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## Pharmacological and Non-Pharmacological

Abstract #610 Shark Tank Winner/presenter

### Therapeutic Play Gym: Feasibility of a caregiver-mediated exercise system for infants and young children with severe neuromuscular weakness

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#### ABSTRACT

**Introduction:** Children need stability, self-produced sensorimotor experiences, and massive amounts of practice to master developmental skills in supine, side-lying, and prone positions.

**Objective:** Evaluate safety and feasibility of caregiver-mediated exercise training with a Therapeutic Play Gym (TPG).

**Methods:** Nine children with severe neuromuscular weakness enrolled in the study. All completed baseline and Month 3 testing with the exploratory TPG-specific FUNctional Measure (FUNM), and Caregiver Impression of Change Questionnaire (CICQ). Testing occurred in home environments or at naturally occurring episodes of care at the University of Florida.

**Mid-study results:** Participants collectively trained for 16,730 minutes with no TPG-related adverse events. FUNM scores (attached) minus (not attached) to TPG was  $p=0.0039$  and change in function (while not attached to TPG) was  $p=0.0078$ . CGIC average score was  $p=0.0039$  and Overall Physical Wellbeing  $p=0.0078$ .

**Conclusion:** Exercise training using the TPG device is yielding promising results in terms of functional and global improvements over 3 months.

Abstract #524 Presenter

## Effect of different corticosteroid dosing regimens on clinical outcomes in boys with Duchenne muscular dystrophy (DMD): a randomized clinical trial

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**Introduction:** Corticosteroids improve muscle function in boys with DMD.

**Objective:** This study compares efficacy and side effects of the three most commonly prescribed corticosteroid regimens in young boys with DMD.

**Methods:** we completed an international randomized, double-blind, parallel-group clinical trial at 32 sites. Participants were randomized to daily prednisone, daily deflazacort or intermittent prednisone. The study enrolled 196 corticosteroid-naïve boys with DMD ages 4-7 years. Boys were assessed for three years.

**Results:** Daily regimen were superior to the intermittent regimen for all motor function outcomes. There were no significant differences in efficacy between daily prednisone and deflazacort. Both daily and intermittent prednisone regimen were associated with greater weight gain than deflazacort. Slowing of growth was less severe with the intermittent regimen than with the daily regimens, with daily deflazacort associated with the greatest slowing of growth.

**Conclusions:** This study establishes the benefit and safety of long-term daily corticosteroid treatment.

Abstract #585

## BALance Training in CMT1A- BALTiC Study- A randomised controlled feasibility trial

M.M. Dudzic, L.E. Lee, C. Massey, D. Tropman, M. Skorupinska, M. Laurá, M.M. Reilly, G.M. Ramdharry  
(London, UK)

**Introduction:** People with Charcot Marie Tooth Disease (CMT) report problems with balance. Few studies have looked at practical interventions to improve this.

**Objectives:** To investigate the feasibility and effect of a home-based programme of multi-sensory balance and strength training for people with CMT1A.

**Methods:** Outcome measures included disease severity, function, patient reported measurements and posturography, performed at baseline and 12 weeks. Fourteen participants were randomised to either 12 weeks of intervention or treatment as usual (TAU). The intervention was a home-based programme of strengthening and multi-sensory balance exercises. Final assessments repeated those carried out at baseline.

**Results:** Thirteen people completed the study. The intervention was well tolerated. Posturography measures demonstrated moderate to large effect sizes in favour of the intervention. Functional measures of balance and mobility showed larger effect sizes.

**Conclusions:** The intervention was safe and feasible with improvements in balance measures.

Abstract #587

## The feasibility and effect of Ankle Foot Orthoses and in-shoe vibrating insoles on standing balance in people with inherited neuropathy- preliminary results

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1. Introduction: People with inherited neuropathy (IN) report problems with balance. External support to the foot and ankle are frequently prescribed, though no data currently looks at the effects of these on balance. Vibration to the foot has shown promise in diabetic neuropathy, though has not been explored in IN.

2. Objectives: To investigate the effect of (1) external support from ankle foot orthoses (AFOs) and (2) vibratory feedback to the sole of the foot on standing balance in people with IN.

