-chromosome inactivation analysis demonstrated non-random inactivation (74:26), supporting the diagnosis of manifesting dystrophinopathy. Follow-up revealed persistent motor incoordination, thigh and calf hypertrophy, restricted ankle dorsiflexion, and a toe-walking tendency.

Conclusions: Early recognition of coexisting dystrophinopathy has direct implications for surveillance, rehabilitation, and genetic counseling.

107 - Near infrared spectroscopy during non-ischaemic handgrip exercise reveals distinct muscle oxygenation signatures in mitochondrial disease and sarcopenia

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Introduction:

Mitochondrial dysfunction is a putative contributor to sarcopenia. Genetically confirmed mitochondrial disease offers a definitive model to validate novel functional assessments as biomarkers for conditions where mitochondrial dysfunction plays a key role.

Objectives:

Determine whether Near-Infrared-Spectroscopy (NIRS) detects impaired oxygen extraction during handgrip exercise in mitochondrial disease, compare oxygenation profiles with sarcopenia, and assess mechanistic biomarker potential.

Methods:

Two cohorts were studied: adults with genetically confirmed mitochondrial disease (n=10) and matched controls (n=19); and MASS Lifecourse participants (n=23), stratified by EWGSOP2 sarcopenia status (7 probable sarcopenia, 16 no sarcopenia). Maximal voluntary contraction (MVC) and 3-minutes intermittent isometric handgrip exercise (40% MVC, 1 Hz) with continuous digital dynamometry and simultaneous NIRS measurement of Tissue Saturation Index (TSI) was performed. MVC peak force, MVC relaxation time, total exercise force, integrated TSI and total haemoglobin (THb) in the last 30 seconds of exercise (compared to pre-exercise baseline) were measured. Statistical significance was assessed using t-tests, Mann-Whitney U, ANOVA, or Kruskal-Wallis tests depending on normality and comparison number.

Results:

Participants with mitochondrial disease showed *attenuated* TSI reduction (-39 for Mito vs -110 for controls, p=0.01). In contrast, participants with sarcopenia, particularly men, showed *exaggerated* TSI reduction (overall -256 for sarcopenic vs -121 for non-sarcopenic, p=0.05; -317 for sarcopenic men vs -36 for non-sarcopenic men, p=0.03). THb responses were comparable across groups. Differences in TSI were not explained by difference in MVC peak force or exercise force.

Conclusion:

Handgrip exercise NIRS identifies distinct muscle oxygenation signatures in mitochondrial disease and sarcopenia.

123 - Retrospective Analysis of MG-ADL Data Outcomes Following Zilucoplan Treatment in Myasthenia Gravis

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Introduction: Myasthenia Gravis (MG) is an autoimmune disease targeting the neuromuscular junction. Since the approval of eculizumab in 2017, several complement inhibitors and Fc receptor (FcRn) blockers have become available, with zilucoplan receiving approval in October 2023. Despite the growing number of targeted therapies, comparative real-world data remain limited.

Objectives: The primary objective of this analysis was to evaluate the real-world effectiveness of zilucoplan based on documented subjective and objective improvement. This poster presents a subset of data from a larger study evaluating and comparing all approved complement inhibitors and FcRn blockers in AChR-positive MG.

Methods: Prospective patients with AChR-positive MG were identified between October 2017 and December 2025. The broader study drugs of interest include all 7 FcRn and terminal complement inhibitors approved since 2017. Exclusion criteria included other causes of weakness. A retrospective chart review was performed, and de-identified patient data were collected.

Results: 174 medication trials were identified across 104 patients. Zilucoplan represented 12.1% of all trials. 57% (n=12) achieved a ≥ 2 -point reduction, and 38% (n=8) achieved a ≥ 3 -point reduction in MG-ADL. Minimal symptom expression was achieved in 1 patient (5%).

Conclusion: A smaller percentage of patients had a meaningful reduction in MG-ADL scores (≥ 3) when compared to the original clinical trial (38% vs 73%). Notably, a large majority of our patient population had failed multiple oral and targeted therapies before zilucoplan. Zilucoplan is effective and a viable first-line or second-line option after failing other targeted immunotherapies.

122 - Dose-Finding Safety and Tolerability Study of Clenbuterol in Facioscapulohumeral Muscular Dystrophy (FSHD)

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Facioscapulohumeral muscular dystrophy (FSHD) is a progressive, DUX4-mediated neuromuscular disorder with no FDA-approved disease-modifying therapies. Clenbuterol, a β 2-adrenergic agonist with established anabolic properties, has shown preclinical efficacy in suppressing DUX4 expression and promoting muscle growth, providing strong biologic rationale for therapeutic repurposing. We are conducting a 6-month, open-label, dose-escalation trial evaluating the safety, tolerability, and preliminary efficacy of clenbuterol in adults with genetically confirmed FSHD (NIH Wellstone Center, P50 AR065139). Thirty participants are planned across three sequential cohorts (20, 40, and 60 mcg twice daily) at three U.S. sites. Primary endpoints include adverse events, safety laboratories, vital signs, and electrocardiographic monitoring. Exploratory efficacy outcomes include functional assessments, RNA sequencing, and quantitative MRI. Cohort 1 (20 mcg BID; n=10) enrollment is complete; nine participants have finished 6 months of treatment, with the last anticipated to complete by July 2026. In this interim analysis, clenbuterol has been well tolerated. Adverse events were predominantly mild and consistent with the known pharmacologic profile, including nervous system, musculoskeletal, and cardiac-related effects. No protocol-defined stopping criteria have been met, and no dose interruptions or discontinuations have occurred. Cohort 2 (40 mcg BID) is currently enrolling. These initial findings demonstrate acceptable safety and tolerability at the starting dose, supporting continued dose escalation and further evaluation of clenbuterol as a potential disease-modifying therapy for FSHD.

I. Investigator Abstracts

7 - COS-PREPARED: Clinical Outcome Study in PRE- and Early-symptomatic Patients with Recessive Dysferlinopathy

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Introduction

Early stage diagnoses are increasingly generated through incidental CK results, screening for segregation analysis, or where families have opted for additional screening following the diagnosis of a symptomatic family member, creating the opportunity to expand current knowledge of early natural history and disease onset.

Objectives

- 1) Define the early natural history of dysferlin-deficient limb girdle muscular dystrophy LGMDR2 by monitoring muscle function, strength, and biomarkers of muscle pathology.
- 2) Identify early indicators of disease onset to inform recognition, diagnosis, care, clinical trial design and treatment indications.

Methods

Assessments include functional and patient reported outcome measures, quantitative MRI (T2, Dixon), and instrumented gait. Functional outcome measures include North Star Assessment for Limb-girdle type muscular dystrophy, 100 metre timed test, selected items from both 1000 Norms project, and Bruininks-Oseretsky Test of Motor Proficiency (BOT).

Results

Five participants (aged 13-19, 3 male, 2 female) with a confirmed diagnosis of dysferlin-deficient LGMDR2 proven by two pathogenic variants in the DYSF gene who can still stand on tiptoes and hop have completed baseline visits.

Annual and further baseline visits will be completed by September 2026. Fat Fraction and T2 are higher than controls, with changes most visible in the Gastromedialis. Functionally, all participants had speeds below the 10th centile on timed tests. Four subjects demonstrated no impairment on the BOTS 'Balance' dimension. Impairments were seen in all subjects in 'Running speed and agility' and 'Strength' subscales.

Conclusions

The recruitment target is 20. We seek the support of Muscle Study Group members for recruitment.

8 - Online Patient Ratings of a Neuromuscular Outpatient Practice: A Retrospective Study

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Introduction: Patients increasingly rely on online reviews and star ratings of physicians when choosing healthcare providers, but the reliability of these ratings, especially in subspecialty fields such as neuromuscular medicine, remains uncertain.

Objectives: Online physician ratings increasingly influence patient choice, yet their trustworthiness and generalizability remain uncertain, particularly in complex specialties such as neuromuscular medicine. Only 5% of patients post reviews, but nearly 40% use online feedback to select physicians.

Methods: We retrospectively analyzed 218 reviews with star ratings posted between May 2016 and June 2025 for a single outpatient neuromuscular practice. Identifiable reviewers were matched to practice records to append referral, diagnostic, and demographic data. Quantitative and thematic analyses were performed.

Results: Among 218 reviews, 182 (83.5%) were positive and 36 (16.5%) negative. Negative themes included feeling dismissed, perceived rudeness, and rushed visits, while positive reviews emphasized thoroughness and effective care. Identifiable negative reviewers were predominantly White female patients (mean age 41) who commonly reported overlapping symptoms including pain, fatigue, motor difficulties, and sensory disturbances. Anxiety or depression was reported in 44.4% of identifiable reviewers.

Conclusions: Online reviews primarily reflect patient experience rather than clinical quality of care or physician competence. Structural pressures—time constraints, diagnostic expectations, and tertiary-care complexity—likely shape negative feedback and should be considered when interpreting online ratings.

13 - Neurofilament Light Chain as a Biomarker for Chronic Inflammatory Demyelinating Polyradiculoneuropathy

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Introduction: The Guillain-Barré Syndrome (GBS)|Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) Foundation proposed standardized definitions of CIDP disease activity based on patient perception of worsening and changes in disability and impairment. Objective biomarkers are needed to supplement clinical assessments of disease activity and treatment response. Neurofilament light chain (NfL) is a promising candidate biomarker to meet this need, but it was not included as a component of the disease activity definitions due to inconclusive data at the time the definitions were developed.

Objectives: To assess the association between elevated NfL levels and evidence of disease activity (EDA) or no evidence of disease activity (NEDA) according to the consensus-based definitions.

Methods: We reviewed the charts of patients with CIDP who were seen at the University of Pennsylvania between 11/2023 and 3/2026 and had their NfL levels tested. We collected scores for Inflammatory Neuropathy Cause and Treatment (INCAT), Inflammatory Rasch-built Overall Disability Scale (I-RODS), Medical Research Council Sum Score (MRC-SS), grip strength, patient perception of symptoms, and NfL levels. An odds ratio was computed to determine the odds of EDA for patients with elevated NfL compared to patients with normal NfL.

Results: 53 patients were included for analysis, and full data was available for 38 patients. Patients with elevated NfL had higher odds of EDA than patients with normal NfL. The results will be updated at the time of presentation.

Conclusions: Elevated NfL is associated with CIDP EDA based on consensus-based definitions integrating objective disability and impairment scales with subjective patient perceptions of worsening.

15 - Electrodiagnostic assessment reveals myasthenia gravis and cervical dystonia in a case of dropped head syndrome: Linked or coincidental?

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INTRODUCTION:

Botulinum toxin (BTX) is considered contraindicated in patients with myasthenia gravis (MG). However, recent reports suggest it may be used safely in selected cases. We present a patient with dropped head syndrome secondary to longstanding, untreated, seronegative, generalized MG who received BTX therapy for cervical dystonia.

CASE REPORT:

An 82-year-old man presented with head drop, fatigable ptosis, and proximal arm weakness. Antibodies to acetylcholine receptor, LRP4, and MuSK were negative, and chest CT showed no thymoma. He was diagnosed with possible seronegative MG and treated with plasmapheresis with marked improvement but was subsequently lost to follow-up.

8 years later, he presented with head drop and neck pain. Examination showed torticollis with hypertrophy of the splenius capitis, levator scapulae and trapezius. There was moderate neck extensor weakness and mild proximal weakness without fatigability. Abnormal neck postures worsened during gait.

Single-fiber EMG (sfEMG) demonstrated markedly increased jitter and blocking, consistent with a generalized neuromuscular junction disorder. Surface EMG showed lack of relaxation of antagonist muscles and co-contraction of agonist and antagonist muscles during neck movements.

Pyridostigmine was ineffective, but prednisone improved neck and limb weakness. Mycophenolate mofetil was initiated.

Given severe neck pain and abnormal posture, low-dose BTX injections were administered, resulting in pain relief while neck strength continued to improve. Repeat sfEMG was essentially unchanged.

CONCLUSIONS:

In this patient with multifactorial dropped head syndrome, electrodiagnostic assessment helped identify contributing factors and guide therapy. Low-dose BTX may be considered for cervical dystonia in carefully selected MG patients after immunotherapy initiation.

17 - Seroreversion and Clinical Recovery Following FcRn Inhibition in Anti-Contactin-1 Autoimmune Nodopathy

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Introduction: Autoimmune nodopathies (AN) are often treatment resistant. Specifically, these types of conditions with IgG4 antibodies specific to proteins within the neuronal axon often do not respond to intravenous immunoglobulin (IVIG). Inhibiting the neonatal Fc receptor (FcRn) can lower the circulating IgG antibodies that are thought to cause these conditions, and this could be an effective treatment for AN.

Methods: Longitudinal clinical, electrophysiologic, and serologic data of a patient with an anti-contactin-1 nodopathy treated with efgartigimod was collected for a case study.

Case Report: A 76-year-old woman developed rapidly progressive weakness, sensory loss, and gait impairment, becoming wheelchair-dependent within 12 weeks. She did not improve with IVIG. Clinical evaluation, lab tests, and an electromyography (EMG) confirmed a demyelinating polyradiculoneuropathy and anti-contactin-1 IgG4 antibodies. Subcutaneous efgartigimod, an FcRn inhibitor, and prednisone were initiated, and this treatment plan showed early stabilization. Over 6 months, with continued efgartigimod and a steroid taper, she improved to reach independent ambulation. Clinically, she showed gains in her Inflammatory Neuropathy Cause And Treatment (INCAT) score, Inflammatory Rasch-built Overall Disability Scale (I-RODS), grip strength, and Medical Research Council Sum-Score (MRC-SS). She also showed improved nerve conduction parameters, normalization of serum neurofilament light chain, and her anti-contactin-1 antibodies disappeared.

Results: In this IgG4 anti-contactin-1 AN, FcRn inhibition was associated with clinical, electrophysiologic, and serologic improvement, including seroreversion.

Conclusion: While this case study showed improvements after treatment with a FcRn inhibitor, more research is required to understand if this will work for future AN patients.

20 - Interrogation of AAV9-induced acute toxicity in large animal models resembling advanced Duchenne muscular dystrophy

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Introduction. Acute lethality is a major safety concern for systemic adeno-associated virus (AAV) gene therapy of neuromuscular diseases. Two nonambulatory Duchenne muscular dystrophy (DMD) patients died within one week of AAV9 dosing.

Objective. To understand high-dose AAV9-induced acute toxicity, we evaluated clinical, molecular, and immunological outcomes in canines that resemble late-stage DMD patients.

Methods. We injected an AAV9 firefly luciferase vector into four affected dogs that were at an advanced disease stage (1.9 to 2.7 years old). One animal dosed with 1×10^{14} vg/kg AAV was terminated at 3 days. One animal dosed with 1×10^{14} vg/kg AAV and two animals dosed with 2.6×10^{14} vg/kg AAV were terminated at 7 days. Studies included clinical observation, chest X-ray, cardiac function, blood biochemistry and hematology, AAV biodistribution and expression, single-nucleus RNAseq and in situ hybridization, serum biomarkers, ELISpot, AAV antibody, and histopathology.

Results. Biodistribution by ddPCR showed robust uptake in the liver and lymphoid tissues, followed by lung, kidney, and skeletal muscle. High levels of AAV transcripts were detected in the liver, skeletal muscle, lymphoid tissues, lung, and kidney. Prominent serum cytokine elevation was detected in two high-dose animals. Importantly, one high-dose animal developed non-infectious pneumonitis resembling acute respiratory distress syndrome seen in the human patient who died following AAV9 delivery. Single-nucleus RNAseq revealed pronounced transgene expression in immune cells in this animal.

Conclusion. Our study modeled acute toxicity seen in nonambulatory DMD patients and revealed potential underlying mechanisms.

30 - Patient-Reported Correlation with Caregiver-Reported Disease Burden in Duchenne Muscular Dystrophy

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Introduction: We previously developed a regulatory-grade, Duchenne muscular dystrophy (DMD)-specific patient-reported outcome measure (the DMD-HI) and caregiver-reported outcome measure (the DMDCR-HI) for use in DMD therapeutic trials. In preparation for future studies, it is important to understand how respondent perspectives influence quantifiable disease burden and be able to calibrate scores based on respondent type.

Objectives: To examine the relationship between patient- and caregiver-reported scores using the DMD-HI and DMDCR-HI and develop methods for calibrating scores across instruments.

Methods: Using matched patient-caregiver dyads, we concurrently evaluated disease burden using the DMD-HI and DMDCR-HI. Associations and agreement between total and subscale scores were evaluated using Pearson correlation and Bland-Altman analyses. We used linear mixed-effects and standard linear models to develop crosswalk formulas between DMD-HI and DMDCR-HI total and subscale scores.

Results: Twenty-one paired patient-caregiver assessments were completed, revealing a strong correlation between DMD-HI and DMDCR-HI total scores ($r = 0.821$, $p < .0001$), with significant correlations in 14/17 subscales. Caregivers consistently reported higher disease burden compared to patients, with an average difference of 13.8 points on the 100-point scale. Bland-Altman analysis indicated all but one observation fell within the limits of agreement. Crosswalk models yielded lower residual error for total scores and specific subscales such as Gastrointestinal Health and Mobility, indicating improved precision.

Conclusions: When comparing the DMD-HI and DMDCR-HI, caregiver-reported disease burden is consistently higher than patient-reported burden, despite strong correlations. Crosswalk models provide a robust approach for calibrating patient- and caregiver-reported scores, facilitating their effective use in longitudinal DMD studies.

35 - The IBM-HI: Correlation between patient-reported disease burden and clinical function in the INSPIRE-IBM study

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Introduction: The Inclusion Body Myositis-Health Index (IBM-HI) is a regulatory-grade patient-reported outcome measure (PRO) developed and validated to measure point-in-time disease burden in 13 symptom areas in IBM patients during therapeutic studies. INSPIRE-IBM is a longitudinal observational study of IBM patients that is using the IBM-HI as a key marker of disease burden.

Objectives: To evaluate the association between IBM-HI scores and clinical function using data from INSPIRE-IBM.

Methods: We compared IBM-HI total and subscale scores to other PROs (EAT-10, Sydney Swallow), functional measures (IBM-FRS, timed up and go), strength measures (manual muscle testing, hand-held dynamometry), and pulmonary function tests (FVC, MIP, MEP). We performed known groups analyses using unpaired t-tests and correlation analyses using Spearman's correlation.

Results: In a cross-sectional analysis of 118 patients from INSPIRE-IBM, the IBM-HI demonstrated known groups validity, detecting higher disease burden in patients who relied on use of a mobility aid. The IBM-HI exhibited variable correlations with other PROs ($r > 0.8$, $p < 0.0001$), functional assessments ($r > 0.6$, $p < 0.0001$), and strength and pulmonary tests ($r < 0.5$, p variable).

Conclusions: In the context of INSPIRE-IBM, the IBM-HI and its subscales demonstrate moderate to strong correlations with other patient-centric and clinician-reported outcome assessments. The convergent validity of the IBM-HI is promising and supports longitudinal investigation to determine its minimal clinically important difference (MCID) as well as to assess its sensitivity in detecting disease worsening or improvement in current and upcoming observational and therapeutic studies.

36 - Using PMP22 Antisense Therapy to Define Disease Pathogenesis in CMT1A

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Introduction: Charcot-Marie-Tooth disease type 1A (CMT1A), caused by PMP22 duplication, is the most common inherited peripheral neuropathy and is characterized by progressive demyelination, impaired nerve conduction and sensorimotor dysfunction. While molecular disorganization of myelin domains has been reported in CMT1A, the temporal relationship between these abnormalities and functional decline remains poorly understood. Antisense oligonucleotide (ASO)-mediated reduction of PMP22 provides a unique opportunity to investigate disease pathogenesis while simultaneously evaluating therapeutic response.

Objectives: To determine whether ASO-mediated normalization of PMP22 expression restores molecular myelin architecture prior to, concurrent with or following improvements in peripheral nerve function in a CMT1A mouse model.

Methods: CMT1A mice received a single subcutaneous injection of PMP22-targeting ASO (10 mg/kg). PMP22 reduction is being quantified with molecular methods. Longitudinal motor phenotyping, peripheral nerve electrophysiology, teased sciatic nerve immunofluorescence and electron microscopy are being evaluated for functional and molecular improvement. Analyses will focus on nodal/paranodal organization, adherens junction integrity and Schmidt-Lanterman incisures structure.

Results: PMP22 expression reduction following ASO treatment was successfully validated in treated CMT1A mice. Studies are ongoing to define the temporal relationship between restoration of molecular myelin organization and improvements in electrophysiological and behavioral outcomes following PMP22 reduction.

Conclusions: These studies will establish PMP22 ASO therapy as a mechanistic tool to investigate disease pathogenesis in CMT1A in addition to its therapeutic potential. Defining the temporal relationship between molecular myelin disorganization and functional decline may provide new insight into early pathogenic events and identify structural features of myelin that are closely linked to peripheral nerve dysfunction.

37 - Limb-onset weakness is associated with loss of independent ambulation in oculopharyngeal muscular dystrophy (OPMD).

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Introduction: OPMD can present with ptosis, dysphagia, and/or proximal muscle weakness. A subset of patients eventually loses “independent ambulation”, defined here as the ability to walk without an assistive device. However, it remains unclear whether eventual loss of independent ambulation is associated with presenting symptomology.

Objectives: To evaluate whether the presence of limb muscle weakness at symptom onset is associated with a higher frequency of loss of independent ambulation in our retrospective OPMD cohort.

Methods: Institutional review board approval was obtained. Age and type of symptom onset (ptosis, dysphagia, and/or limb weakness), follow-up duration, and ambulatory status at the time of the last visit were retrieved from 70 genetically confirmed OPMD patients. Two groups were defined: limb-onset weakness with or without ptosis or dysphagia (n=19) and oculobulbar-onset weakness only at initial presentation (n=51).

Results: Age at both symptom onset and last clinic visit and duration of follow-up did not differ between groups. 13 out of 19 with limb-onset weakness also had ptosis and/or dysphagia at presentation. 34 out of 51 with oculobulbar-onset symptoms eventually developed limb weakness. Ten out of 19 (52%) with limb-onset weakness and only 8 out of 51 (15%) with oculobulbar-onset symptoms had lost “independent ambulation” by the last follow-up visit ($p = 0.002$).

Conclusions: Patients with OPMD who presented with limb muscle weakness (27% of our cohort) more frequently lost independent ambulation during the retrospective follow-up period. In addition to therapies targeting dysphagia, investigational treatments addressing limb weakness are needed for OPMD patients.

39 - Modeling Treatment Response Trajectories in Spinal Muscular Atrophy: Results from the MAP THE SMA study

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Introduction: Spinal muscular atrophy (SMA) has undergone a major therapeutic transformation with the introduction of disease-modifying therapies, although treatment response remains highly variable and incompletely understood.

Objective: This study aimed to develop and validate a predictive framework for forecasting individual treatment trajectories and identifying clinically meaningful response phenotypes.

Methods: We conducted a monocentric observational study including 236 SMA patients (3176 visits). Longitudinal motor outcomes predictions were generated using both full and recursive chain prediction approaches. Multivariate latent class models were applied to identify trajectory-based response groups.

Results: The models showed strong short-term predictive accuracy across functional scales. Latent class analysis identified three main response phenotypes: minimal, mild, and super responders. Age and baseline functional status were the main determinants of class assignment. Super responders showed better motor trajectories, functional independence, and quality of life, whereas minimal responders had persistently poorer outcomes. Patient-reported outcomes confirmed significant differences across classes in daily functioning, perceived health status, and treatment impact. Agreement between predicted and observed classifications ranged from 63% to 84%. Early functional slopes within the first six months showed potential to predict long-term response class.

Conclusions: This integrated framework combining longitudinal modelling and latent class analysis accurately predicts SMA treatment response and identifies clinically relevant response phenotypes. These findings support prediction-driven patient stratification, personalized management, and the use of AI-derived models for dynamic prognostication in SMA care and clinical trial design. This study was funded by the Italian Ministry of Health and the Neuromuscular Study Group.

40 - Beyond Total Scores: A Granular Item Analysis of Functional Changes During 24 Months of DMTs in Type III SMA

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Introduction

While DMTs slowed type III SMA progression, literature largely relies on total HFMSE scores, obscuring granular functional dynamics. This approach fails to distinguish specific motor skills acquired versus those lost. Elucidating long-term trajectories by analyzing item-specific gains and losses is essential to identify which abilities are truly recovered and which remain areas of clinical vulnerability.

Objectives

This study evaluates granular motor activity shifts to map detailed functional trajectories, identifying which HFMSE items are most frequently acquired or lost and determining how these changes impact different age groups and functional levels.

Methods

Using retrospective iSMAC data, we conducted granular shift analyses on individual item changes over 24 months from treatment initiation. We used two approaches: determining functional gain or loss (0 to 1-2 or vice versa) and detecting dynamic changes within the 1-2 range. Patients were stratified by age (<5, 5-9, 10-17, >18 years) and baseline status (walker, sitter, non-sitter).

Results

Evaluating 125 type III SMA patients (93 nusinersen, 32 risdiplam), the cohort showed clear clinical benefit. Per-item analysis revealed 24% showed only gain events, 11.2% only loss, 11.2% stable, and 53.6% mixed results. Items 25-33 proved most resistant to recovery. Age-dependent gains were significant (e.g., item 24 in <5 years, item 21 in >18 years), with distinct functional subgroup patterns.

Conclusions

DMTs at 24 months shift the paradigm from progression-slowing to active functional restoration. Moving beyond total scores to granular, item-specific analysis is essential to reveal therapeutic benefits and support personalized clinical decision-making and tailored rehabilitation plans.

41 - Multivariable prediction of treatment response in type II SMA: beyond single outcome measures

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Introduction: Disease modifying therapies have produced a dramatic change in the progression of disease course in type II spinal muscular atrophy. The changes observed, however, are quite variable, and the interpretation of the response to treatment can be difficult. The aim of this study was to establish whether combining multiple variables might improve prognostic accuracy of 12-month motor outcomes in treated SMA type II, using both HFMSE and the SMA Functional Composite score revised (SMA-FCR).

Methods: Random forest, elastic-net, and linear regression models were compared using baseline predictors including age, motor function, respiratory status, and scoliosis severity. Models stratified patients into tertiles of predicted response.

Results: 200 SMA type II patients from the ITASMAC registry were included in the study. Random forest models achieved optimal performance. Tertile-based stratification revealed gradients in treatment response. For HFMSE, observed 12-month changes were: Q1=0.15 points (95%CI: -0.21;0.51), Q2=0.40 (0.04;0.77), and Q3=3.00 (1.92;4.08). The highest tertile comprised younger patients (median age 2.90 years) with better baseline function, spontaneous breathing, and minimal scoliosis. In the pediatric subgroup (<14 years, N=89), tertile separation was more pronounced. SMA-FCR analysis demonstrated enhanced discrimination, particularly in the pediatric cohort.

Discussion: Our findings demonstrate that the combination of age and motor function with other variables such as respiratory status and scoliosis severity at treatment initiation can help to better predict 12-month motor improvement. SMA-

FCR captured multi-domain improvements better than HFMSE alone, providing clearer separation between response groups.

42 - Oral and Swallowing Abilities Tool- Expanded (OrSAT-E): a new module for assessment of bulbar function in Spinal Muscular Atrophy (SMA)

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Background

The Oral and Swallowing Abilities Tool (OrSAT), originally developed for infants with type I SMA, was limited in scope. This study introduces the OrSAT-Expanded (OrSAT-E), a revised instrument designed for all SMA types and ages, enhancing the assessment of bulbar function across the full spectrum.

Objectives

We aimed to validate the OrSAT-E, comprehensively assessing its applicability, discriminative ability, and sensitivity across the entire SMA patient spectrum compared to a general population control group.

Methods

We analyzed 1,252 OrSAT-E assessments from 251 SMA patients and 217 controls. We evaluated age-related functional trajectories using non-linear modeling and analyzed item-specific impairment frequencies, along with ceiling and floor effects in relation to disease severity and *SMN2* copy number.

Results

Patients showed significantly lower OrSAT-E scores than controls ($p < .001$). In severe phenotypes (type I), impairment was widespread: 71.9% of patients required intervention and 64.1% experienced cough stagnation. Conversely, milder phenotypes exhibited prominent ceiling effects, with 87.6% of type III and 86.4% of pre-symptomatic observations reaching the maximum score of 7. Floor effects were observed exclusively in type I (46.8% of observations). Discrimination was optimal for type I (AUC 0.89) but decreased significantly in milder subtypes, reflecting high functional overlap.

Conclusions

The OrSAT-E demonstrates high sensitivity for severe phenotypes, accurately capturing critical feeding and swallowing difficulties. However, its clinical utility in milder forms is constrained by significant ceiling effects. The tool effectively supports dynamic monitoring of bulbar function, although further refinements are necessary to capture functional variability in less severe populations.

44 - Concordance and discordance between functional outcome measures in Duchenne Muscular Dystrophy: A 12-month longitudinal analysis

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Introduction: In Duchenne Muscular Dystrophy (DMD), the main functional outcome measures are the NSAA, TRF, and 10MWT. Timed items are highly sensitive to functional change, requiring reliable criteria to define improvement, stability, and deterioration. As no standard threshold exists for timed tests, three classification methods were applied: stopwatch range, Minimal Detectable Change (MDC), and MDC velocity.

Objective: To assess concordance and discordance among NSAA, TRF, and 10MWT over 12 months by identifying patients with concordant change across scales. The study also compared methods for defining clinical stability to identify the most appropriate criterion for interpreting functional changes.

Methods: The analysis included 1792 assessments from 567 patients aged 4-7 years enrolled in the Italian DMD Registry and cohorts from the UK and Spain; patients enrolled in clinical trials at the time of assessment were excluded. Longitudinal 12-month data were analyzed using the three stability methods.

Results: In the overall cohort, timed measures worsened over 12 months (+2.12 s TRF; +0.29 s 10MWT), while NSAA remained stable (+0.84 points). At 4 years, all three scales showed concordant improvement. At 5 years, TRF showed the earliest signs of decline, although changes remained within the MDC stability range. At 6 years, both TRF and 10MWT showed decline, while at 7 years all three scales demonstrated concordant deterioration.

Conclusions: Motor progression in DMD is age dependent. Different concordance between scales suggests they assess different motor domains and show variable sensitivity to change over time and should be carefully analyzed in both observational and experimental studies.

48 - Whole-body Electrical Muscle Stimulation Exercise in a Patient with Sporadic Inclusion Body Myositis: A Promising Novel Approach for Disease Management

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1. **Introduction:** Sporadic inclusion body myositis (sIBM) is a degenerative muscle disease whose management focuses on rehabilitation therapies, including exercise, for supportive care in the absence of proven medical treatments. However, current literature shows mixed results of traditional exercise paradigms, demonstrating need for more effective approaches.
2. **Case Report:** A 72-year-old Caucasian male with a 10-year history of sIBM uses a single-point cane for longer-distance walking and grab bars in the bathroom. He reports falling 5-10 times within 6 months prior to enrollment. He is the primary caregiver for his wife and worries about their future as sIBM progresses. He currently engages in no regular exercise and struggles to tolerate moderate-intensity physical activity. He has significant co-morbidities, including type 2 diabetes, coronary artery disease, multiple spinal pathologies, and major polypharmacy.
3. **Methods:** The participant completed an 8-week whole-body electrical muscle stimulation (WB-EMS) exercise intervention utilizing a commercially available system. Each session consisted of 10-12 exercises performed over 20 minutes at mild to moderate intensity, twice weekly. Stimulation parameters were individualized according to tolerance and response. Outcome measures were collected within 1 week prior to and following intervention, testing strength, motor function, power, balance, pain, fatigue, and quality of life.
4. **Results:** Clinically meaningful improvements were seen in power, balance, pain, and fatigue. Functionally, tasks completed at post-test that were impossible at pre-test included descending stairs without handrails and broad jumping. No falls occurred during the 11-week study period.
5. **Conclusions:** WB-EMS Exercise may enhance safety and independence with functional mobility in people with sIBM. Further study is warranted to determine mechanisms and generalizability.

52 - Evaluating the Evidence Behind the Myasthenia Cautionary Drug List

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INTRODUCTION: Certain classes of medications are avoided in Myasthenia Gravis (MG) patients due to the reported risk of MG exacerbation.

OBJECTIVE: To conduct a review of the literature on medications and vaccines that have historically been avoided or used cautiously in patients with MG.

METHODS: Ovid MEDLINE searches were conducted; a study was included if it met the following criteria: peer-reviewed source, published after 1984, and the study described outcomes in MG patients who received a cautionary drug or vaccine. Search categories included cardiac medications, statins, antibiotics, immunosuppressants, minerals, vaccines, and miscellaneous which comprised 17 different drug classes. Studies were screened by two physician reviewers to determine if an MG exacerbation occurred following administration of a cautionary drug. If exacerbation did occur, the Naranjo Adverse Drug Reaction (ADR) Probability Scale was applied to characterize exacerbation as doubtful, possible, probable, or definite. Severity was classified by need for hospitalization or MG crisis.

RESULTS: Seventeen drug classes comprising 7830 patient exposures were included in final analysis. Medications with notable exacerbation rates following exposure included magnesium (33.8%), beta blockers (45.6%), and botulinum toxin (30.8%). Most drug classes had low exacerbation rates (<20%). These included hydroxychloroquine, calcium channel blockers, fluoroquinolones, macrolides, statins, and vaccinations. Across all categories, there were no “definite” exacerbations caused by cautionary drugs by the ADR scoring system.

CONCLUSION: Published evidence to support some MG cautionary drug categories is limited. Certain previously classified cautionary drugs may be safe in MG, expanding therapeutic options for MG patients.

58 - Ten top tips for non-pharmacological management in Facioscapulohumeral muscular dystrophy (FSHD): informed by evidence, clinical practice and lived experience

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Introduction

Facioscapulohumeral muscular dystrophy (FSHD) is one of the most common muscular dystrophies, typically emerging in young adulthood. It has no cure, making conservative non-pharmacological management the mainstay of treatment. FSHD has a variable presentation, and the limited evidence base contributes to clinical guidance gaps and care variability. This paper presents 10 top tips for the conservative management of adults with FSHD.

Objectives

To develop practical guidance for the conservative non-pharmacological management of FSHD by integrating available evidence, best clinical practice and the perspectives of people with FSHD (PwFSHD), carers, and clinicians.

Methods

These tips were derived from key lessons learned across three stages of a mixed-methods study: 1) a systematic review and meta-analysis of non-pharmacological interventions in muscular dystrophies; 2) surveys and ethnographic observations of UK FSHD care; and 3) focus groups with adults with FSHD, carers and clinicians, to define high-quality care.

Results

The 10 tips address: 1) physical activity; 2) safe symptom monitoring and management; 3) exercise modalities including strength and aerobic training, stretching and water-based activities; 4) personalised exercise prescription tailored by type, dosage, intensity and setting; 5) non-pharmacological pain management via massage, heat therapy, hydrotherapy and yoga/Pilates; 6) fatigue management through pacing, rest, relaxation and activity planning; 7) psychological support; 8) patient-clinician communication; 9) information and resource sharing; 10) shoulder surgery: indications and timing.

Conclusions

These 10 tips address a critical gap in clinical guidance for FSHD, offering a readily applicable framework to support equitable, best practice care for adults with FSHD across settings.

59 - Magnetic resonance-compatible handbike platform for clinical investigation of skeletal muscle in ambulatory and disabled patients with neuromuscular disease

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Background & Aim: Magnetic resonance imaging and spectroscopy (MRS) afford comprehensive study of muscle anatomy, biochemistry and physiology in neuromuscular disease (NMD). MR-compatible ergometers, however, typically employ leg exercise, ruling out their use in wheelchair-bound patients. We transformed a leg-cycle ergometer into a handbike accommodating both ambulatory as well as disabled patients. ³¹P MRS recordings of ATP metabolism in biceps brachii (BB) muscle of disabled patients with spinal muscular atrophy (SMA) are presented to demonstrate feasibility.

Methods: An MR-compatible cycle ergometer was fitted with carbon ski poles (Leki, Italy) equipped with 3D-printed handles and mounted on a mobile platform (Lode, NL). Subjects were positioned head-first supine on the patient support of a clinical 3T MR scanner (Philips, NL) and fitted with a 6 cm ³¹P surface coil over the BB. The ergometer platform was positioned over the lower body such that subjects held onto the skipoles with a resting elbow angle of 90°. The ensemble was then moved into the scanner such that the BB was in its center. Dynamic ³¹P MRS data were collected at rest, during arm-cycling and subsequent recovery.

Results: The platform accommodated wheelchair-bound comfortably. The upper-arm remained robustly in position during arm-cycling resulting in high-quality spectra. Unprecedented Pi and pH dynamics were observed providing a window on motor unit recruitment and composition.

Conclusion: Our adapted MR cycle platform affords clinical investigation of skeletal muscles in both ambulatory and disabled patients with NMD and should be readily translatable to commercially available MR cycle ergometers.