3. Methods: This cross-sectional feasibility study used posturography measures to compare shoe only, AFOs and vibrating insoles. Demographic data included disease severity, strength, sensation.

4. Results: Ten people with IN participated. 50% used AFO's prescribed by a health professional. Mean CMT Examination Score was 10.2 (range 6-15). Posturography data is in preparation.

5. Conclusions: The study was safe and feasible. Effect on balance will be assessed and presented.

Abstract #507

## Barriers in decision making for patients with ALS accepting a PEG feeding tube

Introduction: What are barriers and concerns regarding placement of a PEG tube feeding?

Objectives: Identify the level of knowledge about tube feedings and the sources used to obtain knowledge, barriers and concerns that ALS patients have regarding PEG tube feeding.

Methods: Two surveys were given before (when a feeding tube was felt indicated) and at a clinic visit 3 months later, to determine factors influencing their decision for or against a PEG.

Results: Patients have stress, anxiety, and fear regarding placement, which influence choosing PEG. After PEG placement, most report that the procedure and use are easier than expected and they would do it again and would recommend it to others. Several factors were identified that could reduce concerns and lead to placement.

Conclusions: Early introduction and education about PEG placement may be beneficial to improve acceptance of PEGs relieving, fears and stress for ALS patients and caregivers.

Abstract #516



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## USE OF 3D PRINTER IN A REHAB LAB FOR THE CREATION OF CUSTOMIZED ASSISTIVE DEVICES WITH USERS WITH RADIATION-INDUCED BRACHIAL PLEXOPATHY TO INCREASE PARTICIPATION: CASE STUDY

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*Background:* Villa Rosa RehabLab, Trento Italy, aims to design 3D printed personalized Assistive Devices (AD) to facilitate and promote participation through a user-centred co-design process.; direct involvement of the user in the design process ensures a correspondence of the AD to his/her needs, aiming to empower the person in the therapeutic strategy, ensuring the AD's continuous use and avoiding stigmatization. The use of 3D printer is increasingly popular in the medical world, particularly in rehabilitation and occupational therapy for the manufacture of personalized adaptations and assistive devices. M.A. 58 y.o., diagnosed with radiation-induced brachial plexopathy since 2012, at the initial occupational therapy interview reported difficulty in cutting hard foods, reporting pain when he presses the knife with his left arm. Patient's quality of performance was observed and self-perception of performance and satisfaction scored using the Canadian Occupational Performance Measure (COPM)

*Objective:* Improve quality of performance and decrease pain when performing this task

*Method:* After ascertaining that no commercial AD was available, an AD dedicated to this function was designed by the user on paper, and afterwards the occupational therapist created a wood prototype. Once the functionality of the prototype was ascertained, the user, guided by the therapist, drew the object with desired shape and sizes using FUSION360, which was then fabricated with the 3D printer.

*Result:* The client's quality of performance improved using the fabricated AD, as did his COPM scores

*Conclusion:* The RehabLab and use of 3D printer can improve independence and participation with individuals with radiation-induced brachial plexopathy.

Abstract #520

## PHASE 3 STUDY OF ORAL EDARAVONE IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS: 48-WEEK RESULTS

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**INTRODUCTION:** Intravenous (IV) edaravone (Radicava®/Radicut) slows the rate of physical functional decline in ALS. There is interest in a non-IV formulation.

**OBJECTIVES:** To assess the long-term safety and tolerability of recently FDA-approved Radicava ORS® (edaravone) oral suspension in patients with ALS in a global, open-label, phase 3 study (MT-1186-A01).

**METHODS:** A 105-mg ORS dose was administered in treatment cycles that replicated IV edaravone dosing.

**RESULTS:** In the Week 48 safety analysis (n=185), the most common treatment-emergent adverse events (TEAEs) were fall (22.2%) and muscular weakness (21.1%). TEAEs considered to be related to ORS, serious TEAEs, and TEAEs leading to death were reported by 46/185, 48/185, and 12/185 patients, respectively. TEAEs leading to discontinuation included tremor (n=1) and gait disturbance (n=1), both considered ORS-related. There were no serious TEAEs, or TEAEs leading to death, related to ORS.

**CONCLUSIONS:** ORS was generally safe and well tolerated, with no new safety concerns identified.

**Sponsorship:** Mitsubishi Tanabe Pharma Development America, Inc., and Mitsubishi Tanabe Pharma America, Inc.

**Acknowledgements:** p-value communications provided editorial support.

### Disclosure:

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

G.L. Pattee has served as a consultant for Mitsubishi Tanabe Pharma, Inc.

G. Sobue has served as a medical advisor for Mitsubishi Tanabe Pharma Corporation.

P. Couratier has served as a consultant for Biogen and as an editor for Elsevier.

D. Selness and S. Bidani are employees of Mitsubishi Tanabe Pharma Development America, Inc.

M. Hirai and T. Sakata are employees of Mitsubishi Tanabe Pharma Corporation.

A. Salah and S. Apple are employees of Mitsubishi Tanabe Pharma America, Inc.

Abstract #521

PHASE 3B, MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PARALLEL-GROUP STUDY  
TO EVALUATE EFFICACY AND SAFETY OF INVESTIGATIONAL ORAL EDARAVONE  
ADMINISTERED OVER 48 WEEKS IN PATIENTS WITH AMYOTROPHIC LATERAL  
SCLEROSIS (MT-1186-A02)

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**INTRODUCTION:** Intravenous (IV) edaravone (Radicava<sup>®</sup>/Radicut) slows the rate of physical functional decline in ALS. There is interest in a non-IV formulation.

**OBJECTIVES:** Evaluate and compare long-term safety, efficacy, and tolerability of 2 dosing regimens of recently FDA-approved Radicava ORS<sup>®</sup> (edaravone) oral suspension over 48 weeks in patients with ALS in an ongoing, multicenter, phase 3b, double-blind, parallel group, randomized study (MT-1186-A02).

**METHODS:** Patients (n=380 expected, definite/probable ALS, FVC  $\geq$ 70%, ALS duration  $\leq$ 2 years) will be equally randomized into 2 groups: 1) 105-mg ORS daily x28 days, 12 cycles; 2) ORS daily x14 days, then placebo daily x14 days (Cycle 1); followed by ORS daily x10 days, then placebo daily x18 days (Cycles 2-12). The primary objective will evaluate dosing regimen efficacy based on baseline to Week 48 ALSFRS-R score changes.

**RESULTS:** Ongoing.

**CONCLUSIONS:** Safety, efficacy, and tolerability of 2 oral edaravone dosing regimens in patients with ALS will be determined.

**Sponsorship:** Mitsubishi Tanabe Pharma Development America, Inc., and Mitsubishi Tanabe Pharma America, Inc.

**Acknowledgements:** *p*-value provided editorial support.

**Disclosure:**

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

S. DeSilva has nothing to disclose.

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

M. Chum has nothing to disclose.

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



## Abstracts from the 2022 Muscle Study Group Meeting

- A. C. Ludolph has served as a scientific consultant for Mitsubishi Tanabe Pharma America, Inc.
- G. Sobue has served as a medical advisor for Mitsubishi Tanabe Pharma Corporation.
- M. Doyu is a medical advisor for MT-1186-A02 study.
- D. Selness is an employee of Mitsubishi Tanabe Pharma Development America, Inc.
- V. Todorovic is an employee of Mitsubishi Tanabe Pharma Europe Ltd.
- M. Hirai is an employee of Mitsubishi Tanabe Pharma Corporation.
- T. Sakata is an employee of Mitsubishi Tanabe Pharma Corporation.
- A. Wamil is an employee of Mitsubishi Tanabe Pharma Development America, Inc.
- A. Salah is an employee of Mitsubishi Tanabe Pharma America, Inc.
- S. Apple is an employee of Mitsubishi Tanabe Pharma America, Inc.

Abstract #522

Phase 3, Open-Label, Safety Extension Study of Investigational Oral Edaravone Administered Over 96 Weeks in Patients with AMYOTROPHIC LATERAL SCLEROSIS (MT-1186-A03)

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**INTRODUCTION:** Intravenous (IV) edaravone (Radicava®/Radicut) slows the rate of physical functional decline in ALS. There is interest in a non-IV formulation.