61 - Conventional and in-magnet cardiopulmonary exercise testing of patients with neuromuscular disease to investigate peripheral causes of exercise intolerance

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Background & Aim: Exercise intolerance severely affects daily functioning in patients with neuromuscular diseases (NMD), yet the relative contributions of mitochondrial and microvascular dysfunction remain unclear. This study evaluated the feasibility of a non-invasive magnetic resonance (MR) platform to simultaneously assess muscle energy metabolism and microvascular responsiveness during maximal in-magnet cycling.

Methods: Nineteen patients with NMD participated, including nine with Chronic Progressive External Ophthalmoplegia (CPEO; 20-80 years) and ten with Inclusion Body Myositis (IBM; 46-73 years), alongside thirteen healthy older controls (66-84 years). Patients first underwent conventional cardiopulmonary exercise testing (CPET) to assess exercise intolerance. Within two weeks, all participants performed a maximal incremental cycling test on an MR-compatible ergometer (Jeneson this meeting) inside a 3T MRI-scanner. Interleaved quantitative T2*-mapping and phosphorus-31 magnetic resonance spectroscopy (31P-MRS) data were acquired from the vastus lateralis muscle every 4 seconds.

Results: Median predicted maximal oxygen uptake during CPET was 66.9% in CPEO and 70.1% in IBM patients, confirming exercise intolerance. End-exercise phosphocreatine (PCr) depletion and pH reductions were comparable across groups. However, post-exercise PCr recovery time was significantly prolonged in CPEO patients versus controls (214s versus 86s; $p=0.003$), indicating mitochondrial dysfunction. Conversely, IBM patients exhibited a variable range of PCr recovery times (56-206s), reflecting the clinical and histopathological heterogeneity inherent to the disease. Microvascular outcomes, derived from the T2*-maps demonstrated substantial interindividual variability without significant group differences.

Conclusion: Combined qT2* mapping and 31P-MRS during in-magnet cycling is a feasible, non-invasive approach to investigate peripheral mechanisms underlying exercise intolerance in NMD.

62 - Impact of SMN2-modifying treatments on the proteomic profile of plasma and CSF samples from adult Spinal Muscular Atrophy patients

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Spinal muscular atrophy (SMA) is a genetic neuromuscular disorder caused by deficiency of survival motor neuron (SMN) protein resulting from loss of the *SMN1* gene. SMN2-modifying therapies increase functional SMN protein levels and improve clinical outcomes; however, molecular mechanisms underlying treatment response remain incompletely understood. Recent proteomic studies suggest broader biological effects to these therapies. This study aimed to characterise proteomic changes associated with treatment response in adults with SMA.

Plasma samples were obtained from SMA patients pre-treatment with either Nusinersen or Risdiplam; cerebrospinal fluid (CSF) samples were collected from patients receiving Nusinersen. Follow-up plasma and CSF samples were collected at 6 months post-treatment. Quantitative proteomic profiling was performed using Sequential Window Acquisition of all Theoretical Mass Spectra (SWATH-MS), with significant protein alterations defined as $p < 0.05$ and $\geq 25\%$ fold change. Samples were also analysed using the Alamar NULISA™ CNS panel targeting 131 proteins associated with neuronal injury, synaptic function, neuroinflammation, and neurodegeneration.

Proteomic analyses identified treatment-associated alterations in pathways related to neurodegeneration, synaptic remodelling, inflammation, extracellular matrix organisation, and proteostasis. Nusinersen-treated plasma demonstrated reduced neuroaxonal injury markers and changes linked to synaptic plasticity and extracellular remodelling. Risdiplam treatment was associated with reduced inflammatory and microglial activation markers plus altered protein-folding and stress-response pathways. CSF analyses revealed modulation of synaptic, neurovascular, and inflammatory proteins and cytokine-associated pathways.

These findings indicate that SMN2-modifying therapies induce broad molecular changes extending beyond SMN restoration and motor neuron survival, supporting a multisystem model of SMA involving neuroinflammatory, synaptic, vascular, and extracellular matrix pathways.

63 - Neurofilament light chain in Charcot-Marie-Tooth disease and related disorders

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Introduction

Charcot-Marie-Tooth disease (CMT) comprises a heterogeneous group of inherited peripheral neuropathies characterised by chronic axonal degeneration. Neurofilament light chain (NfL) is a biomarker of neuroaxonal injury measurable in blood using ultrasensitive assays and is elevated in several neurodegenerative and peripheral neuropathic disorders. However, its relevance in slowly progressive inherited neuropathies such as CMT remains unclear.

Objectives

To assess serum NfL levels in patients with CMT and explore associations with clinical characteristics.

Methods

Serum NfL levels were measured in 100 adults with genetically or clinically diagnosed CMT. Levels were expressed as a fraction of the age-adjusted upper limit of normal (fULN; value/ULN), with values >1 considered abnormal. Demographic and clinical data were collected.

Results

The cohort included 65 males and 35 females, with a mean age of 48 years and mean disease duration of 23 years. Patients represented a broad spectrum of inherited neuropathies, including CMT1, CMT2, intermediate CMT, hereditary motor neuropathy, hereditary sensory neuropathy, hereditary neuropathy with liability to pressure palsies (HNPP), and CANVAS. Serum NfL levels ranged from 0.14 to 2.86 fULN. No significant associations were found between NfL levels and disease duration ($p=0.752$) or disease severity measured by the CMT Examination Score (CMTES) ($p=0.778$). Elevated NfL levels were observed in 11 patients (11%), predominantly in CMT1A and CMT2.

Conclusions

Serum NfL levels are normal in most patients with CMT, consistent with the disease's slow progression. Longitudinal studies are needed to determine the utility of NfL as a biomarker of disease activity, progression, and treatment response.

66 - Audit of a Needle Muscle Biopsy Service Using the UCH Modified Bergström Needle at a Tertiary Neuromuscular Centre

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Introduction: Open muscle biopsy (OMB) has traditionally been the reference standard for pathological assessment, but needle muscle biopsy (NMB) using the UCH modified Bergström needle became the preferred technique at our centre in 2023.

Objectives: To evaluate the tolerability and safety of our NMB service and compare the adequacy of NMB with OMB.

Methods: We audited 166 consecutive patients undergoing NMB at the Queen Square Centre for Neuromuscular Diseases between February 2023 and May 2026. Pain scores (0-10 numerical rating scale) were recorded during and immediately after the procedure; post-procedural adverse events were collected where available. We also retrospectively reviewed 127 NMB and 137 OMB to compare specimen characteristics and diagnostic adequacy.

Results: Mean age was 49.4 years (SD 16.7); 88/166 (53%) were male. Among 128 patients with pain data, mean pain score was 5.7 (SD 3.0) during the procedure and 3.4 (SD 3.0) immediately after. Among 124 patients with adverse-event data, swelling occurred in 18 (14.5%), mild bruising in 12 (9.7%), moderate bruising in 3 (2.4%), with no severe bruising or infection. NMB yielded smaller specimens than OMB (largest fragment 81 vs 860 mm³, $p < 0.01$), but adequacy was similar: 121/127 (95%) NMB and 133/137 (97%) OMB were diagnostically adequate.

Conclusions: NMB using the UCH modified Bergström needle is well tolerated, safe, and provides high diagnostic adequacy despite smaller tissue volumes, supporting its use as a standard muscle biopsy method in our centre.

71 - Assessing perceived physical fatigability in Charcot-Marie-Tooth disease: learnings from the SMA EFFORT

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Introduction: Fatigue is common in spinal muscular atrophy (SMA) and Charcot-Marie-Tooth disease (CMT).¹⁻⁴ Fatigability, or the objective decline in motor output with sustained activity, is a hallmark of SMA,⁵ and may be problematic in people with CMT.⁶ Fatigue focused patient-reported outcomes (PROs) evaluate the patient's perspective on the severity and impact of this symptom; however, associations with objective fatigability assessments are limited.^{6,7} While in-clinic fatigability measures are valuable, there is a need for valid PROs that can assess this experience with daily activities. The SMA EFFORT, originally developed for SMA, anchors physical activity to intensity and duration to measure perceived physical fatigability (PPF) across phenotypes.⁷ Preliminary data show good test-retest reliability and strong associations with measures of performance fatigability and motor function.

Objective: The purpose of this study was to investigate the SMA EFFORT as a measure of PPF in adolescents and adults with CMT.

Methods: CMT experts were surveyed on the relevance of the SMA EFFORT items. Individuals with CMT (≥ 12 years) completed the scale, rating PPF (5-point Likert scale) with pertinent physical activities performed in the past 30 days. Total and subscale PPF% descriptive scores were generated, and associations with clinical characteristics were explored.

Results: Results will be presented at the NMSG Meeting in San Antonio, TX.

Conclusions: Fatigability may impact daily function in individuals with CMT. An evolving clinical trial landscape necessitates sensitive tools that measure meaningful symptoms. This work explores the utility of assessing PPF in CMT, and its potential to monitor response to treatment.

72 - TDP-43 pathology induces CD8 T cell activation through cryptic epitope recognition

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Introduction

Aggregation and nuclear depletion of the RNA-binding protein TDP-43 are crucial pathological features of amyotrophic lateral sclerosis (ALS), inclusion body myositis (IBM) and multisystem proteinopathy (MSP). The loss of TDP-43 nuclear function results in the aberrant inclusion of cryptic exons in mRNA transcripts, leading to the expression of de novo proteins. Clonally expanded and highly differentiated CD8+ T cells have been observed in individuals with TDP-43 proteinopathies. However, the target antigens mediating T cell activation have remained elusive.

Objectives

Here, we investigate whether the de novo proteins induced by aberrant cryptic splicing due to TDP-43 nuclear loss can act as neo-antigens.

Methods

RNA-sequencing, immunohistochemistry and proteomics were used to identify TDP-43 cryptic peptides and immune gene enrichment in patient samples. TetTCR-SeqHD, a high-throughput and multidimensional single T cell profiling approach, was used to characterise the specificity, clonality and activation of T cells.

Results

We detect the HDGFL2 cryptic peptide and multiple other TDP-43 cryptic exons in IBM skeletal muscle, where their presence correlates with enrichment of T cells and MHC-I antigen presentation. Furthermore, we identify epitopes from HDGFL2 and IGLON5 cryptic peptides, which are recognised by clonally expanded and functionally differentiated CD8+ T cells in ALS and IBM patients. Finally, we demonstrate that T cells engineered to express the identified TCRs can activate in response to the cryptic peptides and are able to kill TDP-43-deficient cells.

Conclusions

This work identifies, for the first time, specific T cell antigens in TDP-43 proteinopathies, directly linking adaptive immune response to TDP-43 pathology.

78 - Dissociation Between Perceived Exertion and Heart Rate Response During Cycling in Myotonic Dystrophy Type 1

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1. Introduction: Fatigue is a highly disabling symptom in myotonic dystrophy type 1 (DM1), yet physiological mechanisms remain poorly understood. Cardiac involvement is common in DM1, but impact of cardiac performance on fatigue has not been explored.

2. Objectives: To characterize heart rate and perceived exertional responses during moderate-intensity cycling in individuals with DM1 compared to healthy controls (HC).

3. Methods: Participants with DM1 and sex/age-matched HCs completed 30-minute moderate-intensity cycling protocol with continuous HR monitoring and repeated ratings of perceived exertion (RPE). Target HR was individualized using the Karvonen equation. HR and RPE trajectories were analyzed over the first 20 minutes to reduce bias from unequal exercise duration. Additional analyses included cumulative target HR achievement and HR-RPE relationships.

4. Results: Five people with DM1 and 4 HCs participated. DM1 participants had received recent echo- and electrocardiograms that were relatively unremarkable. HR trajectory showed blunted cardiovascular responses in DM1 while RPE trajectory demonstrated earlier and greater exertional burden. Scatterplot revealed dissociation between HR and RPE: DM1 participants reported higher RPE at comparable HR levels and peak RPE at lower HR levels. They also had delayed/reduced achievement of target HR during exercise. Three terminated cycling early: one demonstrated heart rate response consistent with deconditioning, but two others experienced chronotropic incompetence, never reaching target heart rate.

5. Conclusions: Individuals with DM1 demonstrated greater exertional burden despite submaximal cardiovascular responses during moderate-intensity cycling. Future research should explore whether this occurs more widely in DM1, requiring additional workup to inform exercise recommendations and interventions for combating fatigue.

80 - Clinical Characteristics of Late-Onset Pompe Disease: A 15-Year Single-Center Experience

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Introduction: Late-onset Pompe disease (LOPD) is a rare lysosomal storage disorder characterized by progressive skeletal and respiratory muscle involvement and frequently delayed diagnosis.

Objective: To characterize the clinical presentation, diagnostic pathways, and treatment patterns of patients with LOPD evaluated at a tertiary neuromuscular center.

Methods: Retrospective review of adults with confirmed LOPD evaluated at Penn State Health Hershey Medical Center from January 2010 to May 2025, with descriptive analysis of demographic, clinical, diagnostic, and treatment data.

Results: This ongoing study includes approximately 44 patients evaluated over a 15-year period; preliminary analysis included 24 patients. The cohort was predominantly female (16/24) and White (22/24). Mean age at symptom onset was 38.7 ± 12.4 years and mean age at diagnosis was 44.8 ± 13.1 years, corresponding to a diagnostic delay of 8.6 ± 7.9 years. Twenty-one patients (87.5%) received disease-specific therapy (11 alglucosidase alfa, 8 avalglucosidase alfa, and 2 cipaglucosidase alfa plus miglustat), while 3 (12.5%) remained untreated. Among treated patients, the mean delay from diagnosis to therapy initiation was 1.86 ± 2.46 years. Mean FVC change from baseline was -0.44 in treated patients versus -0.89 in untreated patients; cardiac function remained stable (mean EF change $+2.43\%$). Muscle biopsy was performed in 15 patients and genetic testing in 14 patients. At last follow-up, 21 patients were alive and 3 had died.

Conclusion: This single-center study highlights diagnostic delays in LOPD, describes real-world clinical presentation and treatment patterns, and compares available enzyme replacement therapies and their effects on muscle strength and respiratory function.

83 - Growing Up with Myotonic Dystrophy Type 1: Clinical Changes Across the Transition to Young Adulthood

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Transition to young adulthood is a critical period for DM1 patients, as early disease manifestations may compromise autonomy and socio-educational adaptation. Managing this phase is challenging due to the high variability between individuals.

We aimed to identify the main clinical features of CDM and ChDM patients during the transition phase and to explore patient and caregiver expectations in the era of emerging therapies.

Thirty-two patients aged 10-18 years (17 CDM, 15 ChDM) with at least two motor, respiratory, and neuropsychological assessments were included. A structured questionnaire was administered once to caregivers and cognitively preserved patients to explore expectations across several domains, including autonomy, relationships, and future therapies.

Comparing the two subgroups, CDM patients showed lower intellectual functioning (FSIQ 40.00 [40.00-43.00] vs 83.50 [72.50-100.50], $p=0.001$) and higher disease burden (CCMDHI total-scores 21.83 [11.65-45.27] vs 5.55 [2.17-13.77], $p=0.02$), with worsening in socialization (-0.30/month, $p=0.0008$) over time. ChDM patients presented greater social-communication difficulties (SCQ total-scores 25.00 [24.00-25.00] vs 20.00 [16.00-22.50], $p=0.01$), a decline in perceptual-reasoning index (-0.68/month, $p=0.04$) and improvements in self-reported emotional-regulation (-0.59/month, $p=0.005$) and quality of life (+0.42/month, $p=0.03$) over time. Motor performance remained stable in both groups. CDM patients showed a slow decline in FVC, whereas ChDM patients remained stable. Speech, strength, and cognitive improvement were the most frequently reported therapeutic goals, with expectations depending on disease subtype.

Despite the relatively small cohort, these findings suggest marked heterogeneity between CDM and ChDM patients during the transition phase, with different patient and caregiver priorities, highlighting the need for subtype-specific care strategies.

85 - Respiratory Muscles Under the Microscope: MRI Biomarkers of Respiratory Impairment in Pediatric FSHD

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Background: Over half of individuals with facioscapulohumeral muscular dystrophy (FSHD) develop symptoms in childhood (≤ 18 years old), and those with early-onset disease (≤ 10 years old) are at increased risk of faster disease progression and a younger age at loss of ambulation. Neuromuscular weakness of the thoracic muscles contributes to spinal deformities, (e.g. scoliosis, lordosis) and impaired respiratory function. Children with FSHD are therefore at high risk for respiratory complications, yet respiratory dysfunction in pediatric-onset FSHD remains uncharacterized. Left untreated, respiratory dysfunction can cause dependence on non-invasive ventilation or death. Quantitative muscle fat fraction (qFF) as measured by whole-body magnetic resonance imaging (WB-MRI) has emerged as a promising biomarker that can predict functional decline but has not been applied to the muscles of respiration to understand how changes in qFF influence respiratory function.

Objective: To determine the impact of FSHD on the muscles of respiration and pulmonary function.

Methods: Baseline WB-MRI and PFT results from the first 10 pediatric participants enrolled in the MOVE Peds natural history study will be evaluated.

Results: qFF of select muscles of respiration (pectoralis, latissimus dorsi, serratus anterior, paraspinal muscles, obliques) will be determined and correlated with baseline PFT measurements. Quantification of percentage of affected muscles, percentage of asymmetry between the left and right side, and mean fat infiltration score for each muscle as determined using the modified Mercuri scale.

Conclusions: This evaluation will provide novel insight into how FSHD affects individual muscles of respiration and the impact this can have on respiratory function.

87 - The impact of prior traumatic experiences on later fatiguability and psychiatric burden in patients with motor neuron disease and muscular dystrophy

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Although fatigue is a frequent complaint associated with motor neuron disease (MND) and muscular dystrophy (MD), it is not clear if and to what extent prior trauma exposure contributes to worse clinical outcomes.

The goal of this study is to assess if prior trauma exposure has worse impact on fatigue in patients diagnosed with MND and MD.

Data extracted from de-identified EHRs from TriNetX database was utilized. After propensity score matching was used to minimize effects of demographic confounds, the final sample size included two matched cohorts of 450 adult patients with minimum 1 year history of MND or MD at index and exposure defined as documented trauma exposure within 5 years prior to index. Risk comparison was used to assess for the following outcomes within 5 years post-index: (a) psychiatric diagnoses and (b) secondary clinical outcomes.

Patients with pre-index documented trauma exposure were shown to have a significantly higher risk of reporting fatigue, mood, and anxiety, all with $p < .001$; and hyperlipidemia, both with $p < .01$. The strongest associations based on risk difference and odds ratio (OR) were observed for anxiety, mood, and fatigue, with ORs of 3.613, 3.492, and 2.296, respectively.

These findings suggests that prior chronic stress may exacerbate clinical symptoms. The results support the integration of mental health screenings and support within multidisciplinary care for those identified to have experienced an adverse event. Future studies should explore whether stress reducing therapies may help reduce fatigue severity in addition to anxiety and mood in this population.

Thirty-two nonambulatory males (weight range 22.6 to 93.0 kg) were included between March 21, 2024, and January 31, 2026. Twenty-eight males (87.5%) required dose modification, with thrombocytopenia (46.9%) and gastrointestinal intolerance (34.4%) being the most common reasons. Among these males, 6 (18.8%) discontinued therapy: 4 due to gastrointestinal intolerance, 1 due to thrombocytopenia, and 1 due to patient preference. At the end of follow up, only 10 males (31.3%) remained at the weight-based initial dose recommended by the study label.

Conclusions:

Among nonambulatory males treated with givinostat, dose modification was frequent and target dosing was often not tolerated. If confirmed in a larger population, findings indicate reduced tolerability in a real-world population that differs from the clinical trial population. Consideration might be given to a lower starting dose for older and heavier males.

94 - Longitudinal Exploratory Evaluation of Bulbar Function in Weaker Non-Ambulatory Adults with Spinal Muscular Atrophy (SMA)

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Disease modifying treatments (DMTs) have been associated with patient-reported changes in bulbar function in spinal muscular atrophy (SMA), yet validated tools to evaluate bulbar integrity remain limited. This study evaluated longitudinal bulbar function in weak, non-ambulatory adults with SMA receiving DMTs.

We recruited 37 non-ambulatory adults with SMA as part of a prospective study (mean [SD] age 36.3 [11.6] years; range 23.4-78.5) from 2022-2025. Bulbar measures included patient reported outcomes (PROs), maximal mouth opening (aMMO), tongue and lip strength (Iowa Oral Performance Instrument), and speech metrics via mobile application (Linus Health's Speech Vitals) in clinic and remotely. Associations were assessed using Wilcoxon rank-sum tests and Spearman correlation; linear mixed-effects models assessed longitudinal change.

Participants included individuals treated with DMT (nusinersen or risdiplam) with 54% male, 59.5% SMA Type 2, 78.4% had 3 copies of SMN2, 67.6% non-sitters, and 64.9% used respiratory support. The cohort were weaker individuals with RULM mean score 10/37 [6.99]) and limited perceived voice deficits (VHI 17.88 [19], mild-moderate). Speech collection included 242 sessions (160 remote, 82 in clinic), with mean follow-up 310 [165] days (range 158-831). Patient-reported and clinical measures differed significantly between functional groups, whereas speech metrics did not. Several speech metrics showed moderate correlations with bulbar measures. Longitudinally, the digital measure that showed significant change was pitch variability.

Speech metrics collected via a mobile application are feasible objective endpoints for assessing bulbar function. This data underscores the complexity of different methods of communication and compensatory mechanisms used by individuals with SMA.

95 - The Trial Sustainability Control Tower: A Finance-Led Decision Model for Sustainable Neuromuscular Trial Delivery Across UCLH & NIHR

Ahsan Ghafoor

Introduction:

Neuromuscular clinical trials are high-complexity, high-cost studies requiring coordinated delivery across investigators, trial coordinators, research nurses, pharmacy, imaging, laboratories, R&D, CRF operations and sponsors. While clinical and regulatory risks are closely monitored, financial sustainability risks often remain fragmented across budgets, contracts, invoices, amendments and operational activity. This can lead to missed income, unrecovered pass-through costs, delayed sponsor payments, unfunded work and hidden pressure on NHS research capacity.

Objectives:

To develop a finance-led Trial Sustainability Control Tower that gives UCLH R&D a single, proactive view of trial cost, income, risk and delivery sustainability.

Methods:

The model translates each protocol, contract, budget and schedule of events into a live sustainability map. Every activity is linked to its responsible team, funding source, invoice trigger, delivery milestone, pass-through cost, amendment status and risk rating. A red-amber-green framework identifies underfunded procedures, missing contract coverage, delayed income, unrecovered costs, unfunded amendments and studies at risk of becoming financially unsustainable.

Results:

The Control Tower creates one shared decision view across QSCTC, R&D and CRF teams. It enables earlier escalation, reduces missed billing opportunities, improves sponsor query resolution, strengthens audit readiness and provides evidence for budget renegotiations, contract amendments and resource planning. It also helps teams assess whether a trial is scientifically valuable, operationally deliverable and financially sustainable.

Conclusions:

This model transforms finance from retrospective reporting into a real-time delivery safeguard. By embedding financial intelligence into trial operations, it protects NHS research capacity, improves legitimate income recovery and supports continued patient access to complex neuromuscular therapies.

96 - LEOPARD-DMD: Interval Results from a Duchenne Muscular Dystrophy Natural History Study

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Introduction: In preparation for therapeutic trials in Duchenne Muscular Dystrophy (DMD), we need sensitive outcome measures that can detect clinically relevant changes in disease burden over time. To satisfy this need, we previously developed and validated the regulatory-grade DMD Caregiver Reported-Health Index (DMDCR-HI).

Objectives: To determine the longitudinal performance metrics of the DMDCR-HI.

Methods: We are conducting a 24-month longitudinal study with caregivers of individuals with DMD. Caregivers are completing a demographics form, DMDCR-HI, parent-reported PedsQL, instrument preference survey, and global impression of change questionnaire at 6-month intervals. We are evaluating: 1) the ability of the DMDCR-HI to measure disease progression, 2) participant preferences for the DMDCR-HI vs. the PedsQL, and 3) meaningful score differences of the DMDCR-HI and its subscales.

Results: We enrolled 92 caregivers of individuals with DMD; 65 caregivers completed the 18-month time point. From baseline to 18 months, caregivers identified significant worsening in the following DMDCR-HI subscales: shoulder and arm function (10.08 points, $p=0.003$), activity participation (4.92 points, $p=0.048$), mobility (6.72 points, $p=0.024$), ambulation (8.46 points, $p=0.012$), and extended ambulation for fully/partly ambulatory patients (6.02 points, $p=0.043$). The PedsQL did not detect any significant changes in disease. A total of 65% of caregivers thought the DMDCR-HI was better able to detect important changes in disease.

Conclusions: The DMDCR-HI is a validated outcome measure that can detect disease progression over an 18-month period and is preferred by users. Future analysis will provide insight into what a meaningful change in DMDCR-HI score is for upcoming clinical trials.

97 - Sensory Neuronopathy as a Presenting Manifestation of Pancreatic Ductal Adenocarcinoma

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Introduction: Sensory neuronopathy is an uncommon disorder of the dorsal root ganglia characterized by prominent large-fiber sensory loss, sensory ataxia, and gait instability. It is most often associated with autoimmune diseases or secondary to paraneoplastic etiology, classically small cell lung carcinoma. We present a case of sensory neuronopathy as the presenting syndrome of pancreatic adenocarcinoma.

Case report: A 77-year-old woman with type 2 diabetes presented with progressive gait instability, sensory loss, and leg weakness associated with unintentional weight loss. Examination demonstrated prominent large-fiber sensory loss in bilateral upper and lower extremities, appendicular and truncal ataxia, proximal-predominant lower extremity weakness, and diffuse areflexia. Electrodiagnostic study showed axonal sensory>motor polyneuropathy with diffuse loss of sensory nerve action potentials. Paraneoplastic antibodies were negative in the serum. CT abdomen identified a pancreatic mass, with biopsy confirming pancreatic ductal adenocarcinoma. The overall picture was most consistent with paraneoplastic sensory neuronopathy associated with pancreatic adenocarcinoma. She underwent resection followed by a 5-day course of IVIG.

Conclusion: Paraneoplastic sensory neuronopathy is a rare neurologic syndrome, and its association with pancreatic adenocarcinoma is particularly uncommon and only rarely described in the literature. This case adds to the reports of pancreatic cancer being associated with paraneoplastic neurological syndromes.

101 - Revelation of Occult Hypermagnesemia: A Case Series on Mg Toxicity Induced by Chronic Supplementation Following Established Guidelines

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¹Independent Researcher as a physician

Introduction: Increased magnesium (Mg) intake via diet and guideline-based supplementation is generally deemed safe, assuming healthy kidneys efficiently eliminate excess. This case report, supported by a historical patient cohort identified via literature review, challenges this dogma.

Case Reports: Two athletic patients with no prior medical history or medication use presented with a severe, diffuse neuromuscular symptom complex. Both had chronically supplemented Mg (200-300 mg/day).

Methods: A clinical work-up was performed, including an electrolyte panel with red blood cell magnesium (RBC-Mg) analysis, complemented by a literature review. Management involved a low-Mg diet combined with high-dose B-vitamin therapy.

Results: Initially, both patients exhibited elevated RBC-Mg alongside normal or low-normal serum Mg (sMg), in the index patient with sMg levels being inversely proportional to RBC-Mg. After five weeks of therapeutic Mg reduction and B-vitamin supplementation, the index patient showed a significant decrease in RBC-Mg, accompanied by a marked rise in sMg. This "scissors effect" was first described by Jean Durlach over four decades ago. Contrary to Durlach's original interpretation, it is posited that markedly elevated RBC-Mg indicates toxic intracellular Mg overload.

Conclusion: The findings augment the historical Durlach cohort and suggest current Mg guidelines may not be universally safe. RBC-Mg is a critical tool for detecting chronic tissue accumulation in exhaustion syndromes. The reciprocal drop in sMg presents a diagnostic pitfall, falsely suggesting deficiency when viewed in isolation. Symptom responsiveness to high-dose B-vitamin therapy implies the reactivation of respiratory chain enzymes previously blocked by Mg excess.

103 - Sensory-Predominant Inflammatory Axonal Neuropathy with Cauda Equina Root Enlargement and CSF HHV-6 Detection

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Background: Sensory-predominant inflammatory neuropathies are difficult to classify when inflammatory features coexist with electrodiagnostic findings that do not meet established demyelinating criteria.

Methods: We reviewed serial electrodiagnostic studies, neuroimaging, cerebrospinal fluid (CSF) analysis, infectious evaluation, and treatment response in a 34-year-old man with progressive distal sensory loss and paresthesias over 2.5 years without objective weakness.

Results: Neurologic examination demonstrated distal sensory loss with impaired vibration and proprioception while motor strength remained preserved. Serial nerve conduction studies showed reduced median, ulnar, radial, and lower-extremity sensory amplitudes with mild latency prolongation and conduction slowing. Motor studies were largely preserved, although delayed F-wave latencies suggested proximal nerve root involvement. Longitudinal review favored a sensory-predominant axonal neuropathy rather than a primary demyelinating process. Lumbar MRI demonstrated smooth enlargement and enhancement of the cauda equina nerve roots. CSF analysis revealed albuminocytologic dissociation (protein 55.5 mg/dL, 3 white blood cells/ μ L). Extensive metabolic, autoimmune, infectious, and neoplastic investigations were unrevealing. CSF PCR was positive for HHV-6, although infectious disease evaluation favored latent reactivation or chromosomal integration rather than active infection. Weekly pulse corticosteroid therapy resulted in approximately 40% improvement in sensory symptoms with interval electrophysiologic improvement.

Conclusions: This case highlights a sensory-predominant inflammatory neuropathy characterized by axonal sensory nerve involvement, albuminocytologic dissociation, and cauda equina root enlargement despite the absence of definitive electrodiagnostic demyelination. CSF HHV-6 detection raises the possibility of a postinfectious immune trigger in a susceptible host.

104 - Prevention of pathogenic Ataxin-1 phosphorylation by RNA trans-splicing ameliorates pathology in a mouse model of spinocerebellar ataxia type 1

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RNA-trans-splicing is an RNA-based gene therapy that creates a hybrid mRNA through a trans-splicing reaction between a target pre-mRNA and an exogenous RNA trans-splicing molecule (RTM). Our objective was to determine whether the pathogenic serine phosphorylation of Ataxin-1 in spinocerebellar ataxia type 1 (SCA1) can be converted to a nontoxic state using RNA trans-splicing. Human and mouse FLAG-tagged RTMs were constructed using traditional cloning methods. Alanine substitutions at S776 (human) or S751 (mouse) were introduced using lentiviral RTM delivery in cells or via AAV2/8 delivery in the well-established Sca1^{154Q/2Q} knock-in mouse model. Mice were treated via intracerebroventricular injections in neonates (P0-2) or with cerebellar stereotaxic injections at symptomatic stage (P100). Motor function and coordination were assessed every 15 days via rotarod. First, accurate *Ataxin-1* reprogramming was demonstrated *in-vitro* and *in-vivo*. Subsequently, a combination of western blot, filter-retardation and Thioflavin T assays of mouse P180 cerebellar lysates revealed diminished Ataxin-1 aggregation and reduction in S776/S751 phosphorylation upon treatment. Additionally, confocal imaging in fixed mouse cerebellar tissue (P150) demonstrated maintained synaptic integrity, with preserved excitatory and inhibitory inputs to Purkinje neurons. Longitudinal rotarod and leg-splaying-test assessment demonstrated marked preservation in motor function and coordination, suggesting a promising therapeutic potential. Finally, adopting a patient-centric view, we delivered the trans-splicing therapy at a symptomatic stage via cerebellar-targeted stereotaxic injections, revealing a significant functional improvement. Together, these findings support the potential of RNA trans-splicing as a promising and versatile therapeutic approach for SCA1.

106 - Atypical Primary Lateral Sclerosis Presenting with Binocular Diplopia: A Case Report

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Introduction: Primary lateral sclerosis (PLS) is an upper motor neuron (UMN) disorder with typically insidious onset of spasticity, most commonly beginning in the lower extremities. Ocular manifestations are rarely described and are not recognized as an initial presenting feature.

Objectives: To describe an atypical presentation of PLS with initial binocular diplopia, expanding the phenotypic spectrum of this disorder.

Methods: We report a 77-year-old woman with a 5-year history of progressive UMN symptoms beginning with binocular diplopia. She underwent extensive evaluation including serial electromyography/nerve conduction studies, single-fiber EMG, MRI of the brain and cervical spine, cerebrospinal fluid analysis, autoimmune and neuromuscular antibody panels, and genetic testing for hereditary spastic paraplegia, ALS genes, and spinocerebellar ataxia.

Results: Neurological exam demonstrated left esotropia with impaired right eye adduction, spastic dysarthria, facial and tongue weakness, diffuse hyperreflexia with pathological reflexes, and upper extremity spasticity. Diagnostic workup was unrevealing for alternative etiologies. Vestibular testing showed central oculomotor dysfunction. The patient met 2020 consensus criteria for definite PLS based on progressive UMN involvement in multiple regions, symptom duration greater than 4 years, absence of lower motor neuron findings on serial studies, and exclusion of mimics. The disease course showed slow progression without lower motor neuron involvement.

Conclusions: This case represents a rare presentation of PLS with binocular diplopia as the initial symptom. It highlights possible supranuclear oculomotor involvement and expands the clinical spectrum of PLS. Recognition of atypical presentations is essential to avoid diagnostic delay and to distinguish PLS from other motor neuron and hereditary disorders.

108 - Long-Read Amplicon Sequencing Method to Measure CTG Repeat Length and Mosaicism for Correlation to Disease Severity in Myotonic Dystrophy Type 1

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Introduction: Myotonic dystrophy type 1 (DM1) is a multisystemic disease caused by expansion of a CTG repeat in the *DMPK* gene, with repeats ranging from 100s to 1000s of triplets. Using current methods, the length of the inherited repeat in the blood is broadly correlated with disease severity (Pearson's R » -0.44; Age-of-onset x modal CTG length), but accurate measurement of individual repeat lengths has technical limitations, particularly with larger alleles.

Objectives: To develop a method to measure CTG repeat length and mosaicism that is amenable to low sample input, economically feasible for large-scale analyses, and allows for sequence-level data.

Methods: We compare (1) Southern blot of genomic DNA, (2) Southern blot of long-range PCR, (3) small-pool PCR, (4) Cas9-mediated genomic DNA enrichment followed by PacBio long-read sequencing, and (5) PacBio sequencing of long-range PCR products using a test-set of patient-derived blood gDNA samples with variable length and mosaicism, and gDNA mixes of known repeat lengths from patient-derived cell lines. Concordance between the methods, limitations of detection of longer or shorter alleles dependent on method, and quantification of mosaicism are measured.

Results: Long-range PCR can amplify highly expanded CTG repeat alleles and represent mosaicism with high concordance compared to gDNA Southern blot (ICC = 0.901 for modal repeat length; ICC 0.888 for range of repeat mosaicism). Long-read sequencing identifies repeat interruptions, and incorporation of unique molecular identifiers to perform bioinformatic amplification correction is explored.

Conclusions: Long-read sequencing of long-range PCR products is an economical alternative to measure CTG repeat length.

111 - A cross-sectional study exploring the alignment between patient-reported and biomechanical dysphagia outcomes in myotonic dystrophy type1 (DM1)

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Studies in myotonic dystrophy type 1 (DM1) consistently demonstrate poor association between patient-reported dysphagia symptoms and instrumental assessment findings. This disconnect complicates clinical assessment and may lead to underdiagnosis of dysphagia. We investigated relationships between biomechanical dysphagia severity and patient-reported symptoms.

Ninety-four adults with DM1 were recruited from across the UK to a tertiary neuromuscular centre. During the same visit, participants completed the Sydney Swallowing Questionnaire (SSQ) and Swallowing Quality of Life Questionnaire (SWAL-QOL), followed by a videofluoroscopic swallowing study using the Modified Barium Swallow Impairment Profile (MBSImP). Participants were stratified into three dysphagia severity groups based on MBSImP oral and pharyngeal sum score tertiles for comparison of symptom scores.

Median age was 45 years (IQR 38, 52); 52 were female. SSQ scores ranged from 20 to 1096 (max 1700), with higher scores indicating greater symptom burden; scores increased across oral dysphagia tertiles: median 136 (IQR 70, 350; n=27), 224 (84, 426; n=20), and 264 (106, 578; n=45), and pharyngeal dysphagia tertiles: median 152 (57, 270; n=22), 194 (78, 398; n=39), and 350 (183, 663; n=31). SWAL-QOL swallowing symptom scores (range 0-100, with higher scores indicating fewer symptoms) decreased across oral tertiles: median 68 (43, 81), 57 (41, 82), and 46 (34, 66), and pharyngeal tertiles: 68 (46, 86), 65 (38, 86), and 43 (30, 59). Individual questionnaire items will be presented, highlighting those with poor sensitivity for detecting differences in dysphagia severity.

Findings suggest that limitations in measurement sensitivity may explain previously observed disconnect between patient-reported and instrumental measures.

112 - Quantitative muscle ultrasound as an assessment and phenotyping tool for oropharyngeal dysphagia in myotonic dystrophy type 1

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Current dysphagia phenotyping focuses on biomechanical function while neglecting pathophysiology. This limits treatment selection in conditions like myotonic dystrophy type 1 (DM1), where dysphagia may result from central nervous system impairment, muscle abnormalities, or both. We integrated biomechanical and muscle pathophysiology assessments to characterise DM1 dysphagia phenotypes.