**OBJECTIVES:** To assess the continued long-term safety and tolerability of Radicava ORS® (edaravone) oral suspension in patients with ALS in ongoing, multicenter, phase 3 studies.

**METHODS:** Study MT-1186-A03 (n=130 anticipated) is a long-term safety and tolerability extension study for MT-1186-A01. Patients who complete MT-1186-A01 and still meet the enrollment criteria will be eligible for MT-1186-A03 and will receive ORS for another 96 weeks.

Patients will continue to be administered a 105-mg ORS dose in treatment cycles that replicate IV edaravone dosing. Study MT-1186-A03 includes a primary safety analysis, and exploratory end points including ALSFRS-R score change from baseline, and time to death, tracheostomy, or permanent assisted mechanical ventilation.

**RESULTS:** Ongoing.

**CONCLUSIONS:** MT-1186-A03 will provide important information on the continued long-term safety and tolerability of ORS in patients with ALS.

**Sponsorship:** Mitsubishi Tanabe Pharma Development America, Inc., and Mitsubishi Tanabe Pharma America, Inc.

**Acknowledgements:** *p*-value communications provided editorial support.

**Disclosure:**

D. Selness is an employee of Mitsubishi Tanabe Pharma Development America, Inc.

M. Hirai is an employee of Mitsubishi Tanabe Pharma Corporation.

T. Sakata is an employee of Mitsubishi Tanabe Pharma Corporation.

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

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Abstract #534

## Evolution of Treatment induced Airway Obstruction in ALS patient on NIV

**Introduction:** Treatment induced Airway Obstruction (TAO) is associated to increased mortality in ALS patients, therefore early detection of this problem is relevant in clinical care. No longitudinal data on the evolution of TAO are available.

**Case Report:** 3 ALS patients showed TAO-associated desaturation after several months of NIV use.

**Methods:** A retrospective analysis of ventilator data, ABGs and sleep studies or night oximetry was performed on these patients.

**Results:** At NIV initiation 3/3 patients showed an AHI weekly average >10/h (respectively 15.7, 13.2, 16.3 event/h). Detection of TAO-associated desaturation occurred at planned follow-ups after respectively 15, 5 and 12 months. AHI from ventilator software was fluctuating, but AHI values >5/h were associated with T89>5 min only in 16/21 nights and with ODI>10 in 8/22 nights.

**Conclusions:** AHI from ventilator software may allow early detection of TAO and predict the risk of developing TAO-associated desaturations.

Abstract #539

## Preliminary data from the ADAPT-NMD study: experiences of patients and clinicians using a new co-designed self-management support programme

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**Introduction:** As there is no cure for most neuromuscular diseases (NMDs), self-managing symptoms is essential for participation in daily activities. The Bridges Self-Management Programme was originally developed in stroke and has now been adapted for people living with neuromuscular diseases (NM Bridges), but this new version needs evaluation.

**Methods:** Ten NMD patients who received NM Bridges, and the six clinicians who were trained in delivering it, participated in semi-structured interviews exploring their experiences of the programme. These interviews will form part of a wider mixed methods feasibility evaluation which is currently ongoing. Reflexive thematic analysis was used to code data and identify key domains and themes.

**Results:** Results will be presented at the 2022 Muscle Study Group Annual Scientific Meeting.

**Conclusion:** Qualitative data generated from this study will form part of an evaluation of the feasibility of delivering and implementing NM Bridges within the context of a specialist neuromuscular service.

Abstract #544

## Patient satisfaction following Phase I and Phase II/III primary mitochondrial myopathy trials

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**Introduction:** Primary mitochondrial myopathies (PMMs) are emerging as a major target for drug development. However, inherent challenges to trial design in this group of rare disease remain. Increasingly, patient preference concerning symptom management is used to inform trial design. Nevertheless, there is limited data for patient-reported experience during participation in PMM drug studies.

**Objective:** We plan to explore patient satisfaction during Phase I and Phase II/III clinical trials in PMMs.

**Methods:** Data will be collected from people with PMMs who have previously participated in Phase I and Phase II/III clinical trials at The National Hospital for Neurology and Neurosurgery, using a patient-administered survey.