Ninety-four adults with DM1 and 63 healthy controls were recruited. Participants underwent videofluoroscopic swallowing study using the Modified Barium Swallow Impairment Profile (MBSImP) and quantitative muscle ultrasound (QMUS) of five swallowing-related muscles. Participants were stratified by MBSImP oral and pharyngeal sum score tertiles. QMUS echogenicity and thickness were converted to sex-, age-, and BMI-adjusted z-scores and compared between tertiles. Median age was 45 years (IQR 38, 52) for DM1 participants and 43 years (IQR 30, 56) for controls. For pharyngeal dysphagia, median geniohyoid echogenicity z-scores decreased across MBSImP tertiles: 2.60 (IQR 2.25, 2.79; n=22), 2.34 (1.48, 3.05; n=38), and 1.73 (1.43, 2.31; n=30), while thickness was reduced in tertiles 1-2 (medians -1.09 and -1.06) but less affected in tertile 3 (-0.40). All oral dysphagia tertiles showed elevated echogenicity (2.18-2.30) and reduced thickness (-1.01 to -1.07). For geniohyoid echogenicity, ICC ranged from 0.73-0.99 in controls and 0.80-0.97 in pwDM1, with 95% LoA of ± 23 and ± 34 grayscale units (scale 0-255) respectively. Results for remaining muscles will be presented.

QMUS indicators of altered muscle thickness and echogenicity were associated with biomechanical dysphagia in DM1, but the relationship was inconsistent, potentially indicating multifactorial dysphagia mechanisms beyond muscle abnormality alone.

115 - Development of a Specialist Research Delivery Unit Supporting Neuromuscular Clinical Trials Within a UK Tertiary Neuroscience Centre

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Introduction: Increasing complexity and volume of neuromuscular clinical trials places growing demands on disease-specific research teams. Limited capacity may affect study initiation, delivery and participant access to research opportunities. The Queen Square Clinical Trials Centre (QSCTC) was established to provide flexible late-phase clinical trial support across neurological specialties.

Objectives: To evaluate the contribution of a specialist research delivery unit to neuromuscular clinical trial activity during its first year of operation.

Methods: A retrospective service evaluation was undertaken of QSCTC activity during its first year of operation. Data collected included portfolio growth, investigator support, participant activity and geographical distribution of participants engaged in clinical research supported by the unit.

Results: During the evaluation period, the active portfolio expanded from 2 to 11 studies including motor neuron disease, Myasthenia gravis, Huntington's disease, multiple sclerosis and inherited neuromuscular disorders. Six principal investigators were supported across multiple neurological subspecialties. Thirty-four studies approached the unit for research support. A total of 83 participant visits were delivered including screening, follow-up and remote assessments. Several newly activated studies achieved first participant screening within 30 days of activation. Participants were recruited from Greater London and multiple counties across South East England including Hertfordshire, Buckinghamshire, Essex, Kent, Oxfordshire, Cambridgeshire and Sussex.

Conclusions: During its first year of operation, a specialist research delivery unit supported substantial growth in neuromuscular clinical trial activity across multiple disease areas and investigators. This model may provide a practical approach to supporting specialist neuroscience research delivery within large academic centres facing increasing research demand while maintaining flexibility across diverse portfolios.

116 - Early Motor Neuron Dysfunction Drives Age-Related Motor Decline: Longitudinal Insights and Therapeutic Modulation with 4-AP

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Introduction: Age-related decline in motor function is a major cause of disability and morbidity and is associated with premature death. While the mechanisms of motor function decline remain incompletely understood, our ongoing work suggests loss of motor neuron (MN) excitability is a major driver and potential therapeutic target. We hypothesize that 4-aminopyridine (4-AP), a potassium channel blocker, offers a translational approach to restore MN excitability.

Objectives: To define the temporal trajectory of MN excitability and neuromuscular decline during aging and evaluate whether 4-AP restores MN excitability.

Methods: Indices of MN and muscle membrane excitability in C57BL/6J mice (n=57) were assessed longitudinally across the natural trajectory of aging from 11-28 months. In a separate ongoing intervention study, aged mice (22-23 months; n=30) were randomized to 4-AP or vehicle to evaluate how acute administration of 4-AP alters these excitability indices.

Results: Longitudinal data showed early electrophysiological deficits, with cervical motor evoked potential (cMEP) and compound muscle action potential, representing indices of spinal MN and muscle excitability, declining at 14-16 months ($p<0.001$), preceding reductions in grip strength at 23-25 months ($p<0.0001$). Acute 4-AP treatment data in old mice showed a nearly two-fold increase in cMEP compared with saline.

Conclusions: Our findings suggest that MN excitability is an early driver of age-related motor decline and represents a modifiable therapeutic target. Furthermore, preliminary results suggest that 4-AP improves MN excitability, supporting this as a potential therapeutic approach. Ongoing chronic 4-AP studies will determine whether restoring MN excitability improves neuromuscular outcomes.

119 - Ulnar Neuropathy in Wild-Type Transthyretin Amyloidosis: A Retrospective Review

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Introduction: Transthyretin amyloidosis (ATTR) is a systemic disorder caused by misfolded transthyretin deposition in multiple organs, including the myocardium and peripheral nervous system. Wild-type transthyretin amyloidosis (ATTRwt) is increasingly recognized to have prominent extracardiac neurological manifestations. Although median nerve entrapment causing carpal tunnel syndrome is well recognized, the prevalence and significance of ulnar neuropathy remain poorly defined.

Objective: To determine the prevalence of ulnar neuropathy in patients with confirmed ATTRwt and characterize its clinical and electrodiagnostic features.

Methods: A retrospective cohort study was conducted of patients with ATTRwt evaluated by a neuromuscular specialist at a single tertiary-care academic medical center between March 2017 and December 2025. Patients were identified through electronic health record review and were included if they met established diagnostic criteria for ATTRwt. Clinical documentation and electrodiagnostic studies were reviewed for evidence of ulnar neuropathy. Ulnar neuropathy was defined by the presence of at least one accepted clinical or electrodiagnostic criterion.

Results: Ninety-four patients with ATTRwt were identified (mean age 81.5 +/- 7.7 years; 90.4% male). Among these, 55 patients (58.5%) demonstrated evidence of ulnar neuropathy based on clinical assessment or electrodiagnostic testing.

Conclusions: Ulnar neuropathy is a common but underrecognized manifestation of wild-type transthyretin amyloidosis. In this single-center cohort, its high prevalence suggests it may broaden the recognized neurologic spectrum of ATTRwt and represent an early clinical indicator. Greater recognition could facilitate earlier diagnosis and inform clinical management.

120 - From Injury to Compensation: Age-Dependent Neuromuscular Responses to CTB-Saporin

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Introduction: Motor neuron (MN) and motor unit (MU) degeneration or injury results in denervation and loss of function but compensation may occur through collateral sprouting of surviving MNs. Yet, prior work suggests that compensatory capacity is limited in the context of aging and neuromuscular diseases such as Amyotrophic Lateral Sclerosis (ALS), spinal muscular atrophy (SMA), and Charcot Marie Tooth and Kennedy's diseases. Ultimately, improving collateral sprouting capacity might offer a strategy to mitigate neuromuscular disease.

Objectives: To define the impact of aging on MU compensation response following CTB-Saporin-induced MN loss in wildtype mice.

Methods: Adult (8-10 months) and aged (26-28 months) mice were injected with 6µg CTB-Saporin and neuromuscular outcomes were assessed longitudinally. Further, a dose finding study was assessed using a range of CTB-Saporin doses in young animals (4 months) to determine the CTB-Saporin dose at which MU compensation is most complete.

Results: At 6µg, CTB-Saporin reduced compound muscle action potential (CMAP) and MU number estimation in both groups, with sustained torque and grip deficits; old mice showed greater repetitive nerve stimulation decrement. Across 0-6µg, CMAP declined dose-dependently. Two-way ANOVA showed a dose effect on CMAP ($p=0.040$); age explained 10.78% and 29.48% of CMAP and single motor unit potential variance, respectively.

Conclusions: Aged mice demonstrate loss of MU repair and compensation following MU disruption. Ongoing dose-ranging will define a submaximal injury level to test age-related limits in MU compensation, a process with potential therapeutic relevancy to disorders of neuromuscular denervation.

121 - Off-label givinostat therapy in a patient with Duchenne muscular dystrophy and early-childhood tuberculosis

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Introduction: Givinostat is a histone deacetylase inhibitor recently approved for Duchenne muscular dystrophy (DMD), an X-linked recessive neuromuscular disorder. This novel disease-modifying therapy prevents muscle damage and fibrosis. Individualized treatment strategies are required when standard corticosteroid regimens are contraindicated.

Methods: Case Report.

Results: An 8-year-old boy with genetically confirmed Duchenne muscular dystrophy was initiated on off-label givinostat therapy. At 2 years old, during active tuberculosis treatment, elevated transaminases were detected alongside calf hypertrophy, frequent falls and fatigue. Past medical history included an inguinal hernia, migrating testes, and a paternal history of Fabry disease. Further laboratory testing revealed markedly elevated CK levels. MLPA confirmed an exon 45 hemizygous deletion. Standard corticosteroid therapy was contraindicated due to repeated tuberculosis treatment and chemoprophylaxis, leaving him without disease-modifying therapy until age 8. Prior to givinostat initiation, neurological examination revealed lumbar hyperlordosis, positive Gower's sign, and impaired heel walking. After 6 months of treatment, functional assessments improved: the North Star Ambulatory Assessment score increased from 30 to 33/34, time to rise decreased from 4.0s to 2.7s, and 4-stair climb improved from 2.0s to 1.6s. The 6-minute walk test remained stable (439m to 425m). The therapy was well-tolerated with no side effects.

Conclusion: This case demonstrates the therapeutic challenge of managing DMD when corticosteroids are contraindicated, proposing that givinostat may remain a viable non-immunosuppressive alternative for patients precluded from standard therapy. While short-term assessment shows functional improvement and excellent tolerability, further follow-up remains necessary for evaluating clinical benefit.

127 - QTc Distribution in Duchenne Muscular Dystrophy Patients: Implications for Therapies with Potential Cardiac Effects

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Background: Concerns have been raised regarding potential QT interval prolongation in patients affected by Duchenne muscular dystrophy (DMD), particularly following the recent approval of givinostat, a medication that may influence QT/QTc duration. This study aimed to characterize QTc values in a cohort of DMD patients not treated with givinostat, including a subgroup receiving medications known to potentially affect QTc.

Methods: The study included 279 patients aged 1.39-46.78 years followed at four neuromuscular referral centers across Italy. All participants underwent routine electrocardiographic (ECG) evaluation as part of standard clinical care. A subgroup of 108 patients received medications associated with increased QTc risk, including proton pump inhibitors, antiepileptic drugs, antidepressants, antipsychotics, stimulants, antihistamines, beta-blockers, diuretics, and antiarrhythmic agents.

Results: The cohort comprised 279 male patients (mean age 15.12 ± 7.41 years). QTc values ranged from 297 to 525 ms. Overall, 254 patients (91.04%) had QTc values <440 ms (mean 397.46 ± 25.28 ms), while 23 (8.24%) had QTc values >440 ms (mean 463.88 ± 24.94 ms). Four patients (1.43%) had QTc values >500 ms (mean 513 ± 8.83 ms). Among the 108 patients receiving medications associated with QT prolongation risk, 95 (87.96%) had QTc values <440 ms (mean 398.48 ± 24.30 ms), and 50 (46.30%) had QTc values <400 ms (mean 380.94 ± 18.78 ms).

Conclusions: In this cohort, only a small proportion of patients (8.24%) had QTc values >440 ms. Patients receiving medications potentially affecting QTc showed a similar prevalence of QTc prolongation, with 12.03% presenting QTc values >440 ms.

128 - Neuropathic Symptoms and Neuropathic Pain Treatment Practices in Patients Receiving Paclitaxel and Nab-Paclitaxel: A Single Center Study

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Introduction: Chemotherapy-induced peripheral neuropathy (CIPN) is a common dose-limiting toxicity affecting 60-70% of patients. Severe CIPN significantly impairs quality of life, making early recognition essential. Duloxetine is currently the only first-line therapy recommended by the American Society of Clinical Oncology.

Objective: This study characterized paclitaxel and nab-paclitaxel-associated neuropathic symptoms, evaluated subsequent chemotherapy regimen modifications, and described real-world pharmacologic management practices.

Methods: EMRs of adult cancer patients treated with paclitaxel or nab-paclitaxel at a single center between January-June 2023 were reviewed up to 2 years.

Results: Of 513 patients identified, 199 were evaluated: 169 (84.9%) paclitaxel and 32 (15.1%) nab-paclitaxel. Mean age 63.3 years; 70.1% female. Overall, 53.8% (n=107) developed symptoms: 84.1% (n=90/107) during active chemotherapy and 15.9% (n=17/107) within 3 months post-treatment. Incidence was 53.8% (n=91/169) for paclitaxel and 50.0% (n=16/32) for nab-paclitaxel.

Among 90 patients with active-treatment symptoms, numbness (78.9%, n=71/90) and tingling (45.6%, n=41/90) predominated, involving feet (62.9%), fingers (60.7%), toes (42.7%), and hands (32.6%). Neuropathic pain occurred in 37.9% (n=33/87). Chemotherapy modifications occurred in 46.1% (n=41/89), including dose reduction in 32.6% (n=29/89) and discontinuation in 13.5% (n=12/89). Pharmacologic therapy was initiated in 42 patients, including 33.3% (n=14/42) without documented pain. Gabapentin was the most common first-line agent (78.6%, n=33/42; median maximum 900 mg/day); duloxetine was used in 9.5% (n=4/42; median maximum 60 mg/day). Combination therapy was used in 19% (n=8/42).

Conclusion: CIPN affects over half of patients, frequently causing chemotherapy modification or discontinuation. Real-world practice heavily favors gabapentin over duloxetine, highlighting opportunities to optimize evidence-based management.

129 - Multidisciplinary Assessment of Brain Involvement in Duchenne Muscular Dystrophy

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Background: Duchenne muscular dystrophy (DMD) is a progressive disorder caused by pathogenic variants in the DMD gene, resulting in loss of dystrophin. Increasing evidence indicates that brain involvement is common in DMD, as dystrophin is expressed in both muscle and the central nervous system. Multiple brain dystrophin isoforms are differentially affected by mutation location, contributing to variability in cognitive, neurodevelopmental, and psychiatric manifestations.

Objectives: This project aims to expand knowledge of brain involvement in DMD through a multidisciplinary approach integrating clinical, neurophysiological, genetic, and computational tools. Specific objectives include characterizing central nervous system involvement, exploring genotype-epigenotype relationships, identifying genetic modifiers, and developing predictive models of neurodevelopmental outcomes.

Methods: The study will include boys older than 6 years with a genetically confirmed diagnosis of DMD followed at our center. Participants will undergo a structured assessment using clinical and neurophysiological tools, including high-density EEG. Genetic investigations will evaluate DMD variants and employ Third-Generation Whole-Genome Sequencing (TG-WGS) to identify modifier loci associated with central nervous system involvement. Machine learning approaches will integrate clinical, neurophysiological, and genetic data to develop algorithms identifying multifactorial risk factors for cognitive and neurodevelopmental disorders.

Expected Impact: This work addresses a major unmet need in DMD by improving understanding of the contribution of DMD mutations and additional genetic factors to brain involvement. It will help define the frequency and severity of neurodevelopmental and psychiatric comorbidities, support more accurate diagnoses and treatment selection, and inform the choice of outcome measures and surrogate endpoints for future interventional trials.

130 - Incidence and Dose-Response Relationship of Neuropathic Symptoms in Patients Receiving Paclitaxel or Nab-Paclitaxel: A Single Center Study

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INTRODUCTION:

Paclitaxel and nab-paclitaxel are widely used taxane chemotherapies for breast, ovarian, and lung cancers. Both are associated with chemotherapy-induced peripheral neuropathy (CIPN), which can impair quality of life and limit treatment. Paclitaxel causes neuropathy in ~60-70% of patients, while nab-paclitaxel rates may be similar or higher. Evaluating incidence and risk factors at our center is important for patient counseling and toxicity monitoring.

OBJECTIVE:

To determine the incidence of neuropathic symptoms with paclitaxel vs. nab-paclitaxel, assess cumulative dose at symptom onset, and evaluate the impact of pre-existing neuropathy.

METHODS:

This retrospective single-center study included adults treated with paclitaxel or nab-paclitaxel (Jan-Jun 2023). Patients were identified via SlicerDicer, with chart review up to 2 years for new or worsening neuropathic symptoms. Incidence and cumulative dose at onset were compared between groups and by neuropathy history.

RESULTS:

A total of 513 patients were identified, of whom 201 have been evaluated (paclitaxel n=169; nab-paclitaxel n=32). Around 53.8% (n=107) had new or worsening neuropathic symptoms, 84.1% (n=90/107) during chemotherapy and 15.9% (n=17/107) within 3 months of treatment. Incidence was similar (53.8% vs. 50%) between both groups. Mean cumulative dose at onset was 869.3±564.6 mg (paclitaxel) and 1,614.2±779.9 mg (nab-paclitaxel). Pre-existing neuropathy did not affect incidence (p=0.66). However, in nab-paclitaxel, it was associated with lower dose at onset (1,208.9 vs. 2,087 mg; p=0.035), but not in paclitaxel.

CONCLUSION:

Neuropathic symptoms are common (~50%) with both agents, with similar incidence. Pre-existing neuropathy may lower the dose threshold for nab-paclitaxel-related symptoms which warrants proactive counseling and monitoring.

131 - Baseline Characteristics and Preliminary Clinical Outcomes in an Observational Study of Advanced Glycation End Products and Chemotherapy-Induced Peripheral Neuropathy

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Background: Chemotherapy-induced peripheral neuropathy (CIPN) is a common and dose limiting toxicity. Informative biomarkers are lacking. Advanced glycation end products (AGEs) have been implicated in pathways associated with oxidative stress, inflammation, and neuronal injury and may contribute to CIPN risk. AGE reduction is a promising therapeutic strategy.

Objective: To develop an electronic health record driven strategy to identify and enroll patients before treatment with platinum or taxane-based chemotherapy. This longitudinal cohort study examines the relationship between AGEs and CIPN risk and severity, laying the foundation for a future CIPN prevention trial.

Methods: Adult patients are prospectively enrolled prior to receiving chemotherapy and followed longitudinally. CIPN clinical assessments include a spectrum of symptom, sign and quality of life-based measures (BPI, CAPPRI, CIPN RODS, EORTC 20, mTCNS). Serum AGEs, metabolic measures and neurofilament light chain (NfL) are collected at baseline and at predefined times through 6 months post chemotherapy.

Results: 54 patients have been enrolled and 21 have completed chemotherapy. Twelve have developed CIPN. The median time to symptom onset was 69 days (range: 10-172 days). Collection of serum samples clinical assessments has been integrated into clinic and infusion visits.

Conclusions: These findings demonstrate the feasibility of this prospective recruitment strategy for biomarker development or CIPN prevention studies. Ongoing analyses will evaluate the relationship between serum AGEs and CIPN incidence and severity, with the goal of designing a trial of AGE reduction (e.g. time restricted eating) for CIPN prevention.

133 - Charcot-Marie-Tooth Disease, Sleep, and Fatigue: Exploring a Complex Interplay to Improve Patient Outcomes

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Introduction Charcot-Marie-Tooth (CMT) disease encompasses a heterogeneous group of inherited polyneuropathies. Fatigue is a prevalent and debilitating symptom that significantly impairs quality of life across CMT subtypes. While the pathophysiology of fatigue remains incompletely understood, sleep disturbances have been documented in CMT1A for approximately two decades; however, systematic characterization across other subtypes is lacking, representing a critical gap in clinical management.

Objective This cross-sectional study aimed to characterize sleep disturbances across genetically confirmed CMT subtypes and evaluate the effect of intervention on objective sleep parameters.

Methods Chart review was performed on 14 patients with genetically confirmed CMT who underwent polysomnography within the preceding ten years. Pre- and post-intervention apnea-hypopnea index (AHI), BMI, Epworth Sleepiness Scale (ESS) score, and mean nocturnal SaO₂ were recorded.

Results Mean age was 47.8 ± 18.0 years; mean BMI was 28.8 ± 4.7 kg/m²; mean AHI was 10.8 ± 8.4 events/hour, and mean ESS was 12.4 ± 5.8 . Subtypes included CMT1A (n=6), CMT2A (n=3), CMTX1 (n=3), CMT2D (n=1), and CMT2E (n=1). Of 14 patients with interpretable data, 85.7% demonstrated at least mild sleep-disordered breathing. Notably, AHI did not significantly correlate with age or BMI. Among 10 treated patients, 8 achieved AHI reduction following CPAP/BiPAP; ESS improvement was modest.

Conclusion CMT patients demonstrate objectively impaired nocturnal breathing responsive to CPAP/BiPAP therapy. The absence of correlation with conventional risk factors underscores the need for proactive, routine sleep screening in all CMT patients, independent of BMI or age. Whether treatment translates to fatigue reduction warrants a prospective study.

134 - Wearable Gait Assessment in Adults with SMA: Preliminary Findings from the SAFE SMA Study

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Individuals with spinal muscular atrophy (SMA) experience progressive muscle weakness and fatigue leading to impaired gait and falls. Falls may result in injury and loss of ambulation, yet no validated tool exists to predict fall risk. Wearable gait devices provide objective gait measures and may help identify characteristics associated with falls and functional decline. This study aims to evaluate the feasibility of wearable devices in adults with SMA and characterize the relationship among gait parameters, muscle fatigability, and fall risk.

A 6-Minute Walk Test (6MWT) was completed in clinic while wearing OpalV2R[®] sensors to measure spatiotemporal measures. Preliminary analyses were performed on eight participants (5-women, 3-male; median age: 34.5; range 25-56). Participants demonstrated slower gait speeds (1.01 ± 0.29 m/s), normal cadence (102.71 ± 15.29 steps/min), and shortened stride length (1.17 ± 0.23 m) compared to healthy. Participants spent $62.51\% \pm 3.12\%$ of the gait cycle in stance phase and $37.47\% \pm 3.14\%$ in swing phase, varying slightly from healthy norms of 60% stance and 40% swing. Slower gait speed was strongly associated with less swing phase time ($\rho=0.92$, $p=0.0011$), longer double support time ($\rho=-0.95$, $p<0.001$), and shorter stride length ($\rho=0.98$, $p<0.001$), whereas faster walkers exhibited opposite patterns. Lateral step variability showed significance with foot strike angle ($\rho=0.74$, $p=0.0366$) and stride length ($\rho=0.71$, $p=0.0465$). Left right gait measurement showed strong agreement for most parameters.

Preliminary findings demonstrate feasibility and suggest that wearable devices capture meaningful gait differences to target interventions and/or bracing. Ongoing data collection will determine whether gait metrics and fatigability measures can predict falls.

135 - Better Balance-CMT: Protocol for a randomised, controlled, efficacy and implementation trial of a home-based, balance training intervention for people with Charcot-Marie-Tooth Disease

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1. Introduction

Charcot-Marie-Tooth disease (CMT) is associated with sensory loss and impaired balance, increasing fall risk. Multi-sensory rehabilitation and resistance training have demonstrated benefits in improving balance and proximal muscle strength when delivered in specialist settings. A pragmatic, home-based programme, Better Balance-CMT, has been developed with proof-of-concept evidence of safety, acceptability, and good adherence.

2. Objectives

This study will evaluate the efficacy of the Better Balance-CMT home-based balance intervention compared with treatment as usual, and to explore factors influencing its real-world implementation.

3. Methods

A randomised, single-blind, two-arm trial will be conducted with a parallel implementation study and economic evaluation. The 12-week intervention will be delivered at home by trained physiotherapists through three face-to-face sessions, supported by web-based materials and remote guidance, using self-management principles. Eighty-four participants will be recruited from six NHS hospitals in England. The primary outcome is change in Berg Balance Scale score, analysed using linear regression adjusted for baseline. A 12-week control period and an additional open-label phase will assess sustained engagement and carry-over effects. Co-production with patients and stakeholders will inform the intervention delivery and implementation strategy.

4. Results

Digital resource development for Better Balance-CMT is underway, with ongoing co-production activities to optimise usability and engagement.

5. Conclusions

Better Balance-CMT will be a scalable rehabilitation approach with potential to improve balance in people with CMT. Funded by the National Institute for Health Research, the trial is scheduled to begin at the end of 2026 with findings expected to inform clinical practice and wider implementation.

136 - Allied Health Professionals Neuromuscular Hub: Empowering Allied Health Professionals to support adults living with neuromuscular conditions

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1. Introduction

Access to specialist knowledge is essential for allied health professionals (AHPs) managing adults with neuromuscular conditions, which are often rare and complex. Limited access to expert-led training can create gaps in care delivery. An online physiotherapy module developed in 2016 demonstrated the value of digital education, prompting expansion to a broader multidisciplinary AHP audience with updated, evidence-based content.

2. Objectives

To develop a comprehensive digital learning hub for AHPs that provides evidence-based guidance on assessment and management of adult neuromuscular conditions, promotes awareness of patient needs, and enables monitoring of engagement and learning through platform analytics.

3. Methods

An expert panel of AHPs specialising in neuromuscular diseases co-developed and updated educational content into 15 structured modules. The programme, funded by Muscular Dystrophy UK in partnership with Treat-NMD, is hosted on an online learning platform (POD-LMS) and accessible via a dedicated website. Resources include recorded lectures, downloadable materials, references, and links to supplementary media.

4. Results

The AHP Neuromuscular Hub has been completed and peer-reviewed. It comprises 15 modules covering key areas such as assessment, exercise, fatigue, orthotics, respiratory care, dietetics, and self-management. Each module includes supporting resources and assessments, with downloadable certification upon completion.

5. Conclusions

This digital hub provides an accessible, scalable approach to improving AHP knowledge and skills in neuromuscular care. Its launch in February 2026 will enable widespread uptake, with ongoing monitoring of engagement to inform further development and optimise impact on clinical practice.

137 - Developing a model of balance impairment for people living with CANVAS: Protocol for a cross-sectional observational study

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1. Introduction

Cerebellar ataxia, neuropathy and vestibular areflexia syndrome (CANVAS) is a rare neurological condition characterised by combined sensory neuropathy, cerebellar and vestibular dysfunction, leading to significant balance impairment and increased risk of falls. Rehabilitation for CANVAS is limited by a lack of condition-specific evidence and an incomplete understanding of how multi-system deficits interact to affect postural control.

2. Objectives

This study aims to characterise postural instability in people with CANVAS and develop a pragmatic model of balance dysfunction to inform future rehabilitation strategies and identify modifiable treatment targets.

3. Methods

A cross-sectional observational study will recruit approximately 30 adults with CANVAS from specialist clinics. Guided by the WHO International Classification of Functioning, Disability and Health (ICF), assessments will examine both impairments and activity limitations. Body function measures include proprioceptive thresholds, vestibulo-ocular reflex parameters, and cerebellar function using smooth pursuit and the Scale for the Assessment and Rating of Ataxia (SARA). Postural control will be evaluated using posturography under varied sensory conditions and during dynamic tasks. Functional balance, patient-reported outcomes, and falls (recorded at baseline and over six months) will also be assessed.

4. Results

The study will generate an integrated profile of balance impairment, combining physiological, functional, and patient-reported data. This will enable identification of key contributors to postural instability and highlight phenotypic patterns relevant to rehabilitation.

5. Conclusions

Findings will provide CANVAS-specific evidence to support the development of a clinically meaningful model of balance dysfunction and guide targeted rehabilitation interventions and future feasibility studies.

138 - Social Determinants of Health in San Antonio Area Myasthenia Gravis Patients

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Introduction:

Generalized Myasthenia Gravis is an autoimmune neuromuscular junction disorder causing fluctuating muscle weakness and affecting >50,000 people in the US. Despite multiple available therapies, many patients face barriers to access to care, contributing to increased disease burden.

Objective:

This research seeks to explore barriers to access by identifying the social determinants of health faced by Myasthenia Gravis (MG) patients treated at a university academic center or a county hospital-affiliated safety-net clinic.

Methods:

We conducted a retrospective chart review and collected data on demographics, home address, employment status, insurance coverage, comorbidities, emergency department (ED) visits, hospitalizations, MG-ADL scores, and clinic no-shows. Data was also collected on antibody profile, time to diagnosis, and treatment types.

Results:

We compared 39 patients seen at the county-affiliated hospital clinic (Group A) with 330 seen at the university academic center (Group B). Group A had higher proportions of Hispanic/Latino and Spanish-speaking patients, higher unemployment and disability rates, and lower use of private insurance. Over half of group A lived in the most disadvantaged neighborhoods. Group A also had higher rates of clinic no-shows, ED visits, and hospitalizations. Antibody profiles and time to diagnosis were similar between groups, however, Group A had lower use of oral immunomodulatory agents and newer infusion therapies.

Conclusion:

The groups varied in demographics, socioeconomic factors, treatment types and health outcomes, despite similar antibody profiles and time to diagnosis, suggesting that differences in access likely drive these disparities. Next steps include implementing dedicated outreach for disadvantaged MG patients.

139 - Investigating Neuromuscular Junction defects in Spinal Muscular Atrophy following central and peripheral SMN restoration

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Introduction

Spinal muscular atrophy (SMA) is associated with impaired neuromuscular junction (NMJ) transmission. We previously demonstrated persistent NMJ defects in adults treated with nusinersen, suggesting that systemic SMN restoration may be required to optimize NMJ function.

Objectives

To evaluate the impact of risdiplam on NMJ transmission compared with historical nusinersen-treated controls and examine associations with strength, function, mobility, and fatigue.

Methods

Adults with 5q-SMA treated with risdiplam for ≥ 12 months. Abnormal repetitive nerve stimulation (RNS) was defined as $>10\%$ compound muscle action potential (CMAP) decrement. Assessments included handheld dynamometry, modified SMAFRS, RULM, FSS, HFMSE, 6MWT, ATEND, ulnar CMAP and MUNE.

Results

Eighteen participants were included (median age 31 years, 56% female, 72% non-ambulatory). Ten participants (56%) demonstrated abnormal RNS decrement. Participants with abnormal decrement had a significantly lower median BMI (22.1 vs 31.1 kg/m², $p=0.026$), whereas age, sex, disease duration, treatment duration, and motor function scores were similar between groups. RNS decrement correlated with 6MWT distance ($r=0.90$, $p=0.037$), elbow flexion strength ($r=0.54$, $p=0.022$), hip abduction strength ($r=0.51$, $p=0.031$), and knee flexion strength ($r=0.55$, $p=0.018$). No significant associations were observed between RNS decrement and SMAFRS, ATEND, fatigue, CMAP, MUNE, or SMUP. Compared with historical nusinersen-treated controls ($n=16$), risdiplam did not improve NMJ transmission ($p=0.80$).

Conclusions

NMJ transmission defects remain prevalent in adults with SMA despite long-term risdiplam treatment. Associations between RNS decrement, mobility, and select strength measures suggest that NMJ dysfunction may contribute to residual weakness. These findings support continued investigation of NMJ transmission as a therapeutic target in SMA.

140 - Evaluation of nutrition in a cohort of adult patients with Spinal Muscular Atrophy (SMA): A preliminary analysis

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¹The Ohio State University

INTRODUCTION

Limited research examines the nutritional status of adults with SMA. Metabolic irregularities and SMA related physical limitations place patients at risk for nutritional deficiencies.

OBJECTIVES

Nutrition is a modifiable factor that may improve health outcomes. Managing nutritional intake and metabolic abnormalities may affect functional abilities and overall health outcomes in SMA. We conducted a cross-sectional study to evaluate the nutritional status of SMA patients.

METHODS

Anthropometric data were collected from the EMR, and patient-reported surveys were conducted including: DHQIII Food Frequency Questionnaire, EAT-10, general GI symptoms questionnaire, demographic questionnaire, GPAQ physical activity questionnaire, and SMAFRS. Data were collected through a one-time virtual encounter and recorded in REDCap.

RESULTS

Twenty patients enrolled. BMI data showed five patients were obese, six overweight, eight normal weight and one underweight (<18). Sixteen completed EAT-10 (abnormal ≥ 3). Ten had a median score of 0.5 (range 0-1); six had a median score of 7.5, indicating swallowing difficulties. Two had a percutaneous endoscopic gastrostomy and both were non-ambulatory. EAT-10 scores were negatively correlated with vigorous/moderate recreational physical activity ($r = -0.52625$, $p = 0.0363$), indicating greater swallowing difficulties were associated with less recreational activity.

CONCLUSIONS

Addressing weight and obesity in adult SMA patients may present an opportunity to optimize nutrition and improve overall health outcomes. These findings highlight the need for targeted interventions to manage weight and support swallowing function as well as physical activity engagement to enhance overall health and quality of life.

141 - Remote Assessment of Central Nervous System Symptoms in Myotonic Dystrophy Type 1

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Introduction: Myotonic dystrophy type 1 (DM1) is an autosomal dominant muscular dystrophy with significant phenotypic variability in severity, multi-systemic involvement, and age of onset. Central nervous system (CNS) symptoms are frequently reported and have significant impact on quality of life for patients.

Objectives: Evaluate the CNS phenotype of patients with DM1 using remote assessments.

Methods: As part of REACH-DM (NCT07505342) and REACH-DM Kids (NCT07630389), individuals with DM1 underwent structured interviews and completed observer-reported outcomes measures (affected children) and patient reported and performance outcome measures (affected adults). For children, these included assessments of adaptive function (Vineland), executive function (BRIEF2), and social skills (SRS). For adults, these included assessment of sleep (FDS), apathy (AES), and executive function (Trail Making Test). Subjects also completed functional assessments. Data was analyzed using descriptive statistics.

Results: Ninety patients with DM1 aged 1-81 years completed at least one remote assessment (19 pediatric and 71 adult patients). In children, memory/thinking problems were reported in 68% (n=13) and hypersomnolence in 26% (n=5). Clinically abnormal scores were noted in 72% (n=13) for the Vineland Composite, 75% (n=9) for BRIEF-2 composite, and 62% (n=8) for SRS-2 Total. In adults, memory/thinking problems were reported in 22.8% (n=24) and hypersomnolence in 80.3% (n=57). Mean FDS total was 14.81 (std=2.97) and mean AES total was 53.43 (std=6.33). Additional analyses are ongoing.

Conclusions: Remote assessments in DM1 reveal frequent neurobehavioral impairments in children and prominent hypersomnolence and apathy in adults. Remote assessments may represent a scalable framework for evaluating and tracking CNS symptom burden in DM1.

142 - AAV9-KIF5A Gene Therapy as a Strategy to Improve Motor Unit Repair and Recovery in a Peripheral Nerve Transection Mouse Model

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Kinesin family member 5A (KIF5A) is an anterograde motor protein that is implicated in the pathogenesis of hereditary neuropathies, hereditary spastic paraparesis, and amyotrophic lateral sclerosis (ALS). Recently, our laboratory reported the phenotype of the first mouse model of an ALS-associated KIF5A mutation, which had an impairment in motor unit recovery following peripheral nerve injury. We have extended these studies and find the impairment in motor unit repair is related to the protein expression levels of KIF5A in neurons, suggesting that ALS-associated KIF5A mutations result in a reduction of KIF5A availability. We hypothesize that restoration or upregulation of KIF5A may rescue this phenotype and that the increase of KIF5A may enhance motor unit repair. To directly evaluate the effect of KIF5A expression on motor unit repair, we have developed an adeno-associated virus (AAV)-based gene therapy approach to increase KIF5A expression in the central nervous system (CNS) of a mouse model of sciatic nerve transection. In our ongoing study, we have identified that AAV-mediated overexpression increases KIF5A levels in the CNS without any observed toxicity up to 8 weeks post-injection. Effects of supraphysiological KIF5A expression on electrophysiological and motor function behavioral assays will be presented. Data from this study will establish a strong proof-of-concept premise for the upregulation of KIF5A as a novel therapeutic target.

143 - Refractory Myasthenia Gravis Four Years After Stiff-Person Spectrum Disorder: Lessons for Malignancy Surveillance

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Introduction:

Stiff-person spectrum disorder (SPSD) is a rare autoimmune neurological disorder that may occur as a paraneoplastic syndrome, with thymoma representing an uncommon but increasingly recognized association. The coexistence of СПSD, thymoma, and myasthenia gravis (MG) remains particularly rare.

Case Report:

A patient with GAD65-positive СПSD responded well to intravenous immunoglobulin (IVIG) and remained clinically stable for four years before developing refractory MG. Evaluation revealed a giant thymoma (5.8 × 5.3 × 4.1 cm). The MG course was complicated by respiratory failure requiring mechanical ventilation and tracheostomy. Neuromuscular symptoms improved following thymectomy and initiation of efgartigimod. Unfortunately, our patient experienced a cardiac arrest and post-anoxic status epilepticus, passing away after transition to comfort care.

Methods:

Clinical data, laboratory studies, neuroimaging findings, treatment course, and relevant literature were reviewed.

Results:

The combination of СПSD, thymoma, and refractory MG represented a rare autoimmune overlap syndrome. Although СПSD symptoms remained stable on IVIG for several years, a giant thymoma was later identified, and the patient subsequently developed refractory MG. Neuromuscular symptoms improved following thymectomy and efgartigimod therapy.

Conclusions:

Standardized guidelines for malignancy screening in GAD65-positive СПSD are lacking. This case highlights the importance of malignancy screening at the time of СПSD diagnosis and continued surveillance during follow-up, as an underlying neoplasm may become clinically apparent years after the initial neurological presentation. Earlier identification and treatment of an underlying malignancy may influence clinical outcomes.

145 - Remote Monitoring and Management of Chemotherapy Induced Peripheral Neuropathy (CIPN-REMOTE), a Randomized Single Blinded Study of a Novel Remote Care Delivery Model

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Introduction: CIPN affects 40-60% of patients receiving neurotoxic chemotherapy and is a major cause of morbidity and reduced quality of life. CIPN-REMOTE aims to improve outcomes through app-based symptom monitoring with remote management by trained nurse practitioners (NPs) utilizing an evidence-based care algorithm.

Methods: CIPN-REMOTE is a 12-week single-blinded randomized controlled trial of a novel CIPN care model. Adults who completed neurotoxic chemotherapy within the last 18 months were randomized to Usual Care (UC) or Symptom Care at Home with NP follow up (SCH-NP). Participants log symptoms daily using an app, website or automated phone system. The clinical oncologist provides standard of care treatment to the UC group. In the SCH-NP group, any moderate to severe symptom triggers an NP call within 24 hours. The primary endpoint is change in NTSS-6 between a 7-day run-in and weeks 11-12. Secondary endpoints include CIPN specific sign, symptom and quality of life outcomes.

Results: 253 participants have completed the study. Preliminary blinded analysis using descriptive statistics alone reveals 125 were randomized to group 1 (G1) and 128 to group 2 (G2). G1 experienced a 1.09 +/- 4.27 and G2 a 2.26 +/- 3.81 improvement in NTSS-6. 49.6% of those in G1 had a clinically meaningful improvement compared to 59.4% in G2.

Conclusions: REMOTE-CIPN has completed enrollment with the last participant expected to exit in Nov. 2026. Preliminary analysis indicates meaningful improvement in CIPN symptoms in both study groups suggesting the home monitoring and remote care delivery model is a promising approach.

II. Industry-Led Abstracts

2 - Post hoc analyses from the Phase 3 SAPPHIRE study evaluating apitegromab in patients with nonambulatory type 2 or 3 spinal muscular atrophy

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Introduction

The Phase 3 SAPPHIRE study (NCT05156320) showed 12mo of apitegromab, an investigational muscle-targeted treatment, reliably improved motor function outcomes for patients with SMA also receiving SMN-targeted treatments, nusinersen or risdiplam.

Objectives

Evaluate the impact of several baseline characteristics on HFMSE outcomes following apitegromab (10 and 20mg/kg) or placebo treatment.

Methods

Post hoc analyses were conducted for the SAPPHIRE population (aged 2-21y). Outcomes are reported as LSM difference (SE) in HFMSE change from baseline for apitegromab vs placebo.

Results

Following 12mo of treatment, the greatest change in HFMSE score was observed for patients with ≤ 2 y of current SMN-targeted treatment: LSM difference (SE) of 2.9 (2.08), favoring apitegromab. For patients with longer treatment exposure (3-4y, 5-6y, and ≥ 7 y), LSM difference (SE) was 1.7 (1.93), 0.8 (0.87), and 1.9 (1.44), respectively. Notable increases in HFMSE score were also observed in patients receiving apitegromab ≤ 5 y since symptom onset: LSM difference (SE) of 2.1 (2.02). Functional improvements continued to favor apitegromab for patients treated 6-10y and ≥ 11 y since symptom onset, with respective LSM differences (SE) of 0.8 (0.81) and 1.7 (1.10). Additionally, apitegromab was associated with greater functional benefit in patients with higher baseline motor function (HFMSE score ≥ 31): LSM difference (SE) of 2.6 (1.08). Patients with HFMSE baseline scores of ≤ 20 or 21-30 also experienced meaningful functional gains following apitegromab treatment: LSM difference (SE) of 0.8 (0.73) and 1.6 (1.93).

Conclusions

These data show that apitegromab treatment resulted in functional benefits regardless of SMN-targeted treatment exposure, SMA symptom onset, and motor function status.

3 - Assessing the impact of ‘any point differences’ or ‘stability’ in the Hammersmith Functional Motor Scale-Expanded on the quality of life of patients with SMA

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Introduction

Validated motor function assessments (eg, HFMSE) are essential for measuring SMA treatment efficacy; however, the meaningfulness of score changes often require patient/caregiver insights.

Objectives

To understand the real-world implications of improvement or stabilization in HFMSE related-tasks, we conducted 60-minute semi-structured qualitative interviews with patients living with SMA and/or their caregivers.

Methods

Using the constant comparative method, we identified four life domains that participants emphasized as being tied to motor function ability: ADLs, psychosocial wellbeing, independence, and QoL. Here we focus on perspectives from pediatric (caregiver proxy/patient-caregiver dyads; aged 2-17y; n=29) and adult (aged ≥18y; n=32) patients related to QoL.

Results

There was a general consensus among pediatric (mean age [SD], 9.2 [4.6]; current function: ‘sitter’ [59%] and ‘walker’ [41%]) and adult (mean age [SD], 44.0y [15.5]; current function: ‘sitter’ [72%] and ‘walker’ [28%]) patients that gaining or retaining the ability to eat, sleep, stretch/reposition, practice self-care, transfer, navigate their environment, work, and play/participate in daily activities would be important for their QoL. For example, improving by a single point in the props on arms HFMSE task would allow a pediatric patient (sitter; caregiver proxy) to participate in school activities, “She would be able to... prop up and color and things like that while on their stomach.” Additionally, an adult patient (walker) highlighted the benefits of stability in HFMSE rolling tasks for sleep, “... I’m able to maneuver myself...get out of bed... get more comfortable.”

Conclusions

These findings underscore the importance of integrating patient/caregiver perspectives for understanding clinically meaningful change.

10 - Evaluation of the Effect of Empasiprubart on Nerve Morphology in Multifocal Motor Neuropathy: Study Design

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Introduction: Multifocal motor neuropathy (MMN) is rare, chronic, autoimmune neuromuscular disease that is predominantly driven by immune-mediated complement deposition. Nerve enlargement is characteristic on ultrasound; however, post-treatment data are limited. Empasiprubart, a first-in-class, humanized, monoclonal antibody that binds complement factor C2, inhibits classical and lectin pathway activation. Empasiprubart showed a favorable safety profile and clinical proof-of-concept in the phase 2 ARDA trial. A phase 3 trial is ongoing.

Objectives: This study will evaluate the effect of intravenous (IV) empasiprubart on nerve morphology by ultrasound in MMN.

Methods: This phase 1b, open-label, single-treatment group study will enroll 30-60 adults. The main cohort includes participants with definite or probable MMN receiving maintenance IVIg. An ancillary cohort includes participants with possible MMN and/or those not meeting the IVIg inclusion criteria for the main cohort. Inclusion criteria include ultrasound-confirmed nerve enlargement and a Rasch-built Overall Disability Scale for Multifocal Motor Neuropathy (MMN-RODS) centile score ≤ 90 . The study includes screening (≤ 8 weeks), treatment (48 weeks), and safety follow-up (60 weeks). IV empasiprubart will be administered on Days 1 and 8, then every 4 weeks. Nerve ultrasound will occur at screening and on Day 1 and Weeks 12, 24, and 48.

Results: The primary endpoint is change from baseline in nerve cross-sectional area at Week 24. Secondary endpoints include muscle strength/function/dexterity (modified Medical Research Council-14 sum score, grip strength, and 9-hole peg test), patient-reported outcomes (MMN-RODS), and safety.

Conclusion: This study will evaluate the empasiprubart's effect on nerve morphology by ultrasound and clinical outcomes in MMN.

11 - Long-Term Safety and Efficacy Data of Empasiprubarb in Multifocal Motor Neuropathy: Phase 2 ARDA+ Study

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Introduction: Empasiprubarb (EMPA) binds C2, inhibiting the classical and lectin complement pathways, leaving the alternative pathway intact.

Objectives: ARDA+ (NCT05405361) assesses long-term safety and efficacy of intravenous EMPA in adults with multifocal motor neuropathy (MMN).

Methods: Participants completing the 16-week, double-blind ARDA trial and entering the long-term open label-extension (ARDA+) received EMPA. Efficacy endpoints at Week 64 included changes from ARDA baseline in grip strength (GS, most-affected hand; kPa) and MMN Rasch-built Overall Disability Scale (MMN-RODS).

Results: Interim results are reported (cutoff: 4 June 2025 [1 year after the last participant rolled over]; median treatment duration: 74 weeks) for this analysis endpoint. Cohort 1: EMPA/EMPA (n=17; received EMPA in ARDA and continued in ARDA+) and placebo (PBO)/EMPA (n=7; received PBO in ARDA and switched to EMPA in ARDA+); cohort 2: EMPA/EMPA (n=18) and PBO/EMPA (n=9). At cutoff, 44/51 participants had ≥1 year with EMPA and remained on treatment. EMPA demonstrated a consistent safety profile, with no deaths/new safety concerns. At Week 64, median change (Q1-Q3) from ARDA baseline in GS (kPa) was 16.7 (2.7-30.7; EMPA/EMPA) and 8.3 (4.0-27.0; PBO/EMPA) in cohort 1, and 44.7 (18.0-53.3) and 10.2 (2.7-19.3) in cohort 2. Median MMN-RODS (Q1-Q3) increased by 9.0 (0.0-23.0; EMPA/EMPA) and 18.0 (-2.0-27.0; PBO/EMPA) in cohort 1, and 13.5 (6.0-32.5) and 0.5 (-2.0-4.0) in cohort 2.

Conclusion: In ARDA+, participants receiving EMPA maintained improvements across efficacy and safety endpoints; those switching from PBO experienced new improvements after EMPA initiation, supporting complement system involvement in MMN pathophysiology.

12 - Design of a Phase 2a Study to Evaluate the Safety, Efficacy, and Tolerability of Intravenous Empasiprubarb as an Add-On Therapy to Intravenous Efgartigimod in Adult Participants With Generalized Myasthenia Gravis

Carrie Johnson¹, Jeff Guptill¹, Raphael Bilgraer¹, Anne Gaëlle-Dosne¹, Sophie Steeland¹, Kristin Heerlein¹, Tony Vangeneugden¹, Maria Ramos Masa¹

¹argenx

Introduction

Generalized myasthenia gravis (gMG) is an immunoglobulin G (IgG)-mediated disease that manifests differently in each patient. In some, a single therapy may insufficiently address all pathogenic mechanisms mediated by IgG autoantibodies, such as complement activation. Efgartigimod, an IgG1 Fc fragment, blocks neonatal Fc receptor-mediated IgG recycling. Empasiprubarb, an IgG1 antibody, selectively inhibits complement C2. For patients with partial response to efgartigimod, empasiprubarb add-on therapy could further improve outcomes.

Objective

To present the design of a Phase 2a, proof-of-concept study evaluating safety, efficacy, and tolerability of empasiprubarb add-on therapy in participants with gMG who partially respond to efgartigimod. This is the first gMG regimen assessed within a platform study.

Methods

The study consists of 3 parts over ~54 weeks. Part A: ~50 adult participants with acetylcholine receptor antibody-positive (AChR-Ab+) gMG receive 1 efgartigimod treatment cycle (4 once-weekly intravenous infusions followed by a 4-week treatment-free period). Part B: participants with partial response to efgartigimod (Myasthenia Gravis Activities of Daily Living [MG-ADL] improvements ≥ 2 with total remaining ≥ 5) receive 2 cycles of efgartigimod with intravenous empasiprubarb coadministered at the first and last infusions of each cycle. Part C (safety follow-up): 4 additional cycles with efgartigimod monotherapy. Participants not meeting partial response criteria during Part A proceed to Part C.

Results

Primary endpoints will evaluate safety and tolerability during Parts A and B. Secondary endpoints will evaluate efficacy, including MG-ADL.

Conclusions

Results of this study will provide proof-of-concept data on empasiprubarb as an add-on therapy to efgartigimod for adults with AChR-Ab+ gMG.

14 - Pathway-Selective Complement Blockade and its Impact on Bacterial Cell Killing

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Introduction: The complement system plays a key role in innate immunity against gram-positive and -negative bacteria. Although inhibition of the terminal complement pathway may increase infection risk, selectively blocking activation pathways upstream of the central complement component C3 may better preserve innate activity.

Objectives: To evaluate how inhibition at different points in the complement cascade affects bacterial killing.

Methods: Four gram-negative species (*Neisseria meningitidis* [H44/76; 2996]; *Haemophilus influenzae* [Eagan; 2093117]; *Escherichia coli* [MG1655; EC014]; and *Klebsiella pneumoniae* [Kpn002 (SF002); Kpn007 (SF007)]) and two gram-positive species (*Streptococcus pneumoniae* [LAC002; TIGR4] and *Staphylococcus aureus* [Newman; Newman Δ SpA/Sbi]) were studied. The bacterial strains were incubated in pooled human serum and studied for C3b complement deposition and bacterial killing with and without complement blockade. For gram-negative species, bacterial killing by serum was assessed using two methods: bacterial survival was measured by enumerating colony-forming units, and complement-mediated membrane permeabilization was measured using the membrane-impermeable deoxyribonucleic acid dye SYTOX Green. *Streptococcus pneumoniae* killing and *Staphylococcus aureus* phagocytosis were assessed using freshly isolated human polymorphonuclear neutrophils. Four complement inhibitors targeting different complement pathway components were tested. These were preincubated in 80% serum for 30 minutes before diluting to 5% and 50% in the final assay conditions. Control conditions included buffer, serum without complement inhibitor, and heat-inactivated serum.

Results: Data will describe how inhibition of different complement components affects bacterial killing.

Conclusion: C2 inhibition preserved complement-mediated bacterial killing across diverse strains, offering insight into how targeting specific complement proteins can effectively modulate immune responses against bacterial pathogens.

18 - Quality of Life in Patients with Generalized Myasthenia Gravis Achieving Sustained vs Transient Minimal Symptom Expression in the Phase 3 Vivacity-MG3 Trial

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Background: In the Vivacity-MG3 trial (NCT04951622), generalized myasthenia gravis (gMG) patients receiving nipocalimab demonstrated improved and sustained efficacy vs placebo. Minimal symptom expression (MSE; MG-ADL score ≤ 1), is a treatment goal in gMG. However, outcomes associated with achieving sustained MSE have not been fully explored.

Objective: To evaluate MSE treatment response and quality-of-life (QoL) in patients achieving sustained vs transient MSE in Vivacity-MG3.

Methods: Participants were stratified into groups based on MSE status over the 24 week double-blind phase: never achieved MSE (No-MSE), achieved MSE sustained for ≥ 8 weeks (sustained-MSE), achieved MSE ≥ 1 times but not sustained for ≥ 8 weeks (transient-MSE). Analyses included likelihood (odds ratio [OR]) of achieving sustained or transient MSE (reference=No-MSE) for nipocalimab vs placebo and MG-QoL-15r total score least-squares mean (LSM) change from baseline (CFB) to week 24 (W24) compared across MSE groups.

Results: Of 153 patients, 35 achieved MSE by W24 (nipocalimab+SOC, n=24/77; placebo+SOC, n=11/76); 19 had sustained MSE (nipocalimab+SOC, n=15/77; placebo+SOC, n=4/76). Nipocalimab- vs placebo-treated patients were significantly more likely to achieve sustained MSE (OR [95% CI]: 4.35 [1.37,13.81], p=0.013). At W24, sustained vs transient MSE patients demonstrated significantly greater improvements in MG-QoL-15r (LSM CFB [95% CI]: -12.7 [-16.3,-9.2] vs -8.7 [-12.5,-5.0], p=0.016) and vs those with No MSE (-4.1 [-7.0,-1.3], p<0.001).

Conclusion: Nipocalimab-treated patients were 4-times more likely to achieve and sustain MSE for ≥ 8 -weeks than placebo. Those achieving sustained vs transient MSE demonstrated greater improvements in QoL. Sustained MSE may be a more impactful treatment goal for gMG patients receiving advanced treatments.

19 - Long-term safety and efficacy of nipocalimab: Approximately 2 years follow-up results from the open-label extension phase of Vivacity-MG3 study

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BACKGROUND: Long-term sustained symptom control remains an important treatment goal in generalized myasthenia gravis (gMG). In a broad population of autoantibody-positive gMG patients, nipocalimab (neonatal Fc-receptor blocker) demonstrated substantial improvement in MG-Activities of Daily Living (MG-ADL) scores over the 24-week double-blind (DB) phase and over 60 weeks (W) of open-label extension (OLE) in Vivacity-MG3 (NCT04951622).

OBJECTIVE: To assess the long-term safety and efficacy of nipocalimab in gMG patients from the ongoing Vivacity-MG3 OLE phase through Week 96.

DESIGN/METHODS: Adult patients with gMG (MGFA Class II-IV), inadequately controlled (MG-ADL $\geq$ 6) on standard-of-care (SOC) therapy were randomized 1:1 to nipocalimab+SOC or placebo+SOC in the 24-week Vivacity-MG3 DB, followed by an option to enter the OLE. Efficacy and safety were evaluated in seropositive (anti-AChR positive, anti-MuSK positive, and/or anti-LRP4 positive) patients who received $\geq$ 1 dose of study treatment.

RESULTS: In the efficacy analysis set (N=137) during OLE, median (range) total duration of treatment for placebo/nipocalimab (n=66) and nipocalimab/nipocalimab (n=71) groups was 69.1W (8-128W) and 62.1W (8-128W) respectively. Among patients with 96W of treatment, mean (SD) change from DB baseline (CFB) in MG-ADL for the placebo/nipocalimab and nipocalimab/nipocalimab groups was -6.69 (3.39) and -6.47 (4.62), CFB in Quantitative-Myasthenia-Gravis (QMG) was -5.81 (4.11) and -5.97 (4.97), and Mean (SD) percent CFB in IgG was -63.24 (14.31) and -64.06 (12.91), respectively. No new safety concerns were reported.

CONCLUSIONS: In autoantibody-positive patients with gMG, long-term treatment with nipocalimab demonstrated sustained disease control through the 24-week phase 3 Vivacity-MG3 study and the 96-week OLE (120 weeks total).

22 - Efgartigimod in Acetylcholine Receptor Antibody Negative Generalized Myasthenia Gravis: Efficacy and Safety Results from ADAPT SERON

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Introduction

Approximately 15%-20% of patients with generalized myasthenia gravis (gMG) are acetylcholine receptor antibody (AChR-Ab) negative. Approved treatment options for this population remain limited. Efgartigimod is a human immunoglobulin G1 (IgG1) antibody Fc fragment that reduces IgG levels via neonatal Fc receptor blockade.

Objective

To evaluate efficacy and safety of efgartigimod in AChR-Ab negative gMG in a Phase 3 trial (ADAPT SERON).

Methods

An MG diagnostic adjudication committee confirmed gMG diagnoses. In double-blind, placebo-controlled Part A, participants were randomized 1:1 to 4 once-weekly infusions of 10 mg/kg intravenous efgartigimod or placebo followed by 5-week follow-up. Part B is an ongoing open-label period.

Results

Overall, 119 participants (n=40, MuSK-Ab+; n=6, LRP4-Ab+; n=73, triple-seronegative) were randomized to efgartigimod (n=58) or placebo (n=61). Efgartigimod demonstrated significantly greater improvement in mean Myasthenia Gravis Activities of Daily Living (MG-ADL) total score from baseline to Week 4 (primary endpoint), relative to placebo ($P=0.007$), with least squares mean change from baseline (90% CI) of -3.35 (-3.98 to -2.72) and -1.90 (-2.51 to -1.28) in each group, respectively. Improvements in MG-ADL scores were observed across all three serostatus subgroups and 30.8% of participants achieved MSE at any time during their first 3 cycles of efgartigimod. Among participants initially treated with efgartigimod, 91.2% achieved clinically meaningful improvement (≥ 2 -point MG-ADL reduction) at Week 4 of any of the first 3 cycles. Efgartigimod was well tolerated, consistent with prior studies.

Conclusions

Efgartigimod demonstrated statistically significant and clinically meaningful improvements in MG-ADL total scores and was well tolerated in AChR-Ab negative gMG.

23 - Durable Responses to Low-Dose Investigational Gene Therapy BB-301 in Patients with Oculopharyngeal Muscular Dystrophy (OPMD) with Dysphagia at 12-Months and 24- Months Post-Treatment and Improved Depth of Response to High-Dose BB-301

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OPMD is an autosomal-dominant degenerative muscle disorder characterized by progressive life-threatening dysphagia and ptosis. BB-301, a gene therapy designed to reduce dysphagic symptoms in OPMD, is being evaluated in a phase 1b/2a, first-in-human study (NCT06185673).

Patients diagnosed with OPMD who were enrolled into the Benitec Natural History (NH) study for ≥ 6 months are eligible to screen onto the BB-301 phase 1b/2a study. Each patient serves as their own control. Clinical and radiographic assessments conducted during the pre-treatment period are compared to an identical set of post-treatment assessments. Serial efficacy assessments comprise videofluoroscopic swallowing studies [VFSS] and a validated patient reported outcome instrument (Sydney Swallow Questionnaire [SSQ]).

A Responder Analysis was developed to facilitate standardized evaluation of BB-301 efficacy. Parameters underlying Response characterization were derived from literature-based methods and include SSQ, VFSS, and cold water timed drinking test.

Six Patients in cohort 1 safely received low-dose BB-301. Six cohort 1 Patients have completed the 12-month statistical follow-up period for the phase 1b/2a study (completers), with 24-month post-treatment results available for Patient 1.

All cohort 1 completers were formal Responders to BB-301, demonstrating durable response to BB-301. At 24-months post-BB-301 treatment, Patient 1 continued to demonstrate robust, disease-modifying outcomes, with deepening improvements in VFSS and SSQ assessments.

Patient 1 and Patient 2 of cohort 2 safely received high-dose BB-301. The interim clinical results demonstrate robust depth of response, with broad improvements in swallowing function.

There have been no treatment-related serious adverse events.

26 - Safety and Efficacy of Riliprubart in CIDP: 76-week Phase 2 Trial Results

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Introduction: Riliprubart, a first-in-class humanized IgG4-monoclonal antibody, selectively inhibits activated-C1s in the classical-complement pathway and can be self-administrated subcutaneously via an auto-injector.

Objective: To report efficacy and safety of riliprubart at Week-76 in participants with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP; NCT04658472).

Methods: This open-label, Phase-2 trial evaluates riliprubart in Standard-of-care (SoC)-Treated, SoC-Refractory, and SoC-Naïve participants for 24-weeks (Part-A) and 52-weeks (optional Part-B). Primary endpoint (Part-A): %-participants relapsing (SoC-Treated)/responding (SoC-Refractory/Naiïve); defined as ≥ 1 -point change in adjusted Inflammatory Neuropathy Cause and Treatment (aINCAT) score. Part-B: safety and efficacy-durability based on %-relapse-free participants (SoC-Treated)/sustained-response (SoC-Refractory/Naiïve); defined as no-increase in aINCAT score ≥ 2 -points at Week-76 relative to Week-24. Exploratory endpoints: additional efficacy measures, change in total-complement, and plasma NfL levels.

Results: At Week-24, 87% (N=42/48) SoC-Treated participants improved/remained stable (52% improved; N=25/48) after switching to riliprubart. 50% (N=9/18) SoC-Refractory, and 75% (N=9/12) SoC-Naïve participants responded. As of April-2025, 74% (N=58/78) entered and 83% (N=48/58) completed Part-B (ongoing:2% [N=1/58]; discontinued:16% [N=9/58]). In SoC-Treated group, at least 80% (N=32/40) who improved/remained stable in Part-A continued to be relapse-free. At least 78% (N=7/9) SoC-Refractory and 86% (N=6/7) SoC-Naïve participants who responded in Part-A had sustained-response. Improvement across all groups was consistent across several outcome measures. Sustained reduction of complement activity and 35% NfL reduction were demonstrated. At least one treatment-emergent adverse event was reported in 74% (N=58/78) participants. Full Part-B data will be presented at the meeting.

Conclusions: Week-76 results suggest sustained clinical benefits of riliprubart in broad spectrum of participants with CIDP, supporting development in Phase-3.

27 - Riliprubart in CIDP: Time and Magnitude of Response Analysis from a Phase-2 Trial

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Introduction: Riliprubart, a first-in-class humanized IgG4-monoclonal antibody, selectively inhibits activated-C1s in classical complement pathway and can be self-administered subcutaneously via auto-injector. In Phase-2 trial (NCT04658472), riliprubart demonstrated favorable safety and encouraging efficacy in chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

Objective: To present time and magnitude of response analyses to characterize clinical benefits of riliprubart.

Methods: The open-label Phase-2 trial evaluated riliprubart across three groups: Standard-of-care (SoC)-Treated, SoC-Refractory, and SoC-Naïve. Participants received 24-week treatment (Part-A), followed by optional 52-week treatment-extension (Part-B). Primary endpoint (Part-A) evaluated %-participants relapsing in SoC-Treated (≥ 1 -point increase in adjusted Inflammatory Neuropathy Cause and Treatment [aINCAT] disability score) and %-participants responding in SoC-Refractory/Naiïve groups (≥ 1 -point decrease in aINCAT score). This post-hoc analysis focused on INCAT responders (≥ 1 -point decrease) in Part-A, and evaluated time-to-first-response, and participant proportion with deep response (≥ 2 -point decrease), overall, and by baseline INCAT score (3-4 versus ≥ 5).

Results: Among 43 INCAT responders in Part-A, first INCAT response was observed as early as Week-2 with $\geq 44\%$ of first responses achieved by Week-4, and $\geq 89\%$ by Week-12 in all three groups. At the last INCAT assessment through Week-24, 44% (19/43) responders achieved deep response with higher rates in participants with severe baseline impairment (INCAT ≥ 5 : 69% [11/16]) versus moderate impairment (INCAT 3-4: 38% [8/21]).

Conclusions: Riliprubart provided rapid and substantial improvement in INCAT score with majority of responders achieving first response by Week-12 and nearly half of responders achieving deep response (≥ 2 -point decrease); supporting Phase-3 development of riliprubart as a potential treatment for people with CIDP.

28 - Telemedicine-Based INCAT Assessment in CIDP: Reliability and Agreement Between Nurse and Neuromuscular Expert Virtual Evaluations

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Introduction:

Inflammatory Neuropathy Cause and Treatment (INCAT) scale is a validated disability measure in chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Recent advances in telemedicine and patient-centric care have driven the demand for virtual-INCAT assessment to facilitate remote monitoring.

Objective:

To evaluate inter-rater reliability of virtual-INCAT assessments among multiple assessors and examine agreement between registered nurse (RN)-administered assessments and neuromuscular-experts' evaluations to establish if RN-assessments can reliably replicate expert findings.

Methods:

We conducted a virtual-INCAT validation sub-study as a part of the ORBIT-CIDP study (Observational, Real-world, Digital Biomarker, and Integrated Treatment Outcomes in CIDP; NCT06968975); planned to enroll 200 participants with ≥ 3 months of therapy and residual disability for virtual-INCAT assessments by RNs using a telehealth platform with 20 randomly selected participants at the time of evaluation. Sessions were video recorded and were subjected to independent INCAT scoring by 7 neuromuscular-specialists. Outcomes included general agreement and scoring reliability between RNs and other experts. Interobserver-agreement was measured using Kendall W coefficient, Fleiss-kappa, mean absolute deviation, and pairwise agreement reliability by interclass correlation coefficients. Pairwise RN vs expert agreement was measured similarly.

Results:

To be presented during the congress.

Conclusions:

This study will provide evidence on the reliability of virtual-INCAT assessments by establishing inter-rater concordance between clinical experts and RNs. If validated, this could transform CIDP patient evaluation by enabling remote monitoring in clinical trials, expanding access in resource-limited settings, and reducing patient burden. This study establishes groundwork for comparing virtual and in-person assessments to validate virtual-INCAT as a reliable and accessible standard-of-care.

29 - ORBIT-CIDP: A Real-World CIDP Study Leveraging Digital and AI-Powered Patient-Centric Innovation

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Introduction:

People with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) often experience residual disability, mobility limitations, and neurological deficits. These challenges increase the burden of regular, in-person clinical assessments required for clinical research. ORBIT-CIDP (**O**bservational, **R**eal-world, **D**igital **B**iomarker, and **I**ntegrated **T**reatment **O**utcomes; NCT06968975) addresses this gap by implementing telehealth-based approach integrating artificial intelligence (AI), digital biomarkers, and patient-centric data collection.

Objective:

To describe the ORBIT study, an innovative, first-of-its-kind study focused on patient-centric approaches to CIDP research.

Methods:

Study includes 200 US adults (≥ 18 years) with CIDP who have received therapy for ≥ 3 months, have residual disability, impairment, or neurologic deficits. Exclusion criteria include participation in interventional clinical trials. The primary objective is to characterize disability changes over up-to 2-years using the patient-reported Inflammatory Rasch-built Overall Disability Scale (IRODS) score.

The secondary objective is to characterize change in disability by the adjusted Inflammatory Neuropathy Cause and Treatment (INCAT) score, including assessing the reliability of virtually administered INCAT. The study will also assess novel digital biomarkers including video-AI movement assessments and insole-derived gait analysis.

Results:

To date, 124 participants have been enrolled in ORBIT-CIDP study. Of which 62.1% are female; 82.3% are white, and 89.5% are not Hispanic or Latino. Additional data will be presented at the congress.

Conclusions:

ORBIT-CIDP pioneers a direct-to-patient approach in CIDP research, enabling real-world disability assessment and feasibility of virtual INCAT administration. By integrating novel digital biomarkers, this study reduces the burden of clinical visits while potentially validating remote monitoring methods, ultimately accelerating patient-centered research in CIDP.

31 - Corticosteroid Usage in Patients with Generalized Myasthenia Gravis Receiving Nipocalimab: Findings from Open-Label Extension Phase of the Phase 3 Vivacity-MG3 Study

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Background: Nipocalimab demonstrated sustained disease control in generalized myasthenia gravis (gMG), improving MG-ADL and QMG scores versus placebo during the Vivacity-MG3 (NCT04951622) 24-week double-blind phase and through Week 60 of the open-label extension (OLE). Corticosteroid dose adjustment was prohibited during the double-blind phase but permitted in OLE, where all patients received nipocalimab.

Objective: To characterize corticosteroid usage, dose reduction/discontinuation, and symptom improvement during the Vivacity-MG3 OLE.

Methods: Corticosteroid dose reductions to ≤ 20 , ≤ 15 , ≤ 10 , and ≤ 5 mg/day prednisone-equivalent were evaluated through OLE Week-60. Among patients achieving low corticosteroid dose (≤ 10 or ≤ 5 mg/day), proportions achieving meaningful clinical improvement (MCI; ≥ 2 -point MG-ADL improvement), minimum symptom expression (MSE; MG-ADL=0 or 1), and ≥ 8 -week sustained outcomes were evaluated.

Results: Of 89 patients receiving corticosteroids at OLE baseline (placebo/nipocalimab:44 [49%], nipocalimab/nipocalimab:45 [51%]), 45% reduced/discontinued corticosteroids by Week-60; mean dose decreased from 23 to 10 mg/day prednisone-equivalent. Dose reduction to ≤ 20 , ≤ 15 , ≤ 10 , and ≤ 5 mg/day prednisone-equivalent were achieved by 85.4%, 71.9%, 60.7%, and 33.7%, respectively. Among patients reaching ≤ 10 mg/day (n=54), 98.1% achieved MCI, 44.4% MSE, and 94.4% and 24.1% ≥ 8 -week sustained MCI and MSE, respectively. For those reaching ≤ 5 mg/day (n=30), 100.0% achieved MCI, 60.0% MSE, and 93.3% and 33.3% ≥ 8 -week sustained MCI and MSE, respectively.

Conclusion: Through OLE Week-60, nearly half of patients receiving corticosteroids at baseline reduced or discontinued corticosteroids. Many patients who tapered to low-dose corticosteroid (≤ 10 or ≤ 5 mg/day) sustained MCI and/or MSE for ≥ 8 -weeks, supporting the corticosteroid-sparing effect of nipocalimab and concurrent meaningful clinical improvement in nipocalimab-treated patients with gMG.

32 - Pregnancy Enhanced Tracking with Neonatal and Infant Assessment (PETUNIA): Design of a Safety Study for Nipocalimab in Generalized Myasthenia Gravis

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Introduction:

Generalized myasthenia gravis (gMG) is a rare autoantibody-mediated disease frequently affecting individuals of childbearing potential. Nipocalimab is a neonatal Fc receptor blocker currently approved in the U.S., Europe, and other regions globally for treatment of gMG. However, its safety has not been studied in pregnant individuals with gMG.

Objective:

Pregnancy Enhanced Tracking with Neonatal and Infant Assessment (PETUNIA) aims to determine the prevalence of pregnancy, maternal, and infant outcomes after exposure to nipocalimab during pregnancy.

Methods:

PETUNIA is a global, non-interventional study using an enhanced pharmacovigilance approach aiming to estimate the prevalence of pregnancy outcomes, maternal complications, and neonatal and infant health outcomes among pregnant individuals with gMG exposed to nipocalimab in the post-marketing setting. From time of first approval, prospective and retrospective reports of nipocalimab exposure during pregnancy will be followed through the end of pregnancy, and for corresponding live births, through one year of life, via structured, targeted questionnaires administered to healthcare providers. The projected sample size is ≥162 total pregnancies with 50 prospectively reported over a 10-year-period from geographies where nipocalimab is approved.

Results:

Primary endpoints include pregnancy outcomes and maternal complications (fetal growth restriction, hypertensive disorders of pregnancy, placental abruption, small for gestational age), serious infections in neonate/infant, and major congenital malformations. Proportions of nipocalimab-exposed pregnancies or neonates/infants with each endpoint will be calculated with 95% confidence intervals using exact methods.

Conclusion:

PETUNIA is designed to obtain real-world safety data on pregnant individuals with gMG exposed to nipocalimab in pregnancy to support clinical decision-making.

34 - Update on Phase 2 of KYSA-6, an Open-Label, Single-Arm, Multicenter Phase 2/3 Study of Miv-cel (Mivocabtagene Autoleucel; KYV-101), a Fully Human CD19 Chimeric Antigen Receptor (CAR) T-Cell Therapy in Generalized Myasthenia Gravis (gMG)

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Introduction: gMG is a neuromuscular autoimmune disease typically causing substantial disability. Novel therapies that provide greater absolute reduction in MG-ADL to minimize/eliminate disease symptoms are needed. Miv-cel is a fully human, autologous CD19 CAR T-cell therapy with CD28 costimulation, designed for potency and tolerability.

Objective: Evaluate clinical outcomes with miv-cel in patients with gMG in Phase 2 of KYSA-6 (NCT06193889).

Methods: Adults (18-75y) with gMG (MGFA class IIb-IV), a history of AChR or MuSK autoantibodies, an MG-ADL score ≥ 6 , and ≥ 2 immunosuppressant/immunomodulator failures, received low-dose lymphodepletion and a single infusion of 1×10^8 CAR T cells.

Results: As of 2/25/2026, 7 patients were dosed (mean [range]: age 46.1y [21-62]; MG-ADL 10.6 [7-16]; QMG 16.9 [9-28]). Median follow-up was 10.2 months (range, 3.3-16.0; n=3 with ≥ 12 months). All patients had robust CAR T-cell expansion and B-cell depletion. With a single dose, all patients had ≥ 3 -point MG-ADL improvement versus baseline; 57% (4/7) achieved MSE (MG-ADL ≤ 1) at their last follow-up. At 24-weeks (n=6), miv-cel treatment resulted in 8.5-point (range, 7-13) and 11.3-point (5-27) mean reductions from baseline in MG-ADL and QMG scores, respectively. All 7 patients became immunotherapy-free (86% at last follow-up). No ICANS or high-grade CRS occurred.

Conclusions: These findings support the potential of a single dose of miv-cel to deliver durable, drug-free, disease-free remission in patients with moderate to severe gMG. Miv-cel treatment resulted in robust, sustained improvements in disease severity with an acceptable safety profile and eliminated background immunosuppressants in the majority of patients. Phase 3 is ongoing.

38 - Phase 1 ASCEND Study Evaluating INS1201 Adeno-Associated Virus Serotype 9 (AAV9) Gene Therapy in Ambulatory Pediatric Males with Duchenne Muscular Dystrophy (DMD): Trial in Progress

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Introduction

INS1201 is an investigational intrathecally administered AAV9 vector-based micro-dystrophin gene therapy for potential treatment of DMD. Preclinical studies demonstrated histopathological improvement and functional efficacy in *mdx* mice, with efficient skeletal and cardiac muscle targeting, and high expression at low doses in mice and non-human primates.

Objectives

ASCEND is a phase 1, first-in-human, dose-escalation study assessing INS1201 safety and biodistribution in ambulatory males with DMD aged 3-<5 years (Part 1: Cohorts 1 and 2) and 2-<3 years (Part 2: Cohorts 3 and 4).

Methods

ASCEND (NCT06817382) will evaluate up to 12 participants across two parts, each comprising two sequential dose cohorts (each n=3): 5.0E+14 vector genomes (vg) in Cohorts 1 and 3, and 1.0E+15 vg in Cohorts 2 and 4. Enrollment is staggered, with a 30-day safety observation period between each participant; an independent data monitoring committee will convene following completion of the last participant's observation period in each of Cohorts 1, 2, and 3. Primary endpoint is incidence and severity of treatment-emergent adverse events (AEs), AEs of special interest, and serious AEs. Secondary endpoints include identification of a recommended phase 2 dose (RP2D) and change from baseline in micro-dystrophin DNA and expression. Exploratory endpoints include micro-dystrophin biodistribution and expression, functional outcomes, and caregiver-reported outcomes. Participants will be followed up for 96 weeks post-administration, followed by a 3-year safety extension study.

Results

As of May 2026, ASCEND is actively enrolling at 10 US sites.

Conclusions

ASCEND will assess INS1201 safety and biodistribution and will inform RP2D selection.

45 - CIC-1 inhibition improves neuromuscular function and accelerates reinnervation in pre-clinical models while sustained functional effects are observed clinically in CMT patients

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CIC-1 inhibition enhances muscle excitability and improves neuromuscular transmission; however, its ability to induce sustained biological effects beyond acute functional improvement remains unclear. Here, we investigated the effects of CIC-1 inhibition across complementary preclinical models of neuromuscular dysfunction and related these findings to emerging clinical observations.

In a CMT2D mouse model, repeated dosing with a CIC-1 inhibitor (NMD712) improved neuromuscular transmission, as evidenced by a reduction in CMAP decrement, and was associated with increased grip strength and body weight. These effects developed progressively with repeated dosing, suggesting a cumulative biological response beyond acute pharmacological action. Ex vivo analyses of muscle preparations obtained following repeated in vivo dosing further demonstrated reduced neuromuscular transmission failure, indicating improved reliability of nerve-driven muscle activation.

In a sciatic nerve crush model, CIC-1 inhibition significantly accelerated recovery of motor function, as assessed by gait parameters, and promoted restoration of muscle mass following denervation, consistent with enhanced reinnervation. Importantly, recent data from an exploratory Phase 2 trial in CMT patients (SYNAPSE-CMT; NCT06482437) demonstrated improvements in muscle strength and motor function that persisted 7 days after treatment discontinuation. Together with preclinical evidence of improved neuromuscular function, reduced transmission failure, and accelerated reinnervation, these findings support the hypothesis that CIC-1 inhibition may underlie sustained biological effects beyond acute neuromuscular facilitation, consistent with disease-modifying effects and may be mediated by activity-dependent mechanisms linking muscle and nerve function.

46 - Clinical Validation of the Association Between Micro-Dystrophin Expression and Muscle MRI with Functional Outcomes: A Pooled Analysis of Delandistrogene Moxeparvovec in Patients Treated with Duchenne Muscular Dystrophy

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Introduction: Delandistrogene moxeparvovec, an approved gene transfer therapy, addresses the root cause of Duchenne Muscular Dystrophy (DMD) through targeted skeletal and cardiac muscle expression of micro-dystrophin protein containing key functional domains of dystrophin.

Objectives: To report correlations of micro-dystrophin expression and skeletal muscle magnetic resonance imaging (MRI) with functional outcomes post-treatment with delandistrogene moxeparvovec.

Methods: Data were pooled from Studies SRP-9001-102 (NCT03769116; N=40, 4-7 years, ambulatory), SRP-9001-103 (NCT04626674; N=40, 3-20 years, ambulatory), and SRP-9001-301 (NCT05096221; N=126, 4-7 years, ambulatory). Correlation of changes in functional outcomes (North Star Ambulatory Assessment [NSAA], Time to Rise [TTR], 10-meter Walk/Run [10MWR], 100-meter Walk/Run [100MWR]) with micro-dystrophin expression (western blot at Week 12), and change in skeletal muscle MRI fat fraction (FF) was measured at 1- and 2-years post-infusion.

Results: Micro-dystrophin expression and functional outcomes were significantly correlated at both 1-year (NSAA $r=0.34$, $P<0.001$; TTR $r=-0.23$, $P=0.018$; 10MWR $r=-0.36$, $P<0.001$; 100MWR $r=-0.24$, $P=0.016$) and 2-years (NSAA $r=0.46$, $P<0.001$; TTR $r=-0.28$, $P<0.03$; 10MWR $r=-0.5$, $P<0.001$; 100MWR $r=-0.53$, $P<0.001$) post-treatment, demonstrating durable treatment effect. MRI FF across all skeletal muscle tissues showed a statistically significant correlation ($P<0.05$) with all functional endpoints, with higher fat composition indicating worse functional efficacy.

Conclusions: These results provide confirmation on the mechanism of action, whereby delandistrogene moxeparvovec produces micro-dystrophin protein demonstrating functional benefit and slowing DMD disease progression. These findings are further supported by skeletal muscle MRI, a clinically meaningful endpoint for DMD disease progression, where levels of FF post-treatment show a strong association with functional efficacy.

47 - A Novel Guillain-Barré Syndrome Clinical Progression Scale to Characterize the Patient's Care Journey: Utilization in a Phase 3 Trial of Tanruprubart

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Introduction: Guillain-Barré syndrome (GBS) is a rare, acute, life-altering autoimmune polyneuropathy with rapidly progressive weakness and prolonged recovery. In GBS-02, a Phase 3, randomized, double-blind, placebo-controlled trial, tanruprubart (ANX005) 30 mg/kg led to rapid complement inhibition and clinical improvement with sustained clinical benefit over 6 months in patients aged ≥ 16 years (n=241) with GBS (NCT04701164).

Objective: Characterize the patient's care journey using a novel GBS Clinical Progression Scale (CLIPS).

Methods: CLIPS was adapted from the WHO Covid-19 Clinical Progression Scale by the study sponsor and GBS experts. This ordinal measure is based on 8 levels of care from 0 (discharged home, independent activities of daily living, capable of self-care) to 7 (death). During GBS-02, clinical status on the scale was physician-recorded weekly for 4 weeks and at 2, 3, 4, and 6 months in a subset of patients (tanruprubart 30 mg/kg n=41, 75 mg/kg n=45, placebo n=45). Treatment impact on level of care was evaluated using a proportional odds logistic regression adjusted for baseline covariates.

Results: All patients were hospitalized and most required medical intervention (Grade ≥ 3). By Day 8, care requirements decreased. At Week 4, the odds of requiring less care favored tanruprubart 30 mg/kg (aOR 2.3, 95% CI (0.99-5.39; p=0.054) over placebo, consistent with overall clinical outcome.

Conclusions: CLIPS captured patients' transitions through levels of care, providing a pragmatic lens to interpret treatment benefit. Early separation at Week 4 favoring tanruprubart supports a clinically meaningful shift toward lower resource intensity during early GBS.

49 - Safety and Exposure of SRP-1003, an $\alpha\text{v}\beta 6$ Integrin-Targeting siRNA Therapy for Patients With Myotonic Dystrophy Type 1: Interim Findings From a Phase 1/2 Study

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Introduction: Myotonic dystrophy type 1 (DM1) is an inherited, progressive, multi-system, autosomal dominant muscular dystrophy.

Objective: To present SRP-1003, an investigational alpha-v beta-6 ($\alpha\text{v}\beta 6$) integrin-targeting ligand-conjugated small interfering RNA (siRNA) that knocks down *DMPK* messenger RNA in the nucleus by targeting toxic RNA for degradation.

Methods: This ongoing, phase 1/2, randomized, placebo-controlled, 2-part trial (NCT06138743) includes patients aged 18–65 years. In part 1, randomized (2:1) patients receive a single ascending siRNA SRP-1003 dose [approx. 1 mg/kg (n=12); 2 mg/kg (n=6)] or placebo. In part 2, randomized (2:1) patients receive multiple ascending siRNA SRP-1003 doses [approx. 3 mg/kg (n=6); 4 mg/kg (n=6); or 8 mg/kg (n=12)] or placebo. Primary/secondary endpoints: safety and tolerability/plasma pharmacokinetics. Key exploratory endpoint: siRNA muscle concentration.

Results: The mean (standard deviation) participants' age was 39.1 (10.32; N=36) years. Overall, 28 patients experienced treatment-emergent adverse events (TEAEs); mostly mild to moderate and not dose dependent. Two patients experienced severe serious TEAEs unrelated to study drug (patient 1: limb abscess, fatal arrhythmia; patient 2: emotional distress [leading to study discontinuation]). The most common TEAEs were headache and upper respiratory tract infections (13.9% each). SRP-1003 had a half-life of ~5 hours and showed consistent dose-dependent increase in plasma exposure, supportive of overall pharmacokinetic linearity. A single low dose (approx. 1 mg/kg) yielded robust muscle siRNA delivery (12 nM; n=7).

Conclusions: SRP-1003 showed an acceptable safety and tolerability profile without dose-limiting safety signal. Plasma exposure increased proportionally with high-level muscle delivery using the $\alpha\text{v}\beta 6$ integrin-targeting approach, supporting continued investigation of SRP-1003.

50 - Safety and Exposure of SRP-1001, an $\alpha\beta6$ Integrin-Targeting siRNA Therapy for Patients with FSHD1: Interim Findings From a Phase 1/2 Study

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Introduction: SRP-1001 is an investigational $\alpha\beta6$ integrin-targeting ligand-based siRNA therapy designed to silence aberrant *DUX4* expression in facioscapulohumeral dystrophy type 1 (FSHD1).

Objectives: To present the preliminary data from the first-in-human trial for SRP-1001 in patients with FSHD1.

Methods: This ongoing, phase 1/2, randomized placebo (PBO)-controlled trial (NCT06131983) included patients aged 16-70 y. In part 1, patients had a single ascending dose (mg/kg) of siRNA (approx. 1 mg/kg, n=5; 2 mg/kg, n=4; 4 mg/kg, n=4; or 8 mg/kg, n=5) or PBO (n=9). In the 12-month part 2, patients had multiple ascending doses (approx. 4 mg/kg, n=11; 8 mg/kg, n=11) or PBO (n=7). Primary and secondary endpoints were safety and tolerability, and plasma pharmacokinetics, respectively. Other endpoints were siRNA muscle concentration, levels of *DUX4*-regulated gene expression, and serum creatine kinase (CK).

Results: The mean (standard deviation) age at baseline was 44.9 (12.75; N=56) years. Overall, 43 patients had any treatment-emergent adverse events (TEAEs). Most were mild to moderate in severity, with 1 serious, unrelated TEAE (chest discomfort) reported. SRP-1001 showed consistent dose-dependent increase in plasma and muscle exposure with no evidence of saturation. Compared with PBO, pooled SRP-1001 single doses suppressed *DUX4*-regulated gene expression by ~90% and reduced CK levels by ~33%.

Conclusions: SRP-1001 suppressed *DUX4*-regulated genes while showing an acceptable safety profile and dose-dependent increases in plasma and muscle concentration.

51 - The Long-Term Safety and Efficacy of Efgartigimod PH20 SC in Adult Participants with Active Idiopathic Inflammatory Myopathy: Results from the Phase 2 Randomized ALKIVIA and Open-Label Extension ALKIVIA+ Trials

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Introduction: Idiopathic inflammatory myopathy (IIM) is a rare, systemic, rheumatic disease. Immunoglobulin G (IgG) autoantibodies may drive several IIM subtypes. Efgartigimod, an IgG1 antibody Fc fragment, has demonstrated clinically meaningful improvements in IIM.

Objectives: Describe efficacy and safety results from phase 2 of ALKIVIA (NCT05523167) and ALKIVIA+ (NCT05979441).

Methods: In ALKIVIA (a phase 2/3, randomized [1:1], double-blinded, placebo-controlled trial), adults with IIM received weekly subcutaneous efgartigimod co-formulated with recombinant human hyaluronidase (EFG) or placebo plus background therapy (PBO). After 24 weeks, eligible participants continued into ALKIVIA+. The primary endpoint was Total Improvement Score (TIS) per 2016 American College of Rheumatology/European Alliance of Associations for Rheumatology Myositis Response Criteria. Changes in Physician Global Assessment of Disease Activity (MDGA), Patient Global Assessment of Disease Activity (PGA), and Manual Muscle Testing-8 (MMT8) were evaluated.

Results: In ALKIVIA, 89 participants received EFG (n=47) or PBO (n=42); 69 switched from PBO to EFG (PBO-EFG; n=34) or continued EFG (EFG-EFG; n=35) in ALKIVIA+. At Week 24, mean TIS was higher with EFG vs PBO (50.67 vs 38.96) and more EFG participants achieved improvements (TIS ≥20: 91.5% vs 73.8%, TIS ≥40: 78.7% vs 47.6%, TIS ≥60: 34.0% vs 9.5%). Greater mean improvements were observed with EFG vs PBO in MDGA (-3.06 vs -2.36), PGA (-2.88 vs -1.11), and MMT8 (15.2 vs 10.8) scores. At Week 52, PBO-EFG and EFG-EFG groups achieved similar improvements. Safety remained consistent.

Conclusion: Clinically meaningful efficacy and consistent safety were observed with EFG, supporting its continued evaluation.

53 - Tanrurubart in GBS: Targeting Early Complement-Associated Inflammation Conserved Across the Clinical Spectrum and Regions

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Introduction: Guillain-Barré syndrome (GBS) is an acute, immune-mediated polyradiculoneuropathy resulting in mild weakness to severe paralysis. Converging evidence supports a short pathogenic window where classical complement activation and innate immune effector mechanisms drive neuroinflammation and early nerve injury.

Objective: To Investigate acute inflammatory effectors in GBS and assess their modulation by upstream complement inhibition.

Methods: Unbiased serum proteome-wide longitudinal profiling (Olink[®] Explore HT) was conducted in GBS patients from a Phase 3, randomized, placebo-controlled study of anti-C1q therapy tanrurubart in Asia (n=115), an IVIg/PE-treated US cohort (n=14) and healthy controls (n=10). Longitudinal analyses and pathway-based interpretation were performed.

Results: Across tanrurubart Phase 3 and IVIg/PE US cohorts, 352 proteins were elevated at baseline, with 2- to 4-fold higher levels versus healthy controls. The top 3 Reactome pathways were all inflammation-related and included 81 unique proteins. In placebo-treated patients, this signature remained high, peaking at ~Day 8, then declining by Day 29, consistent with a transient, early inflammatory phase. In contrast, tanrurubart produced rapid, broad suppression of the inflammatory signature by Day 8, confirmed in a panel of the top 12 inflammatory proteins spanning cytokine signaling, interferon signaling, innate immune pathways, and neutrophil activation. The IVIg/PE US cohort did not demonstrate a comparable early reduction.

Conclusion: These findings identify a temporally defined early inflammatory phase in GBS across geographically and clinically distinct cohorts. Rapid suppression of complement-linked inflammatory pathways following C1q inhibition supports a mechanism-aligned therapeutic approach and suggests a window during which upstream complement targeting may have greatest biological impact.

54 - A First-in-Human Dose-Escalation Study of Intrathecal INS1202 Gene Therapy in Adults with Amyotrophic Lateral Sclerosis (ALS): Trial in Progress

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Introduction

ALS is characterized by progressive brain and spinal cord motor neuron degeneration. Misfolded mutant superoxide dismutase 1 (SOD1) protein aggregates are a pathological hallmark of SOD1-ALS, and misfolded wild-type SOD1 has been observed in sporadic ALS (sALS). INS1202 is an investigational, intrathecally administered, adeno-associated virus serotype 9 (AAV9) vector-based gene therapy that delivers a short hairpin RNA which selectively targets *SOD1* mRNA, ultimately reducing toxic SOD1 protein aggregates. INS1202 improved muscle function and survival in SOD1-mutant mice and reduced toxicity of sALS patient-derived astrocytes in co-culture with healthy mouse motor neurons, supporting evaluation of INS1202 in humans.

Objectives

ARMOR (NCT07290062) is a first-in-human, multi-center, phase 1 study evaluating safety, tolerability, and pharmacodynamics of a one-time intrathecal administration of INS1202 in participants aged 18 to <80 years with ALS who carry *SOD1* mutations or harbor no known ALS-related genetic mutation. Eligible participants meet Gold Coast diagnostic criteria with ALS Functional Rating Scale-Revised (ALSFRS-R) score ≥ 24 , disease duration ≤ 42 months, and predicted vital capacity $\geq 50\%$.

Methods

Three ascending dose cohorts are planned. Dose escalation includes a 30-day safety monitoring period between initial patients and cohorts, with Independent Data Monitoring Committee review and endorsement.

Results

The primary study period is 48 weeks with long-term safety assessed in a 4-year extension study. Endpoints include incidence and severity of adverse events (primary); identifying recommended phase 2 dose and evaluating viral vector shedding (secondary); assessing SOD1 and neurofilament light chain protein levels, clinical efficacy including ALSFRS-R score, and patient-reported outcomes (exploratory).

Conclusions

ARMOR is actively recruiting.

56 - PGN-EDODM1: Data from the FREEDOM-DM1 single-ascending dose study and the initial cohort of the FREEDOM2-DM1 multiple-ascending dose trial.

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1. Introduction: PGN-EDODM1 is an investigational peptide-conjugated oligonucleotide in clinical trials for myotonic dystrophy type 1 (DM1). PGN-EDODM1 binds to pathogenic CUG trinucleotide repeat expansions in *DMPK* mRNA, liberating MBNL1 protein through steric blocking, and is expected to restore mis-splicing of downstream transcripts.

2. Objectives: Data from a single-ascending dose study and the interim readout of Cohort 1 of a multiple-ascending dose study will be presented.

3. Methods: FREEDOM-DM1 is a completed Phase 1 randomized, double-blind, placebo-controlled, single ascending dose (SAD) study of PGN-EDODM1 (NCT06204809). FREEDOM2-DM1 is an ongoing multiple ascending dose study (NCT06667453) with 3 ascending dose levels (n=8, randomized 3:1); each cohort receives 4 doses administered every 4 weeks. Endpoints include safety, tolerability, pharmacokinetics, pharmacodynamics (correction of mis-splicing), and multiple measures of function.

4. Results: FREEDOM-DM1 demonstrated dose-dependent improvements in mean splicing correction of 12.3%, 29.1%, and 53.7% 28 days after single doses of 5 mg/kg, 10 mg/kg, and 15 mg/kg, respectively (22-gene panel). Following a single dose, improvements in functional measures were not observed. PGN-EDODM1 was generally well-tolerated, with one serious treatment-related adverse event (abdominal pain) at 10 mg/kg. Transient mild-moderate changes in renal biomarkers were observed, which met dose-limiting toxicity criteria in one participant at 15 mg/kg. These were asymptomatic and resolved without intervention.

In FREEDOM2-DM1 4 doses of 5 mg/kg PGN-EDODM1 resulted in mean splicing improvement of 7.3% (n=6) vs. 6.8% in the 2 placebos. Middle finger vHOT in treated participants showed a positive trend towards improvement. PGN-EDODM1 was well-tolerated with no cumulative toxicity.

5. Conclusions: Data are encouraging and support escalation to higher doses in the ongoing FREEDOM2-DM1 study.

57 - HARMONIA STUDY DESIGN: A GLOBAL PHASE 3 TRIAL ASSESSING THE EFFICACY AND SAFETY OF Z-BASIVARSEN IN MYOTONIC DYSTROPHY TYPE 1 (DM1)

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DM1 is a spliceopathy that results in multi-system clinical manifestations. Zeleciment basivarsen (Z-basivarsen or DYNE-101) consists of a Tfr1-binding Fab conjugated to an ASO designed to target mutant nuclear *DMPK* RNA in both muscle and CNS with the goal of correcting the underlying spliceopathy.

Data from the ongoing Phase 1/2 ACHIEVE trial informed the initial safety and efficacy of z-basivarsen, which will continue to be evaluated in HARMONIA, a Phase 3, placebo-controlled, randomized, double-blind study to assess the efficacy, safety, and tolerability of z-basivarsen in participants with DM1.

HARMONIA plans to enroll ~150 participants aged ≥16 years. Participants will be randomized 1:1 to receive either z-basivarsen 6.8 mg/kg Q8W or placebo during the 48-week placebo-controlled period, after which they will be eligible to enter an LTE portion. The primary objective is to evaluate the effect of z-basivarsen compared with placebo on improvement in muscle function as measured by the change from baseline in 5 Times Sit-to-Stand (5xSTS). 5xSTS is a validated and reliable measure of lower-extremity strength and functional mobility. It measures the ability to perform activities of daily living and has been shown to be an independent predictor of fall risk. Key secondary objectives include measures of myotonia, muscle strength and function, and patient and clinician-reported outcomes. Given DM1's significant CNS component, the study will evaluate potential effects on CNS-related disease burden, using actigraphy, clinical, and patient-reported outcome measures. HARMONIA is designed to evaluate the multi-systemic impact of spliceopathy correction using functional endpoints related to activities of daily living.

60 - Impact of delandistrogene moxeparvovec treatment delays for ambulatory patients with Duchenne muscular dystrophy

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Introduction: Delandistrogene moxeparvovec is approved in the U.S. to treat ambulatory patients ≥ 4 -years-old with Duchenne muscular dystrophy (DMD). Given the progressive muscle damage in DMD, it is important to understand how treatment delays impact functional outcomes.

Objectives: To model the clinical impact of delandistrogene moxeparvovec treatment delay versus standard of care (SoC) or immediate treatment (no delay).

Methods: A health-state simulation of a prevalent DMD population (ambulatory patients, ≥ 4 -years-old, range of baseline ages) was used. Patients were simulated to receive SoC (corticosteroids and/or medical management), immediate delandistrogene moxeparvovec treatment, and delayed (0.5-2 years from baseline) treatment. Clinical outcomes included 5-year cumulative incidence of loss of rise from floor (RFF), ambulation (LoA), and overhead reach to the scalp or higher with compensation (Brooke score ≥ 3). Delandistrogene moxeparvovec was simulated to delay progression based on hazard ratios (HRs) by age from EMBARK (NCT05096221) Year 3 data on RFF loss and RFF loss < 5 seconds. Both HRs were used to simulate LoA and Brooke ≥ 3 , accounting for outcome uncertainty when extrapolating to other clinical milestones.

Results: At 5 years, RFF loss incidence was 69.6% with SoC, 24.0% with no treatment delay, and 28.8-43.4% with 0.5-2-year delays. LoA incidence was 55.7% (SoC), 17.4-27.2% (no delay), and 21.0-37.8% (0.5-2-year delays). Brooke ≥ 3 incidence was 44.8% (SoC), 4.8-15.1% (no delay), and 8.3-25.5% (0.5-2-year delays).

Conclusions: Applying 3-year EMBARK data, this model estimates lower clinical event incidence with delandistrogene moxeparvovec treatment regardless of administration timing. However, even short delays have a noticeable impact on incidence versus SoC.

64 - U.S. Healthcare Provider Consensus on Definitions of Delayed Diagnosis, Misdiagnosis, and Suboptimal Management in Myasthenia Gravis

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Introduction: Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disease associated with disparities in care across patient subpopulations. Lack of consensus among healthcare providers (HCPs) on definitions of medical unmet needs limits standardized assessment of care quality in clinical practice and research.

Objectives: Develop consensus-based definitions of delayed diagnosis, misdiagnosis, and suboptimal management in MG among U.S. HCPs.

Methods: A two-round Delphi process was conducted among U.S. HCPs experienced in managing MG. In Round 1, participants rated agreement with proposed definitions and provided qualitative feedback. In Round 2, definitions were re-evaluated after review of aggregated responses and themes of disagreement. Consensus was predefined as $\geq 70\%$ agreement.

Results: 110 HCPs (91% MD, 90% neuromuscular specialty, 85% with >5 years managing MG) completed both rounds. Consensus agreement was achieved for definitions of delayed diagnosis (>90 days from first healthcare contact for MG-related symptoms; 96%) and misdiagnosis (alternative neurological or unrelated diagnosis preceding MG; 99%), and for multiple indicators of suboptimal management, with low-to-moderate variance (0.219-0.566). Highest consensus indicators of suboptimal management ($>95\%$ agreement) spanned aspects of care, including delayed diagnostic imaging, lack of timely thymectomy, prolonged high-dose prednisone use without immunosuppressive or other therapy, and failure to adjust treatment with worsening symptoms. Maintenance IVIg monotherapy >3 months did not reach consensus as suboptimal management (42% agreement).

Conclusions: This Delphi study establishes consensus-derived definitions for key diagnostic and management gaps in MG. These standardized definitions have potential to improve assessment of high-quality care in MG and thereby demonstrate and reduce gaps in care.

67 - Treatment Patterns and Clinical Outcomes in Multifocal Motor Neuropathy: Descriptive Insights from the iMMersion Study

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Introduction: Multifocal motor neuropathy (MMN) is a rare, chronic, autoimmune neuromuscular disease that is predominantly driven by immune-mediated complement deposition that drives pathophysiology. iMMersion (NCT05988073) is a global, prospective, longitudinal study to characterize disease course, management, and burden in adults with MMN.

Objectives: Describe the baseline characteristics, treatment patterns, and clinical outcomes of participants enrolled in iMMersion.

Methods: Outcome measures (MMN-Rasch-built Overall Disability Scale [MMN-RODS]; modified MRC-10 [mMRC-10]) and the impact on health-related quality of life (chronic acquired polyneuropathy patient-reported index [CAP-PRI]) will be assessed for ≥ 48 months. Site visits coincide with existing treatment visits (approximately every 3 months).

Results: Of 400 participants, 65.8% had definite, 17.6% probable, and 16.6% possible MMN. Mean (standard deviation [SD]) age was 56.8 (13.0) years; 34% were female and 73% were White. Mean (SD) time since initial symptoms and diagnosis was 13.7 (10.2) and 9.5 (8.3) years, respectively. At study entry, 64.8% of participants were receiving intravenous immunoglobulin (IVIg) monotherapy, 15.5% no MMN treatment, and 13.5% subcutaneous immunoglobulin (SCIg) monotherapy. At data cutoff (January 8, 2026) or study discontinuation, 63.5%, 18.3%, and 13.5% were receiving IVIg, no MMN treatment, and SCIg, respectively. At 12 months, mean (SD) changes from baseline in MMN-RODS centile score (n=259), mMRC-10 sum score (n=251), and CAP-PRI (n=258) were -2.6 (10.5), 0.5 (6.6), and -0.4 (4.4), respectively.

Conclusion: This analysis provides insights into treatment patterns and clinical outcomes in MMN. Although most participants were receiving treatment, changes in outcome measures were modest, highlighting an unmet need for additional therapeutic options.

68 - Interim Analysis from the Ongoing Phase 3 FORTIFY Study of BBP-418 Shows Significant Improvements Across Biomarker and Functional Endpoints in LGMD2I/R9

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Introduction: Limb-girdle muscular dystrophy 2I/R9 (LGMD2I/R9), an autosomal recessive disorder caused by pathogenic variants in *FKRP* impairing α -dystroglycan (α DG) glycosylation, leads to progressive, irreversible muscle damage and cardiopulmonary decline. No approved therapies exist.

Objective: FORTIFY (NCT05775848) is an ongoing randomized, double-blind, placebo-controlled, phase 3 study evaluating BBP-418, an oral small molecule designed to restore α DG glycosylation and maintain muscle integrity during contraction.

Methods: An interim analysis assessed change from baseline (CFB) in α DG (% of control) in muscle at Months 3 and 12; CFB at Month 12 in serum creatine kinase (CK), 100MTT (m/s), and forced vital capacity (FVC; % predicted, seated); and responder rates for NSAD, PUL 2.0, 10MWT, and 10MTT. Safety was assessed.

Results: BBP-418 increased glycosylated α DG 1.8-fold at 3 months, which was sustained at 12 months (both $P < 0.0001$) vs. placebo. CK decreased 82% at Month 12 ($P < 0.0001$). Improvements were observed in 100MTT velocity (+0.14 m/s from baseline; +0.27 m/s vs. placebo; $P < 0.0001$) and FVC (+3% predicted from baseline; +5% predicted vs. placebo; $P = 0.0071$). At Month 12, more participants treated with BBP-418 vs. placebo achieved improvement/stability in NSAD (72.3% vs. 37.5%; $P = 0.0028$), PUL 2.0 (80.0% vs. 53.8%; $P = 0.0224$), 10MWT (86.5% vs. 23.8%; $P < 0.0001$), and 10MTT (81.0% vs. 22.7%; $P < 0.0001$). FVC response rates numerically favored BBP-418. No participants treated with BBP-418 discontinued due to adverse events; serious adverse events were infrequent and balanced.

Conclusions: BBP-418 demonstrated benefit across multiple endpoints with a favorable safety profile, supporting its potential as the first disease-modifying therapy for LGMD2I/R9.

69 - Tanruprubart Monotherapy in Guillain-Barré Syndrome: Early Week 1 Improvement in MRC Sum-Score in FORWARD Study

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Introduction:

Guillain-Barré syndrome (GBS) is a rare, life-altering, neuromuscular emergency where classical complement activation contributes to progressive muscle weakness. Although intravenous immunoglobulin (IVIg) and plasma exchange (PE) are recommended treatments, early clinical progression may still occur and recovery is often incomplete. Tanruprubart is a monoclonal antibody that inhibits C1q, the initiating molecule of the classical complement pathway.

Objective: To describe muscle strength changes through Week 1 in GBS patients treated with tanruprubart in the ongoing FORWARD study.

Method: FORWARD is an open-label, single-arm study of a single intravenous tanruprubart 30 mg/kg dose in recently diagnosed GBS (onset within 10 days; baseline GBS-Disability Score [GBS-DS] 3-5) without prior or planned IVIg/PE. Change in Medical Research Council Sum-Score (MRCss) from baseline through day 7 was summarized.

Results: Among the first 4 treated participants, baseline GBS-DS was 3 in 1 patient and 4 in 3 patients; baseline MRCss ranged from 39 to 53. By Week 1, all patients showed improved muscle strength, with MRCss gains of 7 to 19 points from baseline. Improvement started the day after infusion in all patients. No IVIg/PE was administered during the first week. Tanruprubart was generally well tolerated.

Conclusion: In these initial FORWARD cases, rapid improvement in MRCss was observed by Week 1, following tanruprubart monotherapy. These early findings are consistent with data from the pivotal Phase 3 study conducted in Bangladesh and the Philippines where tanruprubart treatment resulted in highly consistent, rapid improvement. Longer-term and functional outcomes remain important to assess clinical benefit.

70 - Design of a Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study of Adimanebart in Adult and Pediatric Participants with DOK7-, MUSK-, AGRN-, or LRP4-CMS

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Introduction: Congenital myasthenic syndromes (CMS) are caused by mutations at the neuromuscular junction (NMJ) that impair neuromuscular signal transmission, resulting in muscle weakness and fatigability. CMS include subtypes affecting the acetylcholine receptor (AChR)-clustering pathway, such as DOK7-, MUSK-, AGRN-, and LRP4-CMS. Targeting this pathway represents a potential therapeutic approach in CMS. Adimanebart (ARGX-119) is an agonistic monoclonal antibody that targets and activates MuSK to promote AChR clustering, potentially stabilizing the NMJ and improving muscle weakness, fatigability, and performance across daily activities. Positive Phase 1b results in DOK7-CMS support investigation of adimanebart in additional CMS subtypes.

Objectives: To assess efficacy and safety of intravenous (IV) adimanebart in adult and pediatric participants (aged ≥ 12 years) with DOK7-, MUSK-, AGRN-, or LRP4-CMS.

Methods: This Phase 3 global, multicenter, randomized, double-blind, placebo-controlled study comprises a 24-week double-blind treatment period (DBTP) and 104-week open-label extension (OLE). In the DBTP, all participants will be randomized 1:1 to adimanebart IV or placebo IV. Participants who complete the DBTP will continue to the OLE. The study will include ~105 participants.

Results: The primary endpoint is change from baseline in Six-Minute Walk Test (6MWT) distance. Key secondary endpoints include change from baseline in PROMIS Physical Function-10b T-score, Quantitative Myasthenia Gravis Key Component Composite Score, and 6MWT cadence. Safety, tolerability, pharmacokinetics, and immunogenicity will also be assessed.

Conclusion: This Phase 3 study will confirm efficacy and safety of adimanebart IV in adult and pediatric participants with DOK7-, MUSK-, AGRN-, or LRP4-CMS.

73 - Preliminary baseline demographic and safety data from the first-in-human ArthemiR trial of a novel antimiR drug, ATX-01, for the treatment of DM1

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Introduction

ATX-01 is a novel anti-microRNA in clinical development for the treatment of Myotonic Dystrophy (DM). ATX-01 has a dual mechanism of action as a result of the inhibition of miR-23b, a key player in DM1 pathophysiology. In preclinical experiments, ATX-01 increases translation of the important RNA binding protein MBNL and decreases levels of toxic DMPK RNA foci, leading to an improvement in mis-splicing events characteristic of DM1. Preclinical pharmacology demonstrated broad tissue distribution, including to skeletal and cardiac muscle, and to the central nervous system, supporting the potential for ATX-01 to address the multisystemic manifestations of DM1.

Objectives

ArthemiR is a first-in-human randomized, double-blind, placebo-controlled clinical trial to assess the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary clinical efficacy of ascending single and multiple doses of ATX-01 in adult participants with DM1.

Methods

ArthemiR is an integrated single-ascending dose (Part 1) and multiple-ascending dose (Part 2) trial in participants with DM1 aged 18 to 64 years old. Key inclusion criteria include a CTG repeat count of >150 in the DMPK gene, the presence of grip myotonia of >3 seconds, and ability to walk. Key exclusion criteria include congenital DM1, moderate-advanced cardiac disease, and use of anti-myotonia medication. The ArthemiR study is ongoing at 12 sites across Canada, France, Italy, the Netherlands, Spain, the U.K., and the U.S.

Results and Conclusions

Preliminary baseline demographic and safety data from the initial cohorts of the single-ascending dose part (Part 1) of the trial will be presented.

74 - Effect of Subcutaneous Self-Administered Gefurulimab on Ocular Muscle Function in Myasthenia Gravis in the PREVAIL Trial

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Introduction: Gefurulimab, a novel dual-binding nanobody, blocks complement component 5 activation. The phase 3 PREVAIL trial, assessing the efficacy and safety of gefurulimab in adults with anti-acetylcholine receptor antibody-positive (AChR-Ab+) generalized myasthenia gravis (gMG) (NCT05556096), met all primary and secondary endpoints and demonstrated clinically meaningful improvement from baseline in Myasthenia Gravis Activities of Daily Living (MG-ADL) total score at week 26 compared with placebo.

Objective: To evaluate the effect of gefurulimab on ocular symptoms in adults with AChR-Ab+ gMG.

Methods: Adults with AChR-Ab+ gMG were randomized 1:1 to weekly subcutaneous self-administration of gefurulimab or placebo. The primary endpoint was change from baseline in MG-ADL total score at wk26. MG-ADL and Quantitative Myasthenia Gravis (QMG) subdomain scores were assessed.

Results: 260 patients were randomized (gefurulimab: n=131; placebo: n=129). Mean±SD baseline MG-ADL and QMG total scores were 9.0±2.16 and 14.8±4.37, respectively. Improvements in ocular subdomain scores were observed at first assessment after treatment initiation (MG-ADL, wk1; QMG, wk4) and sustained through wk26. Least squares mean±SEM change from baseline at wk26 in MG-ADL and QMG ocular subdomain scores for gefurulimab versus placebo were -1.2±0.14 versus -0.6±0.13 (treatment difference, -0.6±0.19; 95% CI: -1.0, -0.2; $P=0.0016$) and -1.7±0.14 versus -0.9±0.14 (treatment difference, -0.7±0.19; 95% CI: -1.1, -0.4, $P=0.0002$), respectively. Improvements were also observed in other MG-ADL and QMG subdomains. Adverse events were similar between groups; no meningococcal infections were reported.

Conclusion: Gefurulimab, self-administered once weekly via subcutaneous injection, showed early and sustained improvements in MG-ADL and QMG ocular subdomain scores, demonstrating benefits for patients with gMG experiencing ocular symptoms.

75 - Delivering for DMD: Leveraging the FORCE platform to deliver exon skipping oligonucleotides for a broad set of DMD patients

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Introduction

Approved exon skipping therapies for Duchenne muscular dystrophy (DMD) are designed to restore the reading frame of *DMD* transcripts, enabling translation of near-full length, functional dystrophin. Insufficient delivery to muscle and CNS leads to the modest efficacy of these therapies. FORCE was designed to solve delivery of oligonucleotides by leveraging TfR1 biology. Data in *mdx* mice and the zecicent rostudirsen clinical program in exon 51 skip amenable DMD demonstrate that the FORCE platform enhances delivery to muscle, leading to functional improvement.

Objectives

Leverage FORCE to assess skipping of exon 44, 45, 53, or 55 in preclinical cell and mouse DMD models.

Methods

Exon 44, 45, 53, or 55-skipping payloads conjugated using FORCE were evaluated in DMD-relevant cell models. Subsequently, efficacy was evaluated in the hTfR1/hDMD_{WT}/*mdx* mouse. Additionally, a FORCE-PMO was assessed in the DMD relevant hTfR1/hDMD_{Del52}/*mdx* mouse model amenable to exon 53 skipping.

Results

All four FORCE-PMOs induced nearly complete exon skipping in mutant myotubes, including nearly complete skipping of exon 44 at a very low dose. In the hTfR1/hDMD_{WT}/*mdx* mouse, a single dose of FORCE-PMO provided exon skipping in skeletal and cardiac muscle. Repeat dosing of the exon 53 skipping FORCE-PMO in the hTfR1/hDMD_{Del52}/*mdx* mouse led to dystrophin restoration in muscle and localization to the sarcolemma.

Conclusions

Preclinical data support FORCE-PMO delivery of exon skipping and expression of near-full length, functional dystrophin protein. Four development candidates are in the IND-enabling phase and represent opportunities to improve exon skipping therapies for a larger population of people living with DMD.

76 - Global Phase 3 Study to Evaluate the Efficacy and Safety of Telitacicept in Patients with Generalized Myasthenia Gravis (UPSTREAM MG)

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Introduction: Generalized myasthenia gravis (gMG) is an autoimmune disease that affects the postsynaptic membrane of the neuromuscular junction. Current therapies treat the symptoms of gMG through nonspecific immunosuppression or downstream removal of antibodies and inhibition of complement activation.

Telitacicept is a novel TACI-Fc fusion protein that targets B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL) and may reduce B-cell survival and pathogenic antibody production in autoimmune diseases such as gMG.

Data from phase 2 (NCT04302103) and phase 3 (NCT05737160) studies of telitacicept showed efficacy and safety in adults with acetylcholine receptor (AChR) autoantibody-positive gMG.

Objectives: To present the study design of our global, pivotal, phase 3, 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 a confirmed diagnosis of gMG, Myasthenia Gravis Foundation of America (MGFA) class II-IV, Myasthenia Gravis Activities of Daily Living (MG-ADL) score ≥ 6 with $<50\%$ of the total score due to ocular symptoms, and Quantitative MG (QMG) score ≥ 8 , with 4 items having a score ≥ 2 at screening and baseline. After screening, participants will enter a 24-week, double-blind, placebo-controlled phase with 1:1 randomization to either placebo or telitacicept subcutaneous weekly, followed by an OLE period. The primary outcome is the mean change from baseline in MG-ADL score at week 24.

Results: Study enrollment is currently ongoing.

Conclusions: This study will assess the efficacy, safety, and pharmacokinetics/pharmacodynamics of telitacicept in adult patients with gMG.

77 - Reduced Clinical Deteriorations and Healthcare Resource Utilization After Switching from Efgartigimod to Ravulizumab in Patients with Generalized Myasthenia Gravis in the United States

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Introduction: Generalized myasthenia gravis (gMG) remains suboptimally controlled in patients receiving conventional immunosuppressants and oral corticosteroids (OCS). Efgartigimod (FcRn-antagonist) and ravulizumab (C5-inhibitor) have distinct mechanisms of action, and may be switched in clinical practice when symptoms, exacerbations, or dependence on OCS persist. Real-world evidence evaluating outcomes during these transitions remains limited.

Objective: Estimate clinical deteriorations and healthcare-resource-utilization (HCRU) in patients with anti-acetylcholine-receptor-antibody-positive gMG who switched from efgartigimod to ravulizumab.

Methods: A retrospective cohort study of adults with gMG who transitioned from efgartigimod to ravulizumab was conducted using Veeva Compass US claims data. Outcomes: gMG exacerbations, OCS dose escalations, HCRU endpoints. Incidence rates compared across three periods: conventional therapy ("baseline"), efgartigimod (pre-switch), and ravulizumab (post-switch). Multivariable-adjusted generalized estimating equations to estimate incidence-rate-ratios (IRRs).

Results: 107 eligible patients with median follow-up of 19, 13, and 14 months during baseline, efgartigimod, ravulizumab periods, respectively. After initiation of efgartigimod, there were no differences versus baseline in rates of MG exacerbation (IRR=0.63 [0.33-1.19]; p=0.152) or OCS dose escalation (IRR=1.09 [0.81-1.47]; p=0.561). After switching from efgartigimod to ravulizumab, gMG exacerbation rates decreased by 60% (IRR=0.40 [0.20-0.80]; p=0.009); OCS dose escalation rates decreased by 55% (IRR=0.45 [0.31-0.65]; p<0.001). There were similar reductions for Emergency Department visits and total inpatient days. Neurology outpatient visits increased by 38% during the efgartigimod period (IRR=1.38 [1.06-1.80]; p=0.018) followed by a 63% reduction after switching to ravulizumab (IRR=0.37 [0.28-0.48]; p<0.001).

Conclusions: In patients with gMG, switching from efgartigimod to ravulizumab was associated with reduced clinical deteriorations and HCRU. These findings suggest complement inhibition with ravulizumab may reduce disease burden and HCRU.

79 - Safety Analysis Following Real World Use of Delandistrogene Moxeparvovec for Duchenne Muscular Dystrophy (DMD): Interim Analysis of the Phase 4 ENDURE Study

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Introduction

The US, Phase 4, observational ENDURE study (NCT06270719) measures the effectiveness and safety of delandistrogene moxeparvovec versus standard of care (SOC).

Objectives

In this planned interim analysis, patient characteristics, adverse events (AEs), and the impact of prophylactic immunosuppression on acute liver injury (ALI) are described among participants receiving delandistrogene moxeparvovec.

Methods

Participants were enrolled after the clinical decision to initiate delandistrogene moxeparvovec or if they were receiving SOC. Baseline characteristics, AEs, and adjudicated treatment-related ALI stratified by prophylactic immunosuppressant use are descriptively reported.

Results

Fifty-six delandistrogene moxeparvovec-treated participants (45 baseline ambulatory [mean age 9.4 years], 11 non-ambulatory [mean age 16.0]) and 24 SOC participants (all ambulatory [mean age 9.9]) were enrolled (02/2024-02/2026). Vomiting (30.4%; 17/56) and nausea (25.0%; 14/56) were the most frequent treatment-related AEs among treated participants. Treatment-related ALI occurred in 9/56 (16.1%) treated participants (ranging 33-53 days post-infusion), 7 (12.5%) of which were serious (5 ambulatory, 2 non-ambulatory). Eleven treated participants received prophylactic immunosuppression (all sirolimus; initiation ranging 43 days pre-infusion to 14 days post-infusion [before any ALI signs/symptoms]). No ALI cases were observed in treated participants who received prophylactic sirolimus. Two deaths occurred in treated participants, one from acute liver failure (previously disclosed; treatment-related) and one from empyema 8 months post-treatment (unrelated).

Conclusion

There were no new safety findings in this interim analysis of ENDURE. ALI frequency was consistent with prior disclosures. Preliminary findings of prophylactic sirolimus in a limited number of patients suggest protection against ALI; however, ongoing evaluation is warranted.

81 - Baseline Glycolipid IgG Autoantibodies in GBS are Prevalent and Show Cross-Regional Pattern Concordance

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Introduction: Guillain-Barré syndrome (GBS) is an acute, immune-mediated polyradiculoneuropathy resulting in mild weakness to severe paralysis. Autoantibodies target peripheral nerve glycolipids, triggering complement activation, neuroinflammation, and axonal damage. Diverse antibody reactivity patterns underlie the spectrum of phenotypes e.g. acute motor axonal neuropathy (AMAN) and acute inflammatory demyelinating polyneuropathy (AIDP). Recent studies highlight the mechanistic and clinical significance of these complex profiles, emphasizing the need to define antibody-driven disease biology to guide therapies addressing GBS presentations and outcomes.

Objective: Investigate underlying autoantibody patterns in GBS.

Methods: Baseline serum samples from patients with GBS (n=239) in a Phase 3 trial with tanruprubart (GBS-02), conducted in Bangladesh and the Philippines, and an independent US cohort (n=142) were analyzed. Autoantibody profiling was performed using a harmonized glycolipid microarray.

Results: IgG reactivity to glycolipids/complexes was found in >90% of GBS-02 participants. High-abundance/high-affinity IgG signatures were observed in both cohorts, with broad reactivity to GM1, GD1b, GT1a, GD1a, and/or GalNAc-GD1a. The broad, predominant reactivity pattern was present in 51% of GBS-02 participants and 90% of the US cohort. Although frequencies differed across regions, antigen-specific features were concordant. In GBS-02, AMAN (54%), AIDP (28%), and equivocal electrophysiologic subtypes (18%) were observed in the predominant broad reactivity pattern. US cohort electrophysiologic data were unavailable.

Conclusions: Autoantibodies to glycolipids/complexes were detected in most patients. Data from the pivotal Phase 3 population suggests that key baseline IgG reactivity patterns are shared across regions, supporting the external relevance of the enrolled population. Further studies are warranted.

82 - PROMIS Parent Proxy Mobility Scores in Patients Treated with Delandistrogene Moxeparvovec in EMBARK Part 2 Compared with External Controls

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Introduction: Duchenne muscular dystrophy (DMD) causes progressive muscle weakness, leading to ambulatory function loss. Patient- or caregiver-reported outcomes provide meaningful insight into disease progression to help evaluate a treatment's ability to slow functional decline.

Objectives: This study compared changes in Patient-Reported Outcomes Measurement Information System Parent Proxy Mobility scores (PROMIS Mobility) in patients with DMD treated with delandistrogene moxeparvovec in Part 2 of the EMBARK (NCT05096221) trial to external controls (ECs) treated at Nationwide Children's Hospital.

Methods: Inverse probability of treatment weighting was used to adjust for non-randomized treatment assignment and baseline differences between delandistrogene moxeparvovec-treated and EC groups. Rate of change in PROMIS Mobility mean raw score was evaluated across groups using a linear mixed-effects model. An exploratory analysis assessed the proportion of patients from each group that reached a meaningful improvement in PROMIS Mobility, defined using EMBARK Part 1 data with anchor-based methods.

Results: Patients treated with delandistrogene moxeparvovec (n=60; mean [SD] baseline age=7.18 [1.06]) had a nominally significant and clinically meaningful slower PROMIS Mobility rate of decline versus ECs (n=25; mean [SD] baseline age=6.97 [1.15]; difference in linear mixed-effects model slope, 0.281; 95% CI, 0.041-0.520; $P=0.022$). A Kaplan-Meier analysis showed meaningful PROMIS Mobility improvement events occurred earlier in patients treated with delandistrogene moxeparvovec and more frequently (48% [29/60] versus 12% [3/25]; log-rank $P=0.0246$).

Conclusions: Patients treated with delandistrogene moxeparvovec experienced a nominally significant slower change in PROMIS Mobility and more improvement events versus ECs, consistent with earlier findings and further demonstrating its potential to slow disease progression.

86 - Effect of zilucoplan stratified by age of myasthenia gravis onset: RAISE-XT 120-week post hoc analysis

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Introduction:

RAISE-XT (NCT04225871), a Phase 3 open-label extension study, demonstrated sustained improvements in myasthenia gravis (MG)-specific outcomes in patients with generalized MG (gMG) during zilucoplan treatment up to Week 120.

Objective:

To evaluate the efficacy of zilucoplan by age of gMG onset.

Methods:

In RAISE-XT, adults with gMG who completed RAISE (double-blind; NCT04115293) self-administered daily subcutaneous zilucoplan 0.3 mg/kg. Change from double-blind baseline (CFB) in efficacy outcomes to Week 120 and safety were evaluated post hoc (cut-off: 11 November 2023) in early (≤ 50 years) and late (> 50 years) age-of-onset subgroups.

Results:

Mean (standard deviation) age (early onset [N=106] and late onset [N=77]) was 43.9 (12.4) and 66.2 (5.6) years. At Week 120, mean (standard error) CFB (early versus late) was: MG Activities of Daily Living, -7.47 (0.53) versus -6.66 (0.75); Quantitative MG, -10.14 (0.77) versus -9.39 (1.15); MG Quality of Life 15-item revised, -12.55 (1.18) versus -7.68 (1.73); Quality of Life in Neurological Disorders Short Form Fatigue, -11.34 (1.61) versus -9.65 (2.22). Serious and treatment-related treatment-emergent adverse events occurred in 34.0% (n/N=36/106) and 38.7% (n/N=41/106) of patients (early subgroup) and 49.4% (n/N=38/77) and 33.8% (n/N=26/77) of patients (late subgroup), respectively.

Conclusions:

Zilucoplan demonstrated long-term efficacy irrespective of age at gMG onset.

88 - Response to Rozanolixizumab Across Treatment Cycles in Patients with Generalized Myasthenia Gravis: A Post Hoc Analysis of Final Pooled Phase 3 Data

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Introduction:

In MycarinG (Phase 3, NCT03971422), one cycle of six once-weekly subcutaneous rozanolixizumab (7mg/kg or 10mg/kg) infusions demonstrated clinically relevant improvements in MG-specific outcomes versus placebo. Patients could subsequently enroll in open-label extension studies MG0004 (NCT04124965), then MG0007 (NCT04650854), or MG0007 directly.

Objective:

To evaluate response to rozanolixizumab over multiple treatment cycles in patients with generalized myasthenia gravis (gMG), based on Cycle 1 responder status.

Methods:

In MG0004, patients received chronic once-weekly rozanolixizumab (7 mg/kg or 10 mg/kg) for ≤52 weeks. In MG0007, after an initial cycle of rozanolixizumab 7 mg/kg or 10 mg/kg, subsequent cycles were administered at the investigator's discretion. Data were pooled across MycarinG, MG0004 (first 6 weeks), and MG0007 (final data) for patients with ≥2 symptom-driven cycles. MG Activities of Daily Living (MG-ADL) responders (≥2-point improvement) and Quantitative MG (QMG) responders (≥3-point improvement) at Day 43 of each cycle were assessed. *Post hoc* analyses were conducted by Cycle 1 responder status.

Results:

Overall, 129 patients had ≥2 symptom-driven cycles. In Cycle 1, 74.4% (96/129) were MG-ADL responders and 68.2% (88/129) were QMG responders at Day 43. Among MG-ADL responders, response rates remained consistent across subsequent cycles (74.4% to 88.2% up to Cycle 13). Among QMG responders, rates ranged from 61.0% to 83.3% up to Cycle 13. Among MG-ADL non-responders, 63.6% (21/33) became responders at Cycle 2. Among QMG non-responders at Cycle 1, 50.0% (20/40) became responders at Cycle 2.

Conclusions:

Cycle 1 responders had broadly consistent response rates in subsequent cycles of rozanolixizumab. Non-responders may benefit from additional treatment cycles.

89 - Update on the INSPIRE DUCHENNE Phase 1/2 Study of the Next-Generation Microdystrophin Gene Therapy Candidate SGT-003 for Duchenne Muscular Dystrophy

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Introduction

SGT-003 is a next-generation AAV-based microdystrophin gene therapy candidate that uses a novel muscle-tropic capsid, POLARIS-101™ (formerly known as AAV-SLB101), to deliver a functional replacement for dystrophin. This capsid was designed to improve muscle targeting compared to first-generation capsids. SGT-003 microdystrophin includes the R16/R17 nNOS binding domain, enabling stabilization of the muscle membrane and restoration of local signaling pathways.

Objectives

INSPIRE DUCHENNE is a Phase 1/2, open-label, first-in-human trial designed to evaluate the safety, tolerability, and efficacy of SGT-003 in participants with Duchenne muscular dystrophy.

Methods

Safety and tolerability were assessed through adverse event monitoring. Muscle biopsy analyses were conducted to evaluate vector transduction and microdystrophin expression, and biomarkers of muscle integrity were measured over time.

Results

As of May 12, 2026, 47 total participants received SGT-003 across an age range of 1 to 10 years. Treatment has been generally well tolerated, with the most frequent treatment-related adverse events including nausea, vomiting, and decreased appetite. As of a data cutoff of February 23, 2026, robust transduction and microdystrophin expression were observed in Day 90 muscle biopsies (n=17-20 per method), with means of 11 vector copies per nucleus, 60% of normal expression, and 63% positive fibers. Biomarkers of muscle integrity all demonstrated consistent improvements at Day 90 and were sustained through Day 360 post-dosing.

Conclusions

SGT-003 has demonstrated a favorable safety profile and evidence of robust microdystrophin expression, with associated improvements in biomarkers of muscle integrity. These findings support a positive biological impact of SGT-003 treatment in participants with Duchenne.

90 - SGT-003 gene therapy stabilizes the DAPC and improves muscle integrity in Duchenne muscular dystrophy

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Introduction

Duchenne muscular dystrophy is caused by the absence of functional dystrophin, leading to destabilization of the dystrophin-associated protein complex (DAPC), compromised sarcolemmal integrity, and myofiber degeneration. Persistent muscle injury results in elevated serum biomarkers of membrane damage and, in muscle, increased expression of embryonic myosin heavy chain (eMHC), a marker of active degeneration/regeneration.

Objectives

SGT-003, Solid Biosciences' next-generation AAV microdystrophin gene therapy, was evaluated for its ability to restore DAPC integrity and improve muscle health.

Methods

Sarcolemmal localization of DAPC components were assessed in muscle biopsies obtained pre- and post-treatment with SGT-003. An extensive range of muscle integrity biomarkers including serum CK and titin fragments were quantified as biomarkers of sarcolemmal damage. eMHC expression was measured to assess active muscle degeneration/regeneration cycling.

Results

Treatment with SGT-003 resulted in robust sarcolemmal localization of all sarcoglycans and enzymatically active nNOS, consistent with reconstitution of the DAPC. These changes were accompanied by improvements in biomarkers of muscle integrity including reductions in serum CK and titin fragments. Importantly, a marked decrease in eMHC-positive fibers was observed, indicating protection from myofiber necrosis and regenerative cycling.

Conclusions

SGT-003 demonstrated compelling biological evidence of functional microdystrophin activity, including restoration of the DAPC, enhanced sarcolemmal integrity, and attenuation of chronic muscle injury. The reduction in eMHC suggests protection from the pathological degeneration/regeneration loop that drives disease progression in Duchenne. Together, these findings underscore the potential of SGT-003 to meaningfully alter the disease trajectory in Duchenne muscular dystrophy.

91 - PIERRE Clinical Trial Update: Safety and Performance of ThecaFlex DRx™ for Repeated Intrathecal Delivery of Nusinersen

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Neurological therapeutics often require intrathecal (IT) dosing via lumbar puncture (LP). Use may be constrained by contraindications and barriers, including complex spinal anatomy and procedural anxiety. Repeated LPs add cumulative burden and increase exposure to radiation and anesthesia, limiting tolerability. These challenges highlight the need for alternative IT delivery approaches that reduce procedural complexity and burden. The ThecaFlex DRx™ System is an implantable subcutaneous port and IT catheter designed to expand access to patients requiring repeated LP by providing an easier approach to CSF sampling and therapeutic delivery.

PIERRE (NCT05866419) is an ongoing study assessing implantation and infusion success, along with safety, following ThecaFlex implantation and nusinersen administrations.

As of March 2026, 42 participants underwent device implantation. ThecaFlex was successfully implanted in all attempted participants (100%) with no device implantation failures. Nusinersen administration via device was attempted in 39 of 42 participants, consistent with the dosing schedule as of March 30, with successful delivery in 34/39 attempted participants (87.2%). The safety profile remained consistent with earlier findings, with no deaths or unanticipated adverse device effects observed. Additional data from the March 2026 study synopsis, including a larger cohort and longer follow-up, will be presented to further characterize safety and performance.

Preliminary results suggest acceptable safety and support the feasibility of this unique implantable device for repeat IT therapy delivery in patients with SMA. ThecaFlex may improve the patient experience of repeat IT drug administration and may be clinically useful to utilize with other neurological therapeutics.

93 - Comparing Longitudinal Treatment-related Adverse Risks of Infection in Generalized Myasthenia Gravis

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Introduction: Myasthenia gravis (MG) is a neuromuscular disorder characterized by fluctuating muscle weakness. Approved biologic options for generalized MG (gMG) include complement inhibitors (e.g., ravulizumab) and FcRn antagonists (e.g., efgartigimod), while B-cell-targeted agents (e.g., rituximab) are used off-label. While safety of these approved agents has been characterized in clinical trials, additional real-world evidence is needed to evaluate longer-term infection risks.

Objective: The objective of this study is to estimate and compare the real-world infection rates associated with gMG treatments.

Methods: This study was a retrospective longitudinal cohort study of patients with MG initiating ravulizumab, efgartigimod, rozanolixizumab, or rituximab using the Veeva Compass claims database from January 2017 to August 2025. Generalized estimating equations was used to compare annual infection rates across cohort, with adjustment for known and suspected confounders.

Results: Of 1,515 patients, 689 (46.1%) initiated rituximab, 555 (36.6%) efgartigimod, 218 (14.4%) ravulizumab, and 53 (3.5%) rozanolixizumab. After confounder adjustment, both efgartigimod and rituximab showed statistically significantly higher infection rates versus ravulizumab-efgartigimod by 47% (IRR=1.47, 95% CI: 1.17-1.84, p<0.001) and rituximab by 46% (IRR=1.46, 95% CI: 1.23-1.72, p<0.001). Rozanolixizumab suggested a similar trend but was underpowered to detect differences due to small sample size (IRR=1.34, 95% CI: 0.85-2.11, p=0.208).

Conclusions: This study observed lower infection rates in patients receiving ravulizumab compared to those receiving other biologic therapies for gMG. Understanding real-world, long-term infection risk profiles for these drugs could help inform treatment decisions for MG, particularly for patients at higher risk of infection or infection-related complications.

98 - Clinical Relevance of Minimal Symptom Expression (MSE) in Efgartigimod-Treated Patients with Generalized Myasthenia Gravis (gMG)

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Introduction: Minimal Symptom Expression (MSE; MG-ADL 0-1) has emerged as a patient-centric treatment goal in gMG and has been reported in efgartigimod-treated patients. Additional evidence is needed to evaluate long-term symptom trajectories following MSE achievement and whether MSE reflects meaningful gains in quality of life (QoL) and clinician-assessed outcomes.

Objectives: To evaluate MG-ADL trajectories in efgartigimod-treated patients by MSE status and assess associations with QoL and clinician-assessed outcomes.

Methods: *Post-hoc* analyses pooled AChR-Ab+ patients across ADAPT/ADAPT+, ADAPT-SC/ADAPT-SC+, and ADAPT-NXT. Cumulative MSE attainment and time to first MSE were summarized. MG-ADL trajectories were standardized to 4-week intervals using the lowest score per interval. Concurrent associations between MSE and MG-QoL15r, EQ-5D utility, Quantitative Myasthenia Gravis (QMG), and Myasthenia Gravis Composite (MGC) scores were assessed using linear mixed-effects models.

Results: Among 225 efgartigimod-treated participants, 132 (58.7%) achieved MSE, with a median time to first MSE of 1.2 months. With continued efgartigimod treatment, achievers sustained low disease burden over ~3 years, while non-achievers also experienced sustained, clinically meaningful MG-ADL improvements exceeding the minimal clinically important difference. Estimated concurrent mean scores were significantly better during MSE versus non-MSE intervals: EQ-5D utility (0.84 vs. 0.71), MG-QoL15r (7.03 vs. 10.86), QMG (7.48 vs. 11.95) and MGC (5.48 vs. 13.40) (all $p < 0.001$).

Conclusions: MSE is achieved early following efgartigimod and is associated with sustained low disease burden and QoL scores approaching healthy population. Patients not achieving MSE still derive meaningful benefit, supporting MSE as an aspirational - but not exclusive - treatment target in gMG.

99 - Alglucosidase Alfa to Avalglucosidase Alfa Switch Improves Biomarkers in Infantile-Onset Pompe Disease: Pompe Registry Analysis

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Introduction: Avalglucosidase alfa (Ava), approved for infantile-onset (IOPD) and/or late-onset Pompe disease, contains bis-mannose-6-phosphate, improving cellular uptake and clinical efficacy.

Objectives: This analysis describes outcomes in patients with IOPD from the Pompe Registry (NCT00231400) who switched from Alg (≥ 1 -year) to Ava (≥ 3 -months).

Methods: Registry data were analyzed to estimate annual changes in creatine kinase, alanine aminotransferase, aspartate aminotransferase (CK, ALT, AST, U/L), and urine hexatetrasaccharide (Hex4, mmol/mol creatinine) using linear mixed models during the last 5 years of Alg and first 3.5 years of Ava. Results were stratified by last Alg dose (label-dose: ~20 mg/kg EOW, or high-dose: ~40 mg/kg EOW, ~20 or ~40 mg/kg weekly).

Results: 47 patients with IOPD (49% male) were included. Median ages at Alg and Ava initiation were 0.6 and 8.5 years, respectively, and median time on Ava was 2.2 years. Before switching, 66% received high-dose Alg, and 87% started Ava at 40 mg/kg EOW.

In label-dose Alg patients, CK, Hex4, ALT, and AST significantly increased on Alg and significantly decreased on Ava (differences in pre vs. post slopes all; $P < 0.0001$). In high-dose Alg patients, CK, ALT, and AST decreased during both treatments, with a significantly greater rate of decrease on Ava (differences in pre vs. post slopes; all $P < 0.0001$). Hex4 remained elevated/stable in high-dose Alg patients but decreased significantly after switching to Ava (difference in slopes $P < 0.0001$).

Conclusions: Patients with IOPD showed improved CK, Hex4, ALT, and AST trajectories after switching to Ava, regardless of their Alg dose prior to the switch.

105 - Efficacy and cumulative safety of cemdisiran in adults with generalized myasthenia gravis (gMG): Results from the phase 3 NIMBLE trial

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Introduction: Autoantibody-mediated terminal complement activation damages neuromuscular junctions in gMG, resulting in fatigable muscle weakness.

Objectives: The phase 3 NIMBLE trial evaluated cemdisiran (siRNA inhibiting hepatic C5 production) as subcutaneous monotherapy or in combination with pozelimab (monoclonal antibody targeting C5) in participants with gMG.

Methods: In this double-blind, placebo-controlled trial, 288 participants with gMG were randomized to cemdisiran monotherapy (600 mg Q12W), pozelimab monotherapy (200 mg Q4W), combination (both 200 mg Q4W), or placebo. We present key results (based on database lock on July 8, 2025) for the primary efficacy endpoint, change from baseline in MG-ADL total score at Week 24 (n=239), terminal complement inhibition, and the rate of TEAEs (n=277).

Results: NIMBLE met its primary endpoint. In the cemdisiran (n=64) and combination (n=67) arms, the least-squares mean (SE) change from baseline at Week 24 in MG-ADL was -4.5 (0.4) and -4.0 (0.4), with placebo-adjusted differences of -2.3 (P=0.0005) and -1.7 (P=0.0086), achieving 76.6% (n=60) and 99.6% (n=66) terminal complement inhibition, respectively. TEAEs occurred in 69% (54/78), 82% (40/49), 81% (65/80), and 77% (54/70) of participants in the cemdisiran, pozelimab, combination, and placebo arms, respectively. No meningococcal or serious infections occurred in the cemdisiran arm during the double-blind treatment period (DBTP); SAEs of infections in other arms were low. There were 2 deaths (pneumonia [cemdisiran], septic shock [combination]) after the DBTP in participants on concomitant immuno-suppressive therapies with comorbidities.

Conclusions: Quarterly, subcutaneous cemdisiran was generally well-tolerated, with rapid, sustained symptom improvement following partial complement inhibition in participants with gMG.

109 - Impact of Time Since Diagnosis on Efficacy of Inebilizumab: A Post Hoc Analysis of Phase 3 Myasthenia Gravis Inebilizumab Trial (MINT) Data

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Introduction: The MINT study (NCT04524273) met its primary endpoint (Myasthenia Gravis Activities of Daily Living [MG-ADL]), demonstrating the efficacy of inebilizumab in the AChR⁺ and MuSK⁺ seropositive patients with generalized myasthenia gravis (gMG).

Objectives: To determine if response to inebilizumab differs by time since the diagnosis of gMG in the MINT phase 3 trial.

Methods: Patients (AChR⁺ or MuSK⁺) underwent a protocol-specified glucocorticoid taper to ≤ 5 mg/day and were randomized 1:1 to 300 mg inebilizumab or placebo for 26 (MuSK⁺) or 52 (AChR⁺) weeks. Changes from baseline (CFBs) in MG-ADL and Quantitative Myasthenia Gravis (QMG) scores by time since diagnosis were examined.

Results: Overall, 238 patients (AChR⁺, 190; MuSK⁺, 48) were enrolled and randomized to inebilizumab or placebo. The least squares mean (LSM) CFB in MG-ADL score was numerically greater for inebilizumab versus placebo at week 26 for patients with time since diagnosis of <1 year (-5.4 vs. -3.0), ≥ 1 -<4 years (-4.3 vs. -1.8), and ≥ 4 years (-3.7 vs. -2.5); the LSM CFB in QMG score was also numerically greater for inebilizumab versus placebo at week 26 (-5.2 vs. -4.0; -6.4 vs. -2.2; -4.0 vs. -1.9, respectively). Improvements from baseline with inebilizumab versus placebo were observed at week 52 for MG-ADL (AChR⁺: -5.7 vs. -2.3, -5.0 vs. -2.7, -4.0 vs. -1.5, respectively) and QMG (AChR⁺: -7.4 vs. -1.8, -8.3 vs. -2.9, -3.9 vs. -0.5, respectively) scores.

Conclusions: Efficacy of inebilizumab appears independent of time since diagnosis, although the small size of subgroups limits firm conclusions.

110 - Myasthenia Gravis Inebilizumab Trial (MINT): Adverse Events of Special Interest During the Randomized Controlled Period

Richard J. Nowak¹, Kimiaki Utsugisawa², Michael Benatar³, Emma Cifaloni⁴, Maria Isabel Leite⁵, John Vissing⁶, Fengming Tang⁷, Blanca Canales⁷, Qing Li⁷, Sue Cheng⁷, James F. Howard Jr.⁸

¹Yale University, New Haven, CT, USA, ²Hanamaki General Hospital, Hanamaki, Japan, ³University of Miami Miller School of Medicine, Miami, FL, USA, ⁴University of Rochester, Rochester, NY, USA, ⁵University of Oxford, Oxford, UK, ⁶University of Copenhagen, Copenhagen, Denmark, ⁷Amgen Inc., Thousand Oaks, CA, USA, ⁸University of North Carolina, Chapel Hill, NC, USA

Introduction: B cells play a key upstream mechanistic role in autoimmune generalized myasthenia gravis (gMG) pathogenesis through the production of antibodies targeting the acetylcholine receptor (AChR⁺), muscle-specific kinase (MuSK⁺), or other related proteins. Inebilizumab is a monoclonal antibody targeting CD19⁺ B cells.

Objectives: To examine whether inebilizumab is associated with an increased risk of adverse events of special interest (AESIs) in participants with gMG.

Methods: MINT (NCT04524273) was a phase 3 trial in adults with gMG. During the randomized controlled period (52 weeks for AChR⁺; 26 weeks for MuSK⁺), participants were randomized (1:1) to receive inebilizumab 300 mg or placebo on Day-1, Day-15, and Day-183 (AChR⁺ only). Subsets of adverse events were identified as AESIs due to their relevance to inebilizumab's mechanism of action.

Results: A total of 238 participants were randomized to receive inebilizumab 119 (95 AChR⁺, 24 MuSK⁺) and placebo 119 (95 AChR⁺, 24 MuSK⁺). Baseline demographics and disease characteristics were balanced between the two treatment groups. AESIs were infrequent, occurring in 10.1% (n=12) of the inebilizumab- and 16% (n=19) of the placebo-treated group. Cytopenias occurred in 2.5% (n=3) of inebilizumab-treated and 9.2% (n=11) of placebo-treated participants. Serious and/or opportunistic infections were infrequent (inebilizumab: 3.4% [n=4]; placebo: 5.0% [n=6]), with COVID-19 being the most common (inebilizumab: 2/4; placebo: 3/6) and no instances of progressive multifocal leukoencephalopathy. Infusion related reactions occurred in 5.0% (n=6) of the inebilizumab- and 2.5% (n=3) of placebo-treated participants.

Conclusions: These results support a favorable safety profile of inebilizumab over a 26-52-week period.

113 - Real-world safety profile of delandistrogene moxeparvovec in the US postmarketing setting

Vannary Pizzo¹, Preeti Singh¹, Damon Asher¹, Randal Richardson²

¹Sarepta Therapeutics, Inc., Cambridge, MA, USA, ²Gillette Children's, St. Paul, MN, USA

Introduction: Delandistrogene moxeparvovec, an rAAVrh74 vector-based gene therapy approved in the US, slows Duchenne muscular dystrophy progression in ambulatory patients. Clinical studies demonstrated the safety and tolerability of delandistrogene moxeparvovec to be manageable with appropriate monitoring and treatment of adverse events (AEs), typically occurring within 90 days post-infusion.

Objectives: Evaluate real-world postmarketing safety of delandistrogene moxeparvovec from commercially-treated patients in the US.

Methods: Patients who experienced AEs were identified from the Sponsor's (Sarepta Therapeutics) safety database (cutoff: 2 November 2025).

Results: This analysis included 715 patients (n=338 [4-7 years]; n=377 [>7 years]). Most common treatment-related treatment-emergent AEs ($\geq 15\%$ [events/total exposure]) were vomiting (n=141 [19.7%]), nausea (n=139 [19.4%]), and liver injury (n=132 [18.5%]). There were 57 (7.9%) events of serious acute liver injury (ALI) reported and 50 (7.0%) hospitalizations due to ALI. Serious ALI frequency and hospitalizations were similar in patients aged 4-7 and >7 years (n=26 [7.7%] vs. n=30 [8.0%] and n=23 [6.8%] vs n=26 [6.9%], respectively). One event (0.1%) of acute liver failure was reported (previously disclosed, resulting in death). Other treatment-related serious AEs included myocarditis (n=5), immune-mediated myositis (n=2), and infusion-related reactions (n=2). Limitations include incomplete, biased or under-reporting, and difficulties in attributing causality.

Conclusions: Overall safety of delandistrogene moxeparvovec in a large population of US commercially-treated patients is consistent with clinical trial results to date. Frequency of serious ALI and hospitalizations was comparable in patients aged 4-7 and >7 years, highlighting similar safety and tolerability in younger and older ambulatory patients.

124 - Indirect Treatment Comparisons of Nusinersen Versus Intrathecal Onasemnogene Abeparvovec-brve in Treatment Naïve, Later-Onset Spinal Muscular Atrophy Patients

Camilla Woodsmith¹, Jessica Owen¹, Kurt Taylor¹, Xiaomeng Liao¹, Philipp Arnold², Nadia Tavares², Chrysanthé Peteros², Dajun Tian², Catherine Mak²

¹Petauri Evidence, ²Biogen

Introduction

Nusinersen is the first approved treatment for spinal muscular atrophy (SMA) - a severe rare neuromuscular disorder causing progressive motor neuron decline and eventual death. Intrathecal onasemnogene abeparvovec-brve (OAV101 IT) is a recently approved gene therapy for SMA. In the absence of head-to-head trials comparing nusinersen with OAV101 IT, indirect treatment comparisons can estimate comparative efficacy.

Objectives

This analysis compared the efficacy of nusinersen (CHERISH (NCT02292537), DEVOTE Part B (NCT04089566)), with OAV101 IT, using data from STEER (NCT05089656), in treatment naïve, later-onset SMA patients.

Methods

Anchored matching-adjusted indirect comparisons (MAIC) compared CHERISH data to STEER in participants aged 2 to <5 years. DEVOTE Part B and STEER were compared using unanchored MAIC. Comparative efficacy was assessed using change from baseline (CFB) in Hammersmith Functional Motor Scale-Expanded (HFMSE) and Revised Upper Limb Module (RULM). Reduced effective sample sizes following weighting limited statistical power.

Results

Month 12 (CHERISH)/Week 52 (STEER) results numerically favored nusinersen 12 mg in improved CFB compared to OAV101 IT in both HFMSE (mean difference [MD]: 1.86; 95% confidence intervals [CI]: -1.08, 4.80; effective sample size [ESS]/starting sample [N]: 58.2/97) and RULM (MD: 1.52; CI: -0.57, 3.61; ESS/N: 58.2/97). After MAIC weighting, the DEVOTE Part B (nusinersen 28 mg) versus STEER (OAV101 IT) comparison was not feasible.

Conclusions

Nusinersen may be associated with numerically greater improvements in functional outcomes compared to OAV101 IT in treatment-naïve, later-onset SMA patients. As CHERISH evaluated a lower 12-month cumulative dose (48 mg) than the licensed regimens (72 mg or 156 mg), observed results may underestimate its full efficacy.

125 - Indirect Treatment Comparison of Nusinersen 50/28 mg Versus Intrathecal Onasemnogene Apeparvovec-brve in Treatment Experienced Spinal Muscular Atrophy Patients

Camilla Woodsmith¹, Jessica Owen¹, Kurt Taylor¹, Xiaomeng Liao¹, Philipp Arnold², Nadia Tavares², Chrysanthé Peteros², Dajun Tian², Catherine Mak²
¹Petauri Evidence, ²Biogen

Introduction

Nusinersen is the first approved treatment for spinal muscular atrophy (SMA) - a severe rare neuromuscular disorder causing progressive motor neuron decline and eventual death. Intrathecal onasemnogene abeparvovec-brve (OAV101 IT) is a recently approved gene therapy for SMA, and nusinersen 50/28 mg was also recently approved for SMA. In absence of head-to-head trials, indirect treatment comparisons can estimate comparative efficacy.

Objectives

This analysis compared the efficacy of high dose nusinersen (50/28 mg) with OAV101 IT using data from DEVOTE Part C (NCT04089566) and STRENGTH (NCT05386680) in treatment-experienced SMA patients.

Methods

The DEVOTE Part C population was trimmed to sitting, non-ambulatory, <18 years-old participants for alignment with STRENGTH, following which an unanchored matching-adjusted indirect comparison was conducted. Comparative efficacy was assessed using Hammersmith Functional Motor Scale-Expanded (HFMSE) and Revised Upper Limb Module (RULM) change from baseline (CFB) at Week 42 and last observation (Week 52) in STRENGTH compared with Day 302 (DEVOTE). Reduced effective sample sizes following weighting limited statistical power.

Results

From week 42 onwards, nusinersen showed numerically greater improvements in HFMSE and RULM than OAV101 IT. Mean differences (nusinersen vs OAV101 IT) at Week 42 were 0.48 (95% confidence intervals [95%CI]: -2.26, 3.22) for HFMSE and 1.85 (95%CI: -2.18, 5.88) for RULM; and at Week 52 were 1.28 (95%CI: -1.19, 3.75) for HFMSE (effective sample size [ESS]/starting sample [N]: 4.3/10) and 1.90 (95%CI: -2.10, 5.91) for RULM (ESS/N: 6.1/10).

Conclusions

In treatment-experienced patients, findings suggest that high dose nusinersen may be associated with greater functional improvements compared to OAV101 IT.

126 - Interim 1-Year Open-Label Results from the Myasthenia Gravis Inebilizumab Trial (MINT)

Richard J. Nowak¹, Michael Benatar², Maria Isabel Leite³, Emma Ciafaloni⁴, Kimiaki Utsugisawa⁵, Sarah Bray⁶, Kristina Patterson⁷, Ankur Bhambri⁷, Arati Kiran Kanchi⁷, Sue Cheng⁷, John Vissing⁷, James F. Howard Jr.⁸

¹Yale University, New Haven, CT, USA, ²University of Miami Miller School of Medicine, Miami, FL, USA, ³University of Oxford, Oxford, UK, ⁴University of Rochester, Rochester, NY, USA, ⁵Hanamaki General Hospital, Hanamaki, Japan, ⁶Amgen Ltd., Cambridge, UK, ⁷Amgen Inc., Thousand Oaks, CA, USA, ⁸University of North Carolina, Chapel Hill, NC, USA

Introduction: Myasthenia Gravis Inebilizumab Trial (MINT; NCT04524273), a placebo-controlled, phase 3, randomized trial, demonstrated significant improvements in Myasthenia Gravis Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) scores in participants treated with inebilizumab versus placebo in the randomized, controlled period (RCP).

Objective: To evaluate 1-year efficacy and safety results of inebilizumab during the 3 MINT open-label period (OLP).

Methods: Participants with generalized myasthenia gravis were randomized 1:1 to receive 300 mg of intravenous inebilizumab or placebo for 52 weeks (participants with anti-acetylcholine receptor antibodies; AChR⁺) or 26 weeks (participants with anti-muscle-specific kinase antibodies; MuSK[±]) during the RCP, followed by an optional 3-year OLP wherein all participants received inebilizumab. This 1-year interim analysis includes participants who received inebilizumab during the RCP or OLP.

Results: Overall, 238 participants were enrolled in MINT; 208 entered the OLP (inebilizumab, 109; placebo, 99), and 188 completed 1 year. Baseline RCP MG-ADL and QMG scores were similar among participants. Mean improvements continued from baseline of the RCP to 1 year of the OLP for participants treated with inebilizumab/inebilizumab (MG-ADL, -6.1; QMG, -7.3) and placebo/inebilizumab (MG-ADL, -5.9; QMG, -6.9) in the combined AChR⁺ and MuSK⁺ populations. The safety profile in the OLP was consistent with that in the RCP.

Conclusions: During 1 year of the OLP, participants experienced sustained improvements in MG-ADL and QMG scores with inebilizumab, supporting durability of response for participants originally randomized to inebilizumab and consistency of efficacy and tolerability regardless of initial treatment in the RCP.

A stylized world map in orange and blue tones serves as a background for the top section of the poster.

Neuromuscular Study Group

27th Annual Scientific Meeting



SEPTEMBER 25-27, 2026

The Historic Menger Hotel
204 Alamo Plaza, San Antonio, TX 78205



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- 23 *Map*

THANKS TO:

Amardeep Gill
Livestream Director, StreamGuru.net

Liz Russo Paulk
NMSG Administrative Manager

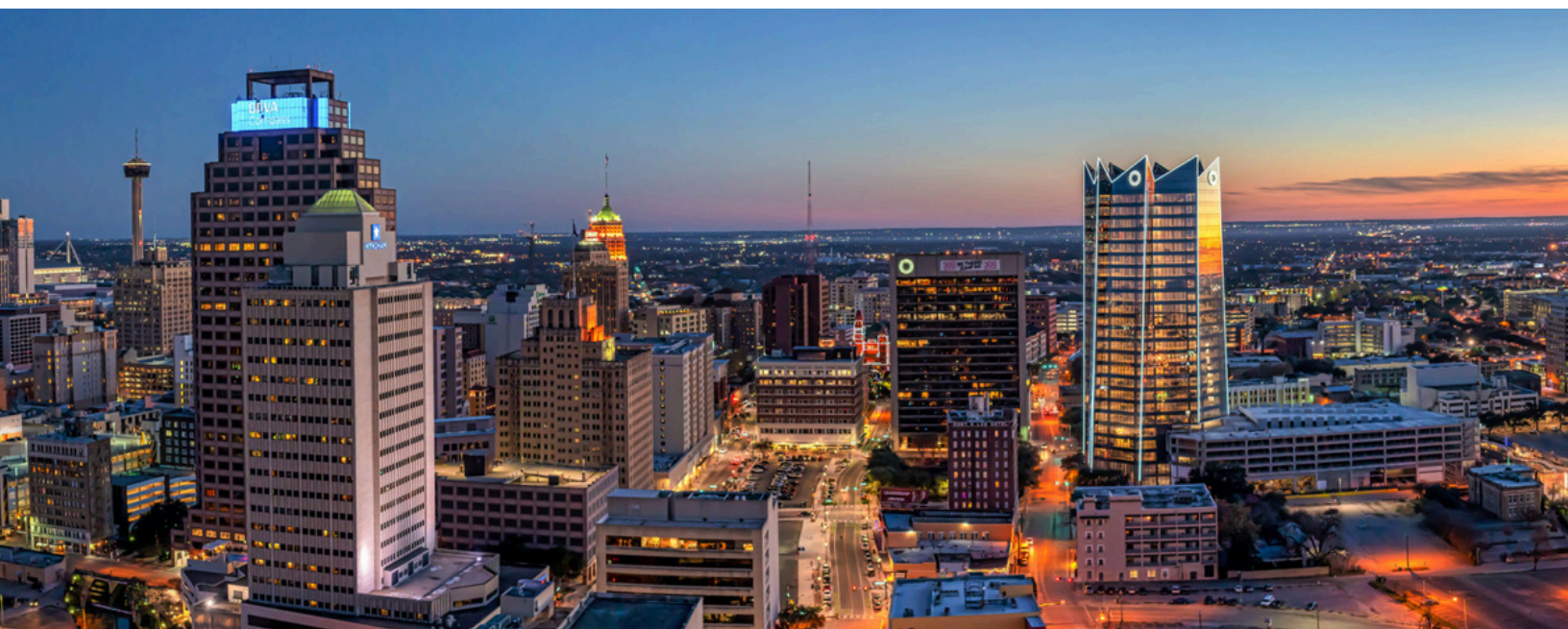
J. Andrea Sierra Delgado, M.D.
University of Missouri

Kelly Gregory
University of Missouri

Megan Galmiche
University of Missouri

Kayla Bunch
University of Missouri

Birda Lewis
University of Missouri



Welcome



Dear Colleagues,

On behalf of the Neuromuscular Study Group (NMSG), we are delighted to welcome you back to San Antonio, Texas, for our 27th Annual Scientific Meeting.

For nearly three decades, the NMSG has united researchers from around the world to collaborate on advancing neuromuscular science. This meeting in particular has become a unique opportunity for our community to come together for a vibrant exchange of ideas that reinforces our commitment to progressing innovation in our field. Whether you are presenting a poster or discussing trials between sessions, we encourage you to engage fully with your colleagues and our industry partners, as your active participation will greatly strengthen the value of our time together.

A few meeting highlights for this year.

- **Emerging Investigators:** We welcome back this valuable session where emerging talent can connect with and learn from established leaders in the field. Join us at 3:40 pm on Friday.
- **Abstract Poster Presentations:** We had 138 submissions this year. Please stop by to see their work at 5 pm on Friday in the Minuet and Patio Rooms.
- **Industry Partners:** We appreciate the immense industry involvement. Please join us for their presentations starting at 2:00 pm on Saturday and visit their tables daily in the Grand Ballroom.
- **Shark Tank:** In its seventh year, the Shark Tank session will feature four exciting proposals, with the winner receiving a \$10,000 grant. New this year: Everyone who attends the session will be able to score the presentations. Join us at 9:00 am on Sunday.

Outside of the scientific program, take time to enjoy the history and charm of the Alamo here in San Antonio. Starting at the historic Alamo, with its cypress-shaded River Walk and tucked-away patios just steps away, San Antonio offers a truly welcoming setting. We hope you will soak in the rich heritage, savor South Texas hospitality and cuisine, and make the most of this charming location during your visit.

We are excited for the continuing opportunity to share breakthroughs, clinical insights, and new ideas that can improve the treatment and care of our patients. Let us continue to embrace the spirit of collaboration as we explore the latest research and inspire one another with our findings.

Sincerely,

A handwritten signature in black ink, appearing to read "Richard J. Barohn".

Richard J. Barohn, M.D.
Professor of Neurology, Immediate Past Executive Vice Chancellor of Health Affairs, University of Missouri
Distinguished Emeritus Professor, University of Kansas
Co-Chairman of the Neuromuscular Study Group

A handwritten signature in black ink, appearing to read "Michael G. Hanna".

Professor Michael G. Hanna
Director, UCL Institute of Neurology
Co-Chairman of the Neuromuscular Study Group



RICHARD J. BAROHN, M.D.
Co-chairman,
Neuromuscular Study Group

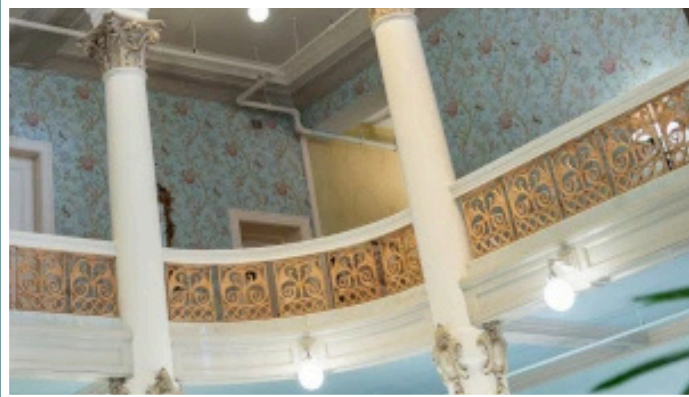
Professor of Neurology,
Immediate Past Executive
Vice Chancellor for
Health Affairs, University of
Missouri;
Distinguished Emeritus
Professor, University of
Kansas



PROF MICHAEL G. HANNA, M.D.
Co-chairman,
Neuromuscular Study Group

Director, University College
London
Institute of Neurology

Committees



EXECUTIVE COMMITTEE

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Director, NMSG Biostatistics Center

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Nicholas Streicher, M.D.

Karen Suetterlin

Prof John Vissing, M.D.
Copenhagen Neuromuscular Center

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Paloma Gonzalez Perez, M.D., Ph.D.

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Jeffrey Statland, M.D.
University of Kansas Medical Center

Gita Ramdharry, Ph.D.
University College London



Information



WIFI

The NMSG has special WiFi access for meeting attendees. This network can be used throughout the hotel.

Network name: NMSG2026

Password: RememberTheAlamo!

WATER AND COFFEE

Water and coffee will be provided all day in the Colonial Room.

SPEAKERS

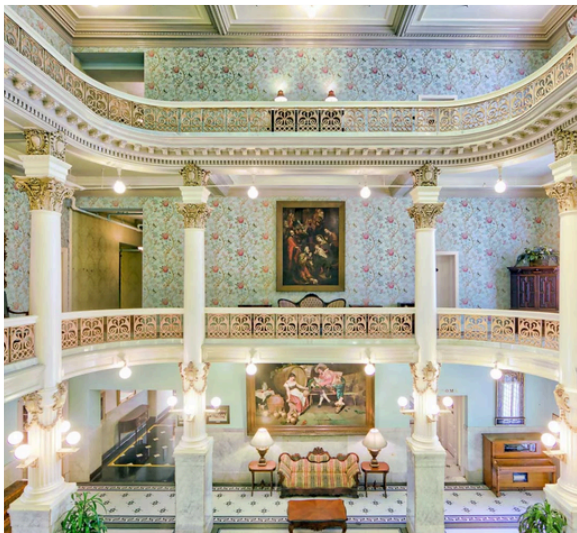
Please provide your presentation on a USB drive to Amardeep Gill, our onsite AV expert, as early as possible so your slides can be loaded into our laptop computer.

PRESENTATION QUESTIONS

If you have a question after a presentation, raise your hand and a microphone will be brought to you.

QUESTIONS

If you have questions not related to a presentation, please ask a member of our staff at the table just outside the Poolside room.



2026 CONTINUING EDUCATION



JOINTLY ACCREDITED PROVIDER™
INTERPROFESSIONAL CONTINUING EDUCATION

JOINT ACCREDITATION STATEMENT

In support of improving patient care, this activity has been planned and implemented by Amedco LLC and Neuromuscular Study Group (NMSG). Amedco LLC is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

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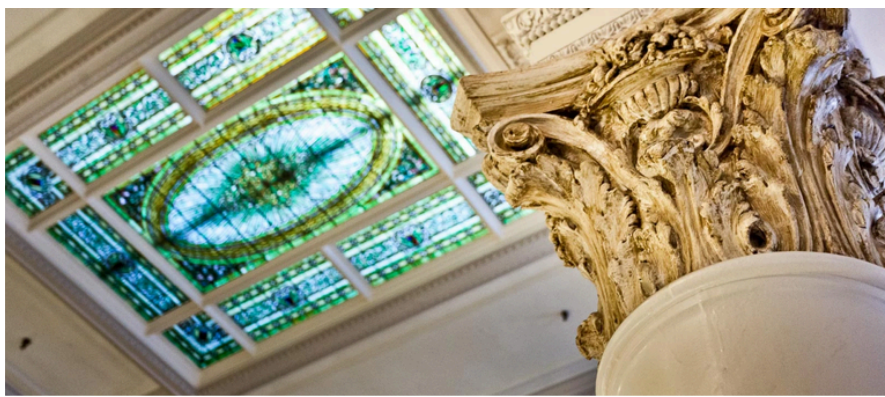
Amedco LLC designates this live activity for a maximum of **11.75** credits *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

*All sessions are granted CME, except **Session 6** and the **Industry Presentations**, both on Saturday afternoon.

GROUP PICTURE

Don't miss the group picture on Friday, September 25th at 7:15 PM in the Victorian Lobby

Agenda



THURSDAY AGENDA

September 24, 11am-6:30pm

11:00 AM - 1:00 PM	<i>Executive Committee Meeting Lunch</i>	Cavalier Room
1:00 PM - 4:00 PM	<i>Clinical Trial Breakout</i>	Renaissance Room
4:00 PM - 5:00 PM	<i>CRC Meeting</i>	Renaissance Room
5:00 PM - 6:30 PM	<i>Welcome Reception</i>	Main Lobby



FRIDAY AGENDA

September 25, 6:30am-11:30pm

6:30 AM - 8:30 AM	Breakfast	Colonial and Minuet Rooms
6:30 AM - 8:30 AM	Breakfast - ALS Military Meeting	Cavalier Room
8:30 AM	Welcome	Grand Ballroom
8:30 AM	State of the NMSG Richard J. Barohn, M.D., Professor of Neurology, Immediate Past Executive Vice Chancellor of Health Affairs, University of Missouri; Distinguished Emeritus Professor, University of Kansas; NMSG Board Chair Professor Michael Hanna, M.D., University College London, NMSG Board Co-Chair	Grand Ballroom
8:45 AM	Today's Agenda Natalie Katz, M.D., Duke, NMSG Planning Committee Co-Chair Matt Wicklund, M.D., University of Texas Health/San Antonio, NMSG Planning Committee Co-Chair	Grand Ballroom



FRIDAY AGENDA

September 25, 6:30am-11:30pm

SESSION ONE

GENETIC THERAPEUTICS

Grand Ballroom

Moderators: Natalie Katz and Valeria Sansone

8:50 AM

Triumphs, Trials, and Future Considerations in Genetic Therapies for Hereditary Neuromuscular Diseases

Grand Ballroom

Andrea Sierra Delgado, M.D., University of Missouri

9:15 AM

Update on Congenital Myopathies in the Genomic Era: From (Rapid) Diagnosis to Trial Readiness

Grand Ballroom

Anna Sarkozy, M.D., Dubowitz Neuromuscular Center, Great Ormond Street Hospital for Children

9:40 AM

Spinal Muscular Atrophy: A Journey from Fatal Disease to Fetal Therapy

Grand Ballroom

Richard Finkel, M.D., St. Jude Children's Research Hospital

10:05 AM

Merging Concepts in Biomarkers and Therapeutics for ALS

Grand Ballroom

Andrea Malaspina, Ph.D., FRCP, University College London

10:30 AM -
10:55 AM

BREAK

Grand Ballroom
Pre-Function



FRIDAY AGENDA

September 25, 6:30am-11:30pm

SESSION TWO

BIOMARKERS

Grand Ballroom

Moderators: Matthew Birkbeck, Ph.D., Newcastle University and Andrea Sierra Delgado, M.D., University of Missouri

10:55 AM

Biomarkers in Myasthenia Gravis

Grand Ballroom

Pushpa Narayanaswami, M.D., Harvard Medical School

11:20 AM

Clinical and Genetic Heterogeneity in Facioscapulohumeral Muscular Dystrophy: Implications for Biomarkers and Trials

Grand Ballroom

Enrico Bugiardi, M.D., Ph.D., University College London

11:45 AM

Peripheral Immune Activation Reflecting CNS Barrier Dysfunction in ALS

Grand Ballroom

Robert Bowser, Ph.D., Barrow Neurological Institute, St. Joseph's Hospital and Medical Center

12:10 PM

Biomarkers in Myotonic Dystrophy

Grand Ballroom

Nicholas E. Johnson, M.D., M.Sci., FAAN, Virginia Commonwealth University

**12:30 PM -
1:30 PM**

LUNCH

Colonial and
Minuet Rooms



SESSION THREE

ABSTRACT PRESENTATIONS

Grand Ballroom

Moderators: James Lilleker and Karen Suetterlin

1:30 PM

Multilevel Neurophysiologic Assessment of Cortical and Peripheral Motor System Dysfunction in Amyotrophic Lateral Sclerosis

Arsh Ketabforoush, M.D., University of Missouri

Grand Ballroom

1:45 PM

Clinical Outcomes and Safety of Nucleoside Therapy for Thymidine Kinase 2 Deficiency in a Brazilian Cohort

Cristiane Araujo Martins Moreno, M.D., Ph.D,
Universidade de São Paulo, Brazil

Grand Ballroom

2:00 PM

Longitudinal assessment of motor function in Duchenne Muscular Dystrophy in a pediatric cohort: development of Italian centile curves for the North Star Ambulatory Assessment, 10-Meter Walk/Run Velocity and Rise from Floor Velocity

Sophia Paolucci, TNPEE, Fondazione Policlinico
Universitario Agostino Gemelli IRCCS

Grand Ballroom

2:15 PM

Neuromuscular junction failure in sarcopenia is linked to Nav1.4 loss and reversed by CLC-1 inhibition

Hiroshi Nishimune

Grand Ballroom

2:30 PM

Real-World Givinostat Tolerability and Dose Modification in Nonambulatory Males with Duchenne Muscular Dystrophy

Abigail B. Crowner, PharmD, MPH, University of Iowa
Health Care

Grand Ballroom



FRIDAY AGENDA

September 25, 6:30am-11:30pm

SESSION THREE, CONTINUED

ABSTRACT PRESENTATIONS

Moderators: James Lilleker and Karen Suetterlin

Grand Ballroom

2:45 PM

Lysosome Remodeling in CMT1A Neuropathy: Pathogenic Mechanism or Compensatory Response?

Abigail Chischolm, M.S., University of Missouri, Columbia

Grand Ballroom

2:52 PM

Manifesting dystrophinopathy in a girl with Williams-Beuren syndrome: a dual molecular diagnosis supported by skewed X-inactivation

Wiktoria Błachut, medical student, Jagiellonian University Medical College, Cracow, Poland

Grand Ballroom

3:00 PM

Near infrared spectroscopy during non-ischaemic handgrip exercise reveals distinct muscle oxygenation signatures in mitochondrial disease and sarcopenia

Helen Devine, Newcastle University

Grand Ballroom

3:07 PM

Retrospective Analysis of MG-ADL Data Outcomes Following Zilucoplan Treatment in Myasthenia Gravis

Carson Barnard, M.D., University of Kansas Medical Center

Grand Ballroom

3:12 PM

Dose-Finding Safety and Tolerability Study of Clenbuterol in Facioscapulohumeral Muscular Dystrophy (FSHD)

Rebecca Clay, CCRP, University of Kansas Medical Center

Grand Ballroom

3:20 PM -
3:40 PM

Break

Grand Ballroom
Pre-Function

FRIDAY AGENDA

September 25, 6:30am-11:30pm

SESSION FOUR

EMERGING INVESTIGATORS WORKSHOP, **SPONSORED BY argenx**

Grand Ballroom

Moderator: Matthew Birkbeck, Ph.D., Newcastle University

**3:40 PM -
4:50 PM**

***Moderator: Matthew Birkbeck, Ph.D.,
Newcastle University***

Grand Ballroom

Mentors: Gita Ramdharry, Ph.D., Karen Suetterlin, MBBS, MRCP, Ph.D., David Arnold, M.D., Jasper Morrow, MBChB, Ph.D., Abdus S. Wahed, Ph.D., Margaret Duku

EVENING ACTIVITIES

EVENING ACTIVITIES

**5:00 PM -
7:00 PM**

POSTER PRESENTATIONS

Minuet and
Patio Rooms

7:15 PM

GROUP PICTURE

Menger Hotel
Victorian Lobby

**7:30 PM -
9:30 PM**

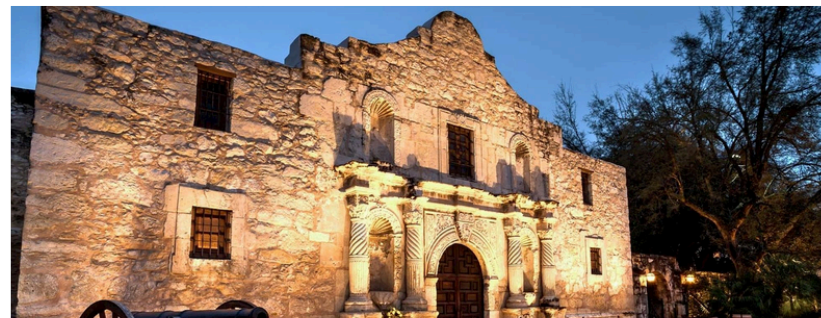
DINNER

The Crockett
Hotel

**9:30 PM -
11:30 PM**

RECEPTION

The Menger Bar



SATURDAY AGENDA

September 26, 6:30am-11:30pm

6:30 AM - 8:30 AM	Breakfast	Colonial and Minuet Rooms
6:30 AM - 8:30 AM	Journal Breakfast	Cavalier Room
8:00 AM	Welcome	Grand Ballroom
8:00 AM	State of the NMSG Richard J. Barohn, M.D., Professor of Neurology, Immediate Past Executive Vice Chancellor of Health Affairs, University of Missouri; Distinguished Emeritus Professor, University of Kansas; NMSG Board Chair Professor Michael Hanna, M.D., University College London, NMSG Board Co-Chair	Grand Ballroom
8:15 AM	Today's Agenda Dr. Miriam Freimer, M.D., Ohio State University Matt Wicklund, M.D., University of Texas Health/San Antonio, NMSG Planning Committee Co-Chair	Grand Ballroom
8:20 AM	Robert C. Griggs Keynote Lecture What exactly are we estimating in a randomized, controlled clinical trial? Professor Michael McDermott, Ph.D., University of Rochester	Grand Ballroom
9:10 AM	NMSG Fellowship Update Sophie Rengarajan, M.D., Ph.D., UCLA Medical Center	Grand Ballroom
9:25 AM - 9:45 AM	Break	Grand Ballroom Pre-Function

SATURDAY AGENDA

September 26, 6:30am-11:30pm

SESSION FIVE

GENETIC THERAPEUTICS

Moderators: Matt Wicklund and John Vissing

Grand Ballroom

9:45 AM

Genetic Nerve Diseases Across the Lifespan/CMT

Michael Shy, M.D., University of Iowa

Grand Ballroom

10:10 AM

CAR-T Cell Therapy in MG

Ali Habib, M.D., UCI Health

Grand Ballroom

10:35 AM

Precision Diagnostics and Targeted Therapies in Primary Mitochondrial Diseases

Professor Robert Pitceathly, MBChB, Ph.D.,
University College London

Grand Ballroom

11:00 AM

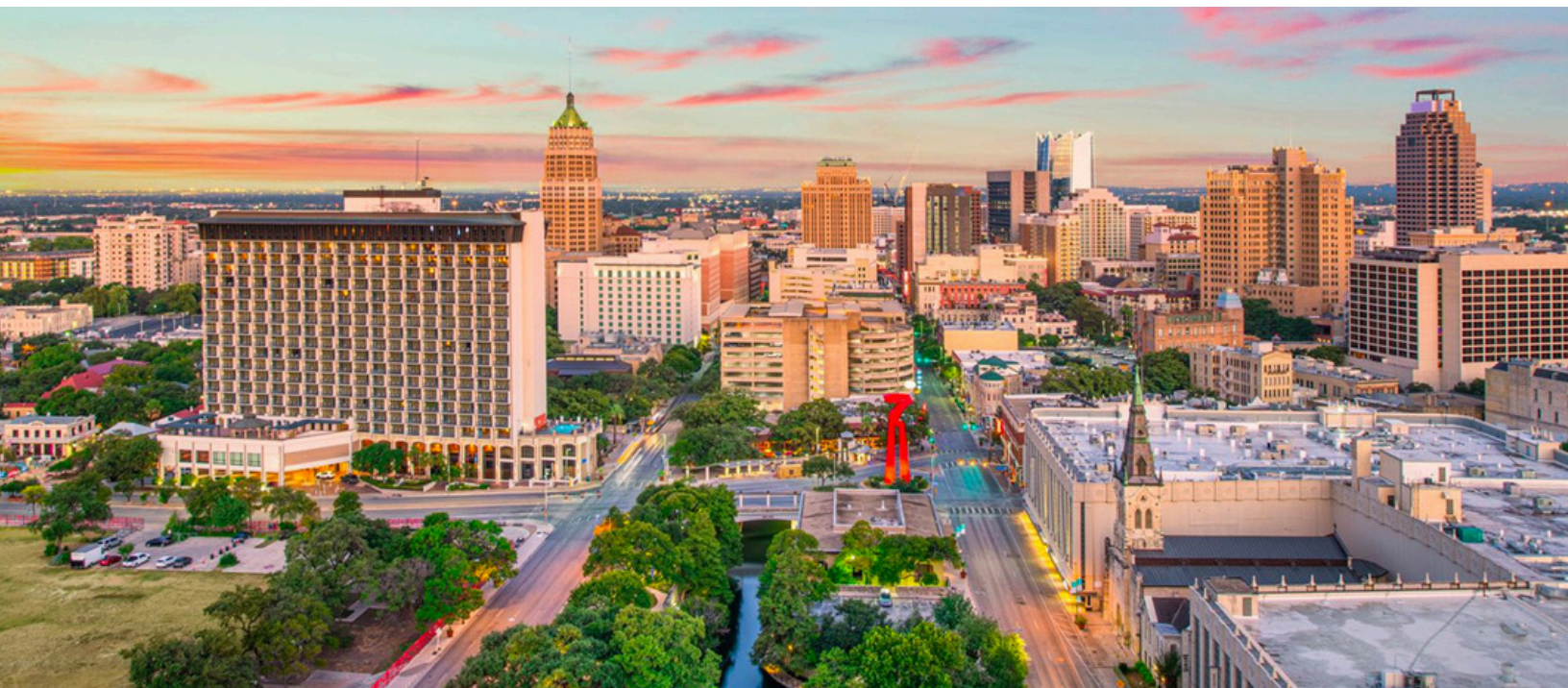
Fellowship Committee Meeting for Endowment possibility

Grant Room

11:25 AM -
12:30 PM

LUNCH

Colonial and
Minuet Rooms



SATURDAY AGENDA

September 26, 6:30am-11:30pm

SESSION SIX - NO CME

TECHNOLOGICAL ADVANCEMENTS

Grand Ballroom

Moderators: Gita Ramdharry and Megan
Iammarino

12:30 PM

Engineered GM1 (TLN): From Preclinical ALS Studies to Clinical Evaluation in Parkinson's Disease

Grand Ballroom

Smita Saxena, Ph.D., University of Missouri

12:55 PM

Spinal Cord Stimulation in Spinal Muscular Atrophy

Grand Ballroom

Marco Capogrosso, Ph.D., University of
Pittsburgh

1:20 PM

Psychometric Testing of Functional Outcome Measures

Grand Ballroom

Katy Eichinger, Ph.D., DPT, University of
Rochester

1:45 PM -
2:00 PM

BREAK

Grand Ballroom
Pre-Function



SATURDAY AGENDA

September 26, 6:30am-11:30pm

INDUSTRY PRESENTATIONS - NO CME

INDUSTRY PRESENTATIONS

Moderators: Matt Wicklund and Miriam Freimer

Grand Ballroom

2:00 PM

Catalyst

***Vamorolone, a Delta-9,11 Corticosteroid:
Exploring the Structural-Activity Relationship***
Keri Kasun, PharmD, Sr Medical Science Liaison -
Rare Neuromuscular Disease

Grand Ballroom

2:25 PM

Johnson & Johnson

***Pregnancy Enhanced Tracking with Neonatal
and Infant Assessment (PETUNIA): Design of a
Safety Study for Nipocalimab in Generalized
Myasthenia Gravis***

Ashley Anderson, Associate Medical Director,
Autoantibody, Johnson & Johnson

Grand Ballroom

2:50 PM

UCB

***Understanding FcRn Biology, Treatment
Durability, Steroid-Sparing Evidence, and
Albumin Considerations in gMG***

Amanda Hernandez, M.D., Ph.D., Assistant
Professor of Neurology, Chief of Neuromuscular
Medicine, Farmington, CT

Grand Ballroom

3:15 PM

MLBIO

***LGMD2I/R9 (FKRP-related) – Disease Overview
and Interim Results from the FORTIFY Phase 3
Study***

Douglas Sproule, M.D., M.Sc.

Grand Ballroom

3:40 PM

argenx

***From strength to function: Understanding the
clinical relevance of grip strength in CIDP and
MMN***

Dr. Allison Crowell, General Neurologist, Clinical
Neurophysiology Penn Medicine Lancaster General
Hospital

Grand Ballroom

SATURDAY AGENDA

September 26, 6:30am-11:30pm

**INDUSTRY
PRESENTATIONS,
CONTINUED
- NO CME**

INDUSTRY PRESENTATIONS

Moderators: Matt Wicklund and Miriam Freimer

Grand Ballroom

4:05 PM

Sanofi

Riliprubart Phase 2 data and Phase 3 trial design.

Asif Paker, M.D., M.P.H.

Grand Ballroom

4:30 PM

Sarepta

Advancing Genetic Medicine Research for Rare Neuromuscular and Central Nervous System Diseases

Elisabeth McGee, APRN, Sarepta Therapeutics, Inc.

Grand Ballroom

4:55 PM

Scholar Rock

Going Beyond the Motor Neuron to the Muscle: Expanding the Focus of SMA Care

Natalie Katz, M.D., Ph.D., Assistant Professor of Pediatrics (Neurology) Co-Director, Duke Children's Neuromuscular Program

Grand Ballroom

5:20 PM

VOR Bio

Our Investigational BAFF/APRIL Inhibitor: Evaluating Telitacicept in Generalized Myasthenia Gravis and Beyond

Nolan Campbell, Ph.D. - Medical Director - Myasthenia Gravis

Grand Ballroom

5:45 PM

Pepgen

FREEDOM2-DM1: Interim results of a multiple-ascending dose clinical trial of PGN-EDODM1 in people with myotonic dystrophy type 1

Paul Streck, M.D., MBA, Executive Vice President, Head of Research & Development, PepGen

Grand Ballroom

SATURDAY AGENDA

September 26, 6:30am-11:30pm

EVENING ACTIVITIES

EVENING ACTIVITIES

The Buckhorn Saloon

7:30 PM -
9:30 PM

DINNER

The Buckhorn Saloon

9:30 PM -
11:30 PM

RECEPTION AND DANCING

The Buckhorn Saloon



SUNDAY AGENDA

September 27, 6:30am-12:30pm

6:30 AM - 8:30 AM	Breakfast	Colonial and Minuet Rooms
8:30 AM	Welcome	Grand Ballroom
8:30 AM	State of the NMSG Richard J. Barohn, M.D., Professor of Neurology, Immediate Past Executive Vice Chancellor of Health Affairs, University of Missouri; Distinguished Emeritus Professor, University of Kansas; NMSG Board Chair Professor Michael Hanna, M.D., University College London, NMSG Board Co-Chair	Grand Ballroom
8:45 AM	Today's Agenda Dr. Natalie Katz Matt Wicklund, M.D., University of Texas Health/San Antonio, NMSG Planning Committee Co-Chair	Grand Ballroom

<u>SESSION SEVEN</u>	<u>SHARK TANK, SPONSORED BY ALEXION</u> Francesco Sacca', M.D., FAAN, Senior Medical Director, GMA Rare Neurology, Alexion Pharmaceuticals Moderator: James Lilleker	Grand Ballroom
9:00 AM	2025 Shark Tank Winner Update Grace McMacken, MBChB, Ph.D., Queen's University Belfast	Grand Ballroom
9:20 AM	Introduction of Sharks Moderators: James Lilleker, MBChB, MRCP, Ph.D., Jasper Morrow, MBChB, Ph.D., Paloma Gonzalez Perez, M.D., Ph.D.	Grand Ballroom
9:30 AM	Shark Tank Presentations	Grand Ballroom

11:00 AM - 11:15 AM	BREAK	Grand Ballroom Pre-Function
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SUNDAY AGENDA

September 27, 6:30am-12:30pm

<u>SESSION EIGHT</u>	<u>THE CLINIC AND BEYOND</u> Moderators: Jacqueline Montes and Nicholas Streicher	Grand Ballroom
11:15 AM	<i>Advancing Our Knowledge of Clinical Phenotypes Using Standardized Outcome Assessments</i> Megan Iammarino, DPT, University of Texas/San Antonio	Grand Ballroom
11:40 AM	<i>Dysphagia in Myotonic Dystrophy Type 1: A Multidimensional Profile and Practical Approach for the Neuromuscular Clinician</i> Jodi Allen, Ph.D., University College London	Grand Ballroom
12:05 PM	<i>Adaptive and Sequential Multiple Assignment Randomized Trials in Neuromuscular Diseases</i> Abdus S. Wahed, Ph.D., University of Rochester	Grand Ballroom
12:30 PM	<i>Announce Shark Tank Winner</i>	Grand Ballroom
12:30 PM	<i>LUNCH</i>	Colonial and Minuet Rooms
<i>AFTER LUNCH</i>	<i>END OF CONFERENCE</i>	THANK YOU!

Notes

DOWNTOWN SAN ANTONIO

*History * Culture * River Walk*



BUCKHORN

**Buckhorn
Saloon & Museum**
318 E. Houston St.

ENTRANCE ON
E. HOUSTON ST.

San Antonio
Visitor Center

COLLEGE ST.

Hyatt Regency
San Antonio
Riverwalk

2

**San Antonio
River Walk**

3

**La Villita
Historic Arts Village**

THE RIVER WALK
The San Antonio River
flows naturally through
downtown and passes beneath
several streets and bridges,
including Losoya St. and
E. Crockett St.



Torch of
Friendship

WALKING ROUTES FROM THE MENDER HOTEL



--- To Crockett Hotel
~ 1 minute walk



--- To Buckhorn Saloon & Museum
~ 7 minutes walk

All distances are approximate.
Wear comfortable shoes and
enjoy the walk!

N. ALAMO ST.

W. HOUSTON ST.

U.S. Federal
Courthouse &
Post Office

E. HOUSTON ST.

3RD ST.



1

The Alamo
300 Alamo Plaza

PLAZA DE VALERO

LOSOYA ST.

E. CROCKETT ST.

BONHAM ST.

The Crockett Hotel
320 Bonham St.



CROCKETT HOTEL

ENTRANCE ON
BONHAM ST.

4

**Shops at
Rivercenter**

MOTOR ENTRANCE &
VALET DROP-OFF
ON E. CROCKETT ST.

MENDER HOTEL

The Menger Hotel
204 Alamo Plaza

E. COMMERCE ST.

E. MARKET ST.

Don't miss LGMD2I/R9.

Genetic testing can guide care planning^{1,2}

When to suspect LGMD2I/R9

Consider LGMD2I/R9 when patients present with^{2,3}:

- Pelvic and shoulder muscle weakness^{2,4}
- Gait disturbance, frequent falls^{1,4,6}
- Scapular winging⁵
- Elevated serum creatine kinase (CK)⁴
- Calf hypertrophy^{4,5}
- Cardiac or respiratory complications over time⁷

Unexplained elevated CK?

Episodic or persistent CK elevation may be an early sign of neuromuscular disease.⁸
Avoid missed or delayed diagnosis—consider genetic testing⁹

Why test early?



Reduce time to diagnosis in rare muscle diseases^{1,9}



Enable accurate subtype identification^{1,8,9}



Support family risk assessment and counseling^{1,9}



Inform appropriate management and referrals^{1,9}

A simple path to diagnosis



1. Suspect LGMD2I/R9

Based on clinical presentation and/or elevated CK



2. Order genetic testing

Use a neuromuscular NGS panel that includes *FKRP*^{2,4,8,10}



3. Results inconclusive?

Consider whole exome sequencing (WES) or genetics consultation^{7,9,11}



4. Confirm diagnosis and next steps

Connect patients to appropriate specialist care and resources^{2,7,9}

CK=creatine kinase; FKRP=fukutin-related protein; LGMD2I/R9=limb-girdle muscular dystrophy type 2I/R9; NGS=next-generation sequencing; WES=whole exome sequencing.

References: 1. Osman H, et al. *Health Expect*. 2025;28(3):e70271. 2. Vissing J, et al. *Neurol Genet*. 2026;12(2):e200370. 3. Murphy LB, et al. *Ann Clin Transl Neurol*. 2020;7(5):757-766. 4. Belhassen I, et al. *Acta Myol*. 2023;42(4):106-112. 5. Jensen SM, et al. *Neuromuscul Disord*. 2023;33(2):119-132. 6. Coffey LN, et al. *Neuromuscul Disord*. 2021;31(12):1235-1240. 7. Narayanaswami P, et al. *Neurology*. 2014;83(16):1453-1463. 8. Ng KWP, et al. *Front Neurol*. 2022;13:997551. 9. Georganopoulou DG, et al. *Protein J*. 2021;40(4):466-488. 10. Uzan GS, et al. *Mol Syndromol*. 2024;15(1):14-21. 11. Caramizaru A, et al. *Clin Genet*. 2026;110(1):46-63.

Learn more about
IMAAVY at
IMAAVYhcp.com



AGAMREE® is FDA approved for the treatment of Duchenne muscular dystrophy (DMD) in patients 2 years of age and older¹



GAVEN
Actual AGAMREE patient

Tough on Duchenne.

"Now that we've been on it for 6 months...he's growing again, and he's happier overall." —Jessica, mother of Gaven



Visit us at the 2026 Annual Neuromuscular Study Group Scientific Meeting or learn more at AGAMREEhcp.com

IMPORTANT SAFETY INFORMATION

Contraindications

AGAMREE is contraindicated in patients with known hypersensitivity to vamorolone or any of the inactive ingredients in AGAMREE.

Warnings & Precautions

- Alterations in Endocrine Function:** Corticosteroids, such as AGAMREE, can cause serious and life-threatening alterations in endocrine function, especially with chronic use. Monitor patients receiving AGAMREE for Cushing's syndrome, hyperglycemia, and adrenal insufficiency after AGAMREE withdrawal. In addition, patients with hypopituitarism, primary adrenal insufficiency or congenital adrenal hyperplasia, altered thyroid function, or pheochromocytoma may be at increased risk for adverse endocrine events. Acute adrenal insufficiency can occur if AGAMREE is withdrawn abruptly, and could be fatal. The risk of adrenal insufficiency is reduced by gradually tapering the dose when withdrawing treatment. For patients already taking corticosteroids during times of stress, the dosage may need to be increased.
- Immunosuppression and Increased Risk of Infection:** Use of corticosteroids, including AGAMREE, increases the risk of new infection; exacerbation of existing infections; dissemination; and reactivation or exacerbation of latent infection and may mask some signs of infection; these infections can be severe, and at times fatal. Tell patients and/or caregivers to inform their healthcare provider if the patient has had recent or ongoing infections or has recently received a vaccine. Advise patients taking AGAMREE to avoid exposure to chickenpox or measles and to alert their healthcare provider immediately if they are exposed.
- Alterations in Cardiovascular/Renal Function:** Monitor for elevated blood pressure and monitor sodium and potassium levels in patients chronically treated with AGAMREE.
- Gastrointestinal Perforation:** Use of corticosteroids increases the risk of gastrointestinal perforation in patients with certain gastrointestinal disorders, such as active or latent peptic ulcers, diverticulitis, fresh intestinal anastomoses, and non-specific ulcerative colitis. Signs and symptoms of gastrointestinal perforation may be masked.
- Behavioral and Mood Disturbances:** Potentially severe psychiatric adverse reactions may occur with systemic corticosteroids, including AGAMREE, and may include hypomanic or manic symptoms (eg, euphoria, insomnia, mood swings) during treatment and depressive episodes after discontinuation of treatment. Encourage patients to seek medical attention if psychiatric symptoms develop.
- Effects on Bones:** Prolonged use of corticosteroids, such as AGAMREE, can lead to osteoporosis, which can predispose patients to vertebral and long bone fractures. Monitor bone mineral density in patients on long-term treatment with AGAMREE.
- Ophthalmic Effects:** The use of corticosteroids, such as AGAMREE, may increase the risk of cataracts, ocular infections, and glaucoma. Monitor intraocular pressure if treatment with AGAMREE is continued for more than 6 weeks.
- Vaccination:** Do not administer live-attenuated or live vaccines to patients receiving AGAMREE. Administer live-attenuated or live vaccines at least 4 to 6 weeks prior to starting AGAMREE.
- Effects on Growth and Development:** Long-term use of corticosteroids, including AGAMREE, can have negative effects on growth and development in children.
- Thromboembolic Events:** Observational studies have shown an increased risk of thromboembolism. Use AGAMREE with caution in patients who have or may be predisposed to thromboembolic disorders.

Adverse Reactions

The most common adverse reactions (>10% for AGAMREE and greater than placebo) are cushingoid features, psychiatric disorders, vomiting, weight increased, and vitamin D deficiency.

Use in Specific Populations

- In patients with mild to moderate hepatic impairment, the recommended daily dose of AGAMREE is 2 mg/kg, preferably with a meal, up to a maximum daily dosage of 100 mg for patients weighing more than 50 kg.
- When used concomitantly with strong CYP3A4 inhibitors, the maximum recommended daily dose of AGAMREE is 4 mg/kg, preferably with a meal, up to a maximum daily dosage of 200 mg for patients weighing more than 50 kg.
- The safety and effectiveness of AGAMREE have not been established in pediatric patients below the age of 2 years.



Scan to view full Prescribing Information at AGAMREEhcp.com/hcp-pi.

To report SUSPECTED ADVERSE REACTIONS, contact Catalyst Pharmaceuticals, Inc. at 1-844-347-3277 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Reference: 1. AGAMREE (vamorolone) Oral Suspension [prescribing information]. Catalyst Pharmaceuticals, Inc.; 2024.



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AGA-0908-1 August 2026

Visit the Catalyst Pharmaceuticals table to learn more about LEMS.

When your patients are experiencing refractory symptoms, LOOK OUT FOR LAMBERT-EATON MYASTHENIC SYNDROME (LEMS)¹⁴

LEMS is an underrecognized autoimmune neuromuscular disorder with symptoms that overlap with myasthenia gravis (MG).^{15,6} However, LEMS can often be identified by autonomic symptoms, including dry mouth, constipation, and orthostatic hypotension.^{2,6} Distinguishing LEMS is critical as up to 60% of cases are associated with an underlying malignancy—most commonly small cell lung cancer.^{2,7-9}



Scan the QR code to learn more about anti-voltage-gated calcium channel antibody testing and a free testing option.



LEMSawarehcp.com

References: 1. Merino-Ramirez MA, et al. *Can J Neurol Sci*. 2016;43(5):635-647. 2. Titulaer MJ, et al. *Lancet Neurol*. 2011;10(12):1098-1107. 3. Evoli A, et al. *Neuromuscul Disord*. 2024;44:104468. 4. Evoli A, et al. Supplementary material. In: 27th ENMC international workshop: Seronegative myasthenia gravis: An update paradigm for diagnosis and management. 9–11 February 2024, Hooftdorp, the Netherlands. *Neuromuscul Disord*. 2024;44:104468. 5. Harms L, et al. *J Med Econ*. 2012;15(3):521-530. 6. Titulaer MJ, et al. *Lancet Neurol*. 2011; 10(12):1098-1107. 7. Kesner VG, et al. *Neurol Clin*. 2018;36(2):379-394. 8. Wirtz PW, et al. *Clin Neurol Neurosurg*. 2002;104(4):359-363. 9. Titulaer M, et al. *J Clin Oncol*. 2008; 26(26):4276-81.



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Transforming the lives of people living with myotonic dystrophy type 1 (DM1).

Driven by our proprietary Enhanced Delivery Oligonucleotide (EDO) platform, PepGen's investigational compound, **PGN-EDODM1**, has the potential to safely and effectively target the root cause of **DM1**.

Want to learn more?
Visit our booth.

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Email us: clinicaltrials@pepgen.com



Our mission

Armed with the most advanced science in genetic medicine, we are in a daily race to rescue lives otherwise stolen by rare disease.

At Sarepta, every day is another twenty-four hours to stand up for patients, advance technology, challenge convention and **DRAG TOMORROW INTO TODAY.**



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SETH
Living with Duchenne
muscular dystrophy

Sanofi is Honored to Sponsor the 2026 NMSG Annual Meeting

Breaking Ground in CIDP with Complement Inhibition



Scan the QR code to
learn more about our
actively recruiting
Phase 3 trial

sanofi

MAT-US-2509023 v1.0 - P Approval date: 08/2025
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your patients or visit
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AMGEN

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USA-335-82351 06/26

argenx-sponsored presentation

From strength to function: Understanding the clinical relevance of grip strength in CIDP and MMN

Saturday, September 26; 3:40–4:05 pm CDT
Grand Ballroom, Menger Hotel,
San Antonio, Texas

Join us on Saturday, September 26, for a symposium about grip strength in neuromuscular diseases. Expert faculty will explore the clinical relevance of grip strength as a sensitive, objective measure of upper limb muscle function and overall muscle strength in neuromuscular diseases, such as CIDP and MMN. Faculty will also discuss insights derived from grip strength data generated in clinical trials and considerations for the use of this measure in future clinical practice.



Save the date to your calendar!

CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; MMN, multifocal motor neuropathy. This event is funded and organized by argenx and is intended for healthcare professionals only. MED-US-a117-2600022 v1 | August 2026 | © 2026 argenx. All rights reserved.

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MEDICAL AFFAIRS



Conner, actual
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NMD PHARMA[®]
NEUROMUSCULAR DISORDERS

*Our purpose is to enable better lives
through novel therapies
to restore skeletal muscle health*

Proud sponsor of
the 27th Annual
NMSG Scientific Meeting



Advancing SMA Care Together

Progress begins with a promise—one made to the people at the heart of our mission. For over a decade, Scholar Rock's commitment to the SMA community has fueled our work to bring innovative solutions to life.

We share your passion for serving those living with SMA, and are here to partner with you in our pursuit of creating new possibilities.

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US-SRK-0060



Ben Gabelman
Living with SMA

RRNMF NEUROMUSCULAR JOURNAL

VOL. 7:2

SEPTEMBER 2026



SAVE THE DATE!

September 17-19, 2027



The background of the image is a photograph of the Alamo mission building in San Antonio, Texas. The building is constructed of light-colored stone and features a prominent arched entrance with a large wooden door. Above the door is a decorative pediment. The building is surrounded by a low stone wall and a paved area. A flagpole with the Texas state flag is visible on the left side of the image. The sky is clear and blue.

27th Annual NMSG Scientific Meeting

Day One: Friday, September 25, 2026

Welcome & Meeting Overview

280+

REGISTERED ATTENDEES

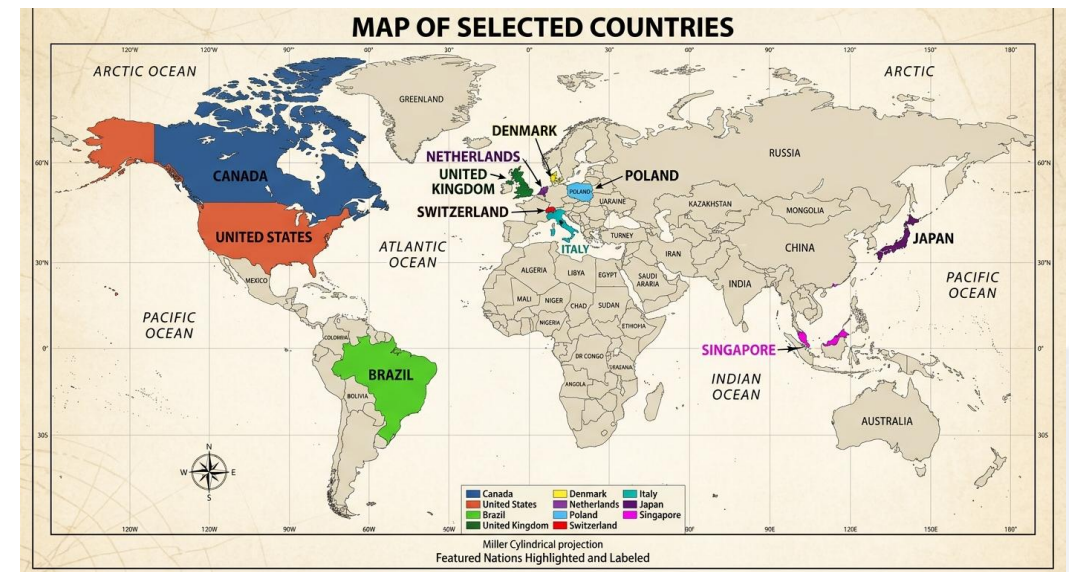
50+

JUNIOR INVESTIGATORS

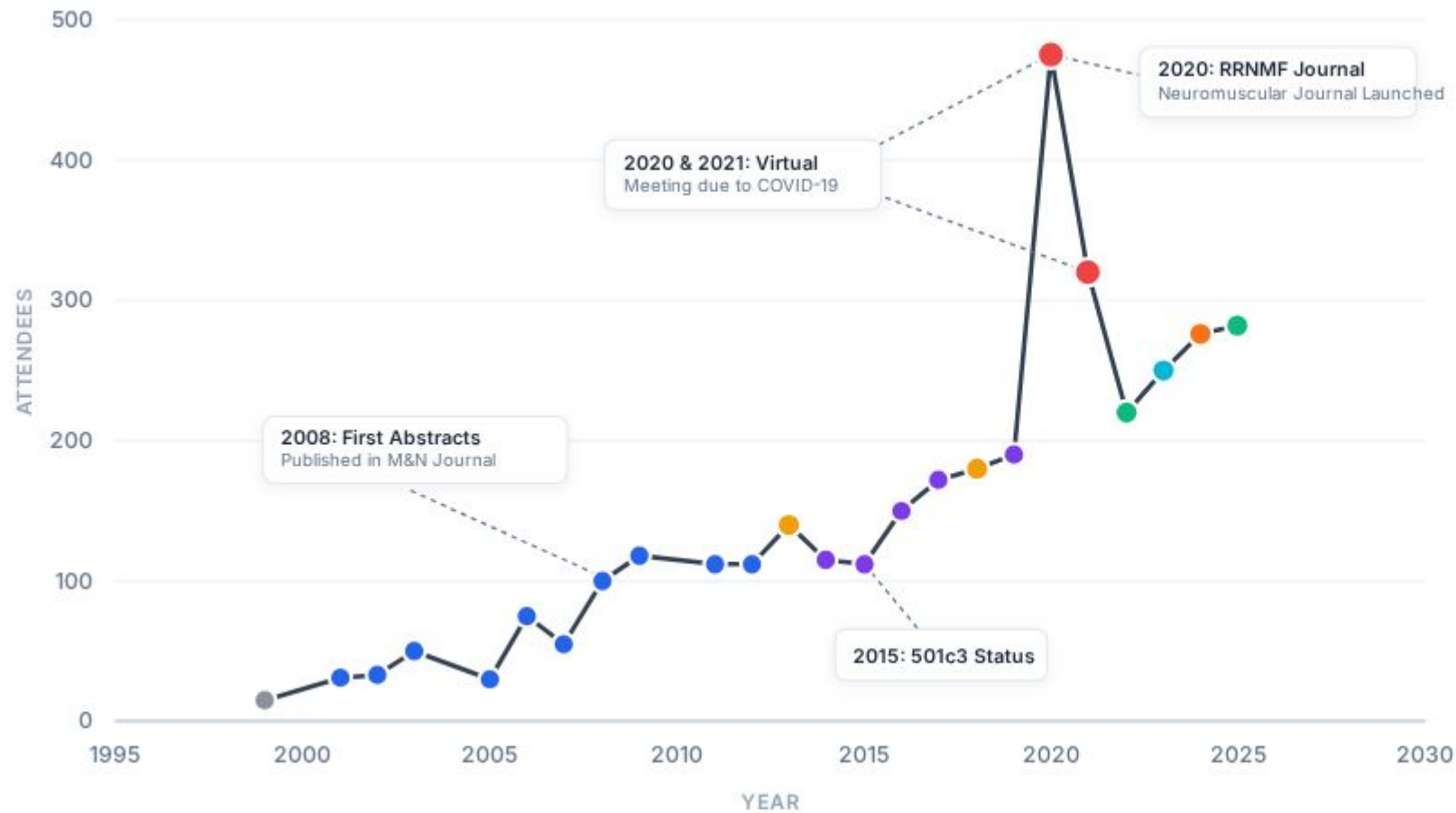
12

PARTICIPATING COUNTRIES

- Brazil
- Canada
- Denmark
- England
- Italy
- Japan
- Netherlands
- Poland
- Singapore
- Switzerland
- United Kingdom
- United States



History of the NMSG Annual Meeting



PEAK ATTENDANCE
475 (Virtual)

IN-PERSON RECORD
282 (Stresa '25)

Meeting Locations

- Chicago, IL
- Beaver Hollow
- England
- Snowbird, UT
- Remote
- Stresa, Italy
- Orlando, FL
- Tarrytown, NY
- San Antonio, TX

NMSG Strategic Goals



Premier Organization & Clinical Trials

Maintain position as the premier organization and annual meeting for neuromuscular clinical trials.



Support Young Investigators

Support and develop young investigators in the field to foster next-generation leadership.



International Collaboration

Foster global partnerships and international clinical trial collaboration.



Pre-Clinical Discovery

Connect to pre-clinical investigators who are exploring potential pathways for new treatments.



Industry Engagement

Engage effectively with pharmaceutical and industry partners to accelerate therapies.

2026 NMSG Planning Committee

Vino Vivekanandam, Ph.D., 2026 Planning Chair

University College London

Matthew Wicklund, MD, FAAN, 2026 Planning Chair

University of Texas Health - San Antonio

David Arnold, MD

University of Missouri

James Lilleker, MBChB, MRCP, Ph.D.

University of Manchester

Gina Ramdharry, Ph.D.

University College of London

Nicholas Streicher, M.D.

University of Michigan

Prof John Vissing, M.D.

Copenhagen University Hospital

Matthew Birkbeck, Ph.D.

University of Michigan

Heidi Fuller, Ph.D.

Keele University

Megan Iammarino, DPT

University of Texas Health - San Antonio

Valeria Sansone, M.D., Ph.D., Co-Chair

NeMO, Milan

Karen Suetterlin, MBBS, MRCP, Ph.D.

Newcastle University

Richard J. Barohn, M.D., NMSG Chair

University of Missouri

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Richard J. Barohn, M.D., Chair
University of Missouri

Michael Hanna, M.D., Chair
University College London

Robert Griggs, M.D., Immediate Past Chair
University of Rochester School of Medicine

Amanda Guidon, M.D., MPH, Investigator Member,
Massachusetts General Hospital

Valeria Sansone, M.D., Ph.D., Incoming Investigator Member,
NeMO Milan

James Lilleker, MBChB, MRCP, Ph.D., Investigator Member,
University of Manchester

Bhaskar Roy, MBBS, MHS, Young Investigator Member,
Yale School of Medicine

Michael Hehir, M.D., Outgoing Investigator Member,

University of Vermont Medical Center

Michaela Walker, MPH, CCRP, Coordinator Member,
University of Kansas Medical Center

Abdus Wahed, PhD, Director, NMSG Biostatistics Center,
University of Rochester Medical Center

Emma Ciafaloni, M.D., FAAN, Director, NMSG Coordination Center

University of Rochester Medical Center

Mazen Dimachkie, M.D., Treasurer
University of Kansas Medical Center

Karen Mul, M.D., Ph.D., Incoming Investigator Member,

Radboud University Medical Center

John Vissing, M.D., Outgoing Investigator Member,

University of Copenhagen

2026 NMSG Special Thanks

Amardeep Gill, *Livestream Director, StreamGuru.net, AV*

Liz Russo Paulk, *NMSG Administrative Manager*

Kelly Gregory, *University of Missouri*

J. Andrea Sierra Delgado, M.D., *University of Missouri*

Susanna Pozzi, *NeMO Milan*



General Meeting Information



RESTROOMS are located just outside Ballroom C.



WATER AND COFFEE all day in the Grand Ballroom pre-function space.



SPEAKERS - Please provide your presentation on a USB drive to Amardeep Gill, our onsite AV expert, as early as possible so your slides can be loaded into our laptop computer.



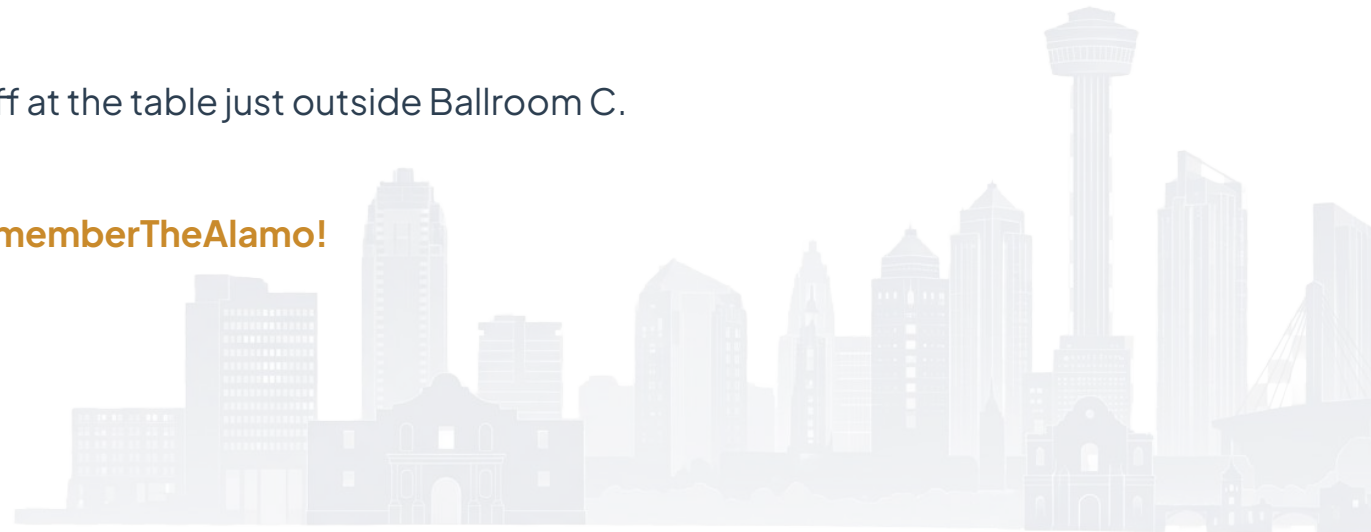
QUESTIONS AFTER A PRESENTATION? Raise your hand and we'll bring a microphone to you.



OTHER QUESTIONS? Please ask a member of our staff at the table just outside Ballroom C.



WI-FI ACCESS Network: **NMSG2026** | Password: **RememberTheAlamo!**



Abstracts

NMSG Abstracts

The accepted abstracts for this conference are published in **RRNMF Neuromuscular Journal**. Use the QR code in your agenda book to retrieve them.



Scan QR Code in Agenda Booklet

Fellowship

Our **Neuromuscular Review Course** returns this spring with a new set of virtual continuing education courses!

Designed with neurologists, physicians, primary care providers, physical medicine specialists, and advanced practice professionals in mind, this course will provide you with up-to-date insights into the clinical approach of diagnosing and managing neuromuscular diseases.

The 2027 Next Generation Research Grant in Neuromuscular Disease will open for applications in mid-June. This early-career research grant consists of a commitment of \$150,000 over two years, and is awarded in partnership between the NMSG and the American Brain Foundation. Applications are due October 1, 2026, and funding begins on July 1, 2027. For additional details and to apply, visit

<https://www.americanbrainfoundation.org/for-researchers/#nrg>.

- June 2026: Fellowship applications open, watch June newsletter for details
- October 1, 2026: Applications close
- October – December 2026: Reviewers evaluate applications
- Mid-January 2027: Reviewers meet to discuss applications and select recipients
- July 1, 2027: Fellowship begins



Continuing Education

- In support of improving patient care, this activity has been planned and implemented by Amedco LLC and Neuromuscular Study Group (NMSG). Amedco LLC is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.
-
- Amedco Joint Accreditation #4008163
-
- Physicians (ACCME) Credit Designation Amedco LLC designates this live activity for a 14.25 credits AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Friday Highlights

- 9:00 am - Genetic Therapeutics
- 10:45 am - Biomarkers
- 1:30 pm - Abstract Presentations
- 3:40 pm - Early Investigators Workshop sponsored by argenx
- 5:00 pm - Poster Presentations
- 7:15 pm - Group Picture
- 7:30 pm - Dinner at the Crockett Hotel
- 9:30 pm - Reception at the Menger Bar



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- Johnson & Johnson
- ML Bio
- UCB/Commercial



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- ITF Pharma



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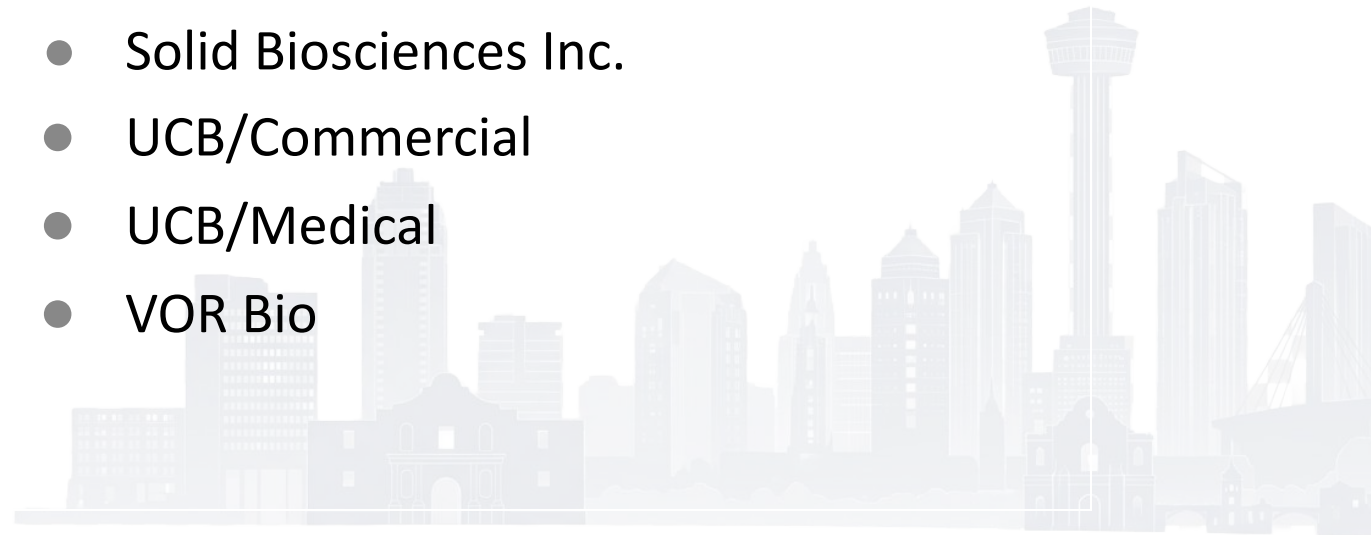
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 - Poster Session



Thank you again all sponsors

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Closing Remarks

“

One Last Thought

"Whether you are presenting a poster or discussing trials between sessions, we encourage you to engage fully with your colleagues and our industry partners as your active participation will greatly strengthen the value of our time together."

The background of the image is a photograph of the Alamo mission building in San Antonio, Texas. The building is constructed from light-colored stone and features a prominent arched entrance with a large wooden door. Above the door is a decorative pediment. The building is surrounded by a low stone wall and a paved area. A flagpole with the Texas state flag is visible on the left side of the image. The sky is clear and blue.

27th Annual NMSG Scientific Meeting

Day Two: Saturday, September 26, 2026

Reminders

- If you have a question after a presentation, raise your hand and we'll bring a microphone to you.
- If you have questions not related to the presentation, please ask a member of our staff at the table just outside the sponsor room.
- The NMSG has a special WiFi access for meeting attendees. This network can be used throughout the hotel.

Network name: NMSG2026

Password: RemembertheAlamo!

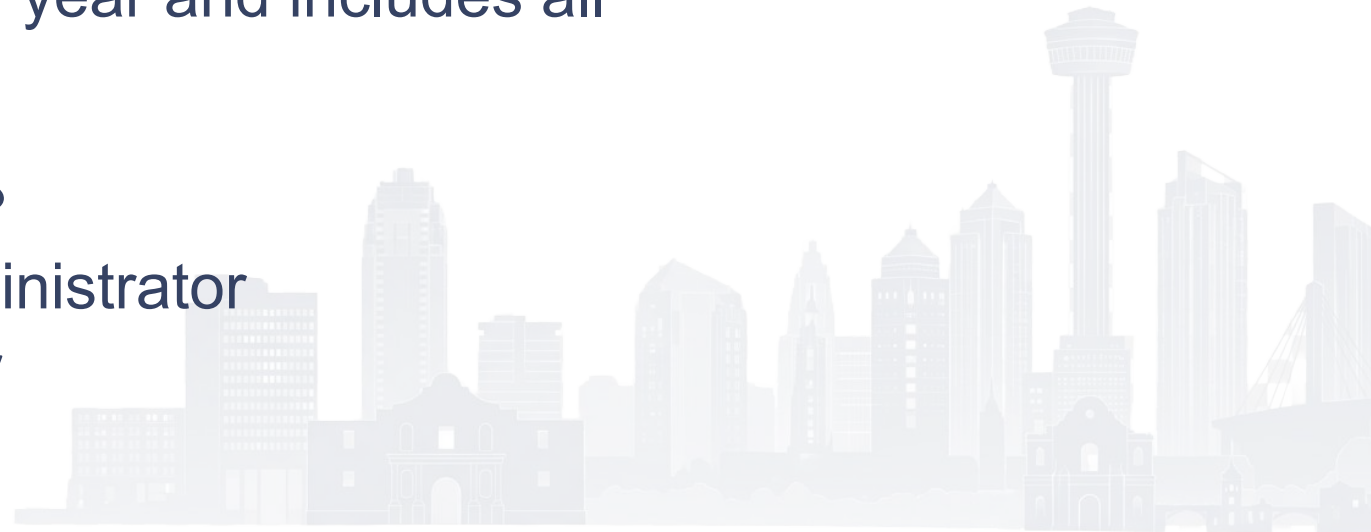


Become a NMSG Member!

1. On the NMSG website the application is under the membership tab.
2. The NMSG Executive Committee will review your application and contact you with any questions.
3. If your site is approved, we will invoice you for \$500 which is good for the calendar year and includes all researchers at your site.

Questions?

Ask our group's administrator
Kelly Gregory



NMSG Member Benefits

- Discounted registration to this meeting
- Brainstorming potential study ideas
 - Steering committee input
- Critiquing grant submissions
- Mentorship
- Database management
- Statistical support
- Funding assistance
- Shark Tank competition
- Hang out in cool places with other neuromuscular academics and industry partners



NMSG Member Sites – Current on Dues

- Beth Israel Deaconess
- Cedar-Sinai Los Angeles
- Common Spirit
- Indiana University
- Northwestern University
- Univ of MASS Medical School
- University of California, Irvine
- University of Kansas Medical Center
- University of Milan
- University of Missouri
- University of Nebraska
- University of Pittsburgh
- University of Rochester Medical Center
- University of Texas Health Science Center, San Antonio
- University of Vermont



Thanks Again to:

- Amardeep Gill, *Livestream Director, StreamGuru.net*
- Liz Russo Paulk, *NMSG Administrative Manager*
- J. Andrea Sierra Delgado, M.D., *University of Missouri*
- Megan Galmiche, *University of Missouri*
- Birda Lewis, *University of Missouri*
- Kayla Bunch, *University of Missouri*
- Kelly Gregory, *University of Missouri*



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Saturday Highlights

- 9:30 am - Genetic Therapeutics
- 12:30 pm - Technological Advancements
- 2:00 pm - Industry Presentations
- 7:30 pm - Dinner at the Buckhorn Saloon
- 8:30 pm - Buckhorn Museum
- 9:30 pm - Dancing at the Buckhorn



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27th Annual NMSG Scientific Meeting

Day Three: Sunday, September 27, 2026

Sunday Highlights

- 9:00 am - Shark Tank sponsored by Alexion
- 11:15 am - The Clinic and Beyond
- 12:20 pm - Shark Tank Winner Announcement
- 12:30 pm - Lunch



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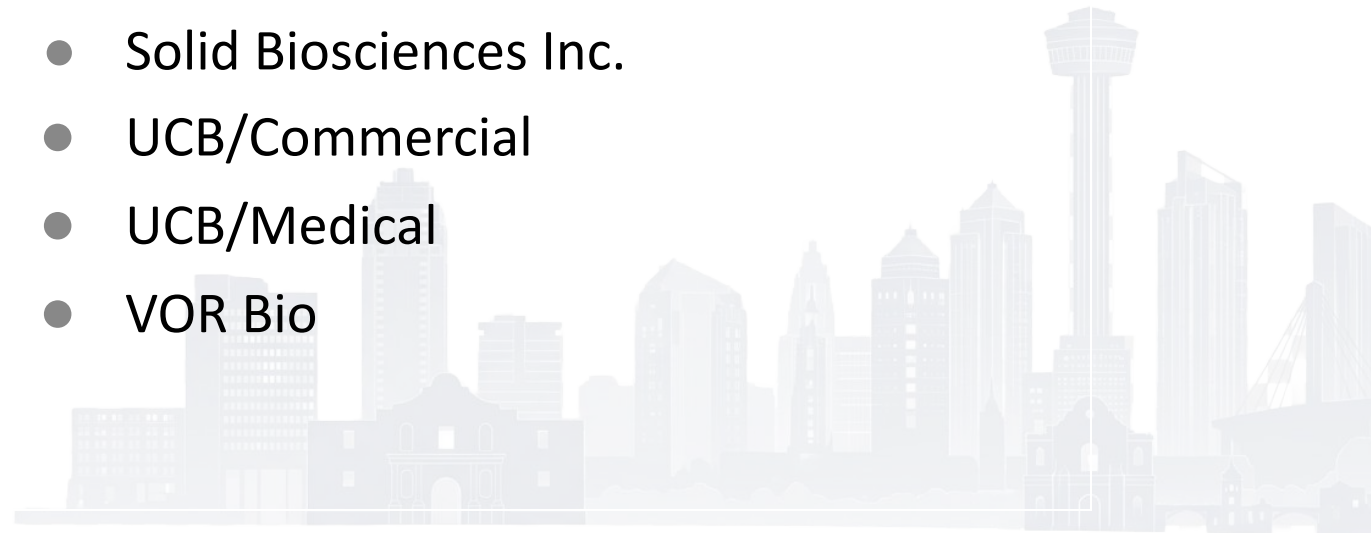
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Sponsors – Thank You

And thanks again to our
2026 sponsors!





**Join us next year in
Tarrytown, NY,
from September 17-19, 2027**