**Conclusion:** We anticipate our data informing the early stages of study design to ensure recruitment and retention of patients during PMM clinical trials are maximised. This work will have potential implications for other rare disease interventional studies.

Abstract #548

## Baseline Characteristics of Patients with Myasthenia Gravis Enrolled in an Expanded Access Programme (EAP) for Efgartigimod

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**Introduction:** In the phase 3 ADAPT study, efgartigimod was well-tolerated and efficacious in patients with generalised myasthenia gravis (gMG).

**Objective:** The EAP is for patients with gMG and ineffectively controlled symptoms (IgG  $\geq$ 4g/L in previous month), who cannot enrol in a clinical trial.

**Methods:** Enrolment is ongoing across Europe (USA ceased following efgartigimod approval). Country-specific/individual protocols aligned to local practice apply (US protocol: NCT04777734).

**Results:** Enrolled patients (N=46) receive intravenous efgartigimod 10mg/kg according to fixed/flexible treatment cycles. As of 8 April 2022, most are female (56.5%), aged 45–64 years (39.1%); 69.6% are AChR-Ab+, 21.7% are seronegative and 8.7% are MuSKAb-positive. 86.9% had IgG >6g/L. 54.5% (N=44) are MGFA class III; previous/current treatments ( $\geq$ 30 patients) include: steroids 95.3%, pyridostigmine 72%, intravenous immunoglobulin 69.7%, and 25% had prior thymectomy, 63.6% had  $\geq$ 2 comorbidities.

**Conclusions:** The EAP addresses an unmet need and provides insights into characteristics and management of patients with gMG.

Abstract #553

## Design and Implementation of the Tofersen Early Access Program

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### **Presenting author:**

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### **Abstract:**

**Introduction:** Tofersen (BIIB067) is an investigational drug in people with amyotrophic lateral sclerosis associated with mutations in the superoxide dismutase 1 (*SOD1*) gene (*SOD1-ALS*).

**Objectives:** To describe the design and implementation of the tofersen EAP.

**Methods:** The tofersen EAP, initially limited to persons with rapidly progressive disease, began in July-2021 when the last randomized participant received their first dose in the open-label extension (NCT03070119) of the Phase 3 VALOR (NCT02623699). In October-2021, VALOR results revealed that although the primary endpoint did not achieve statistical significance, consistent evidence suggested slowing of decline in faster-progressing participants. The EAP was then expanded to the broader *SOD1-ALS* population.

**Results:** As of 30-April-2022, the tofersen EAP was available in 31 countries and 115 people had been treated in 12 countries.

**Conclusions:** The tofersen EAP is designed to be inclusive, consistent with principles of medical ethics and prudent medical practice.

Abstract #556

## One-year ENDEAVOR data (ambulatory, ≥4- to <8-year-olds): Phase 1b trial of delandistrogene moxeparovec in Duchenne muscular dystrophy (DMD)

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C. Wandel,<sup>5</sup> S. Lewis,<sup>4</sup> J. Malhotra,<sup>4</sup> D.A. Griffin,<sup>4,7</sup> R.A. Potter,<sup>4</sup> R. Salazar,<sup>4\*</sup> L.R. Rodino-Klapac,<sup>4</sup> J.R. Mendell<sup>7,8</sup>

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\*Presenting on behalf of the authors

**Introduction:** Delandistrogene moxeparovec (SRP-9001) is an investigational gene transfer therapy being studied in DMD.

**Objectives:** ENDEAVOR (NCT04626674) is a two-part, open-label, Phase 1b study assessing expression/safety of commercially representative delandistrogene moxeparovec material in four cohorts of patients with DMD.

**Methods:** Participants received a single intravenous dose ( $1.33 \times 10^{14}$  vg/kg, linear qPCR) of delandistrogene moxeparovec. The primary outcome measure is change in micro-dystrophin protein expression from baseline to Week 12 (Part 1). Secondary outcome measures include safety (over 260 weeks).

**Results:** Data from the first 11 patients (Cohort 1; ≥4- to <8-year-old ambulatory boys) demonstrated micro-dystrophin protein expression at Week 12. We present 1-year safety and functional data and 12-week expression data from all Cohort 1 patients (n=20).

**Conclusion:** Data suggest that safety of commercially representative delandistrogene moxeparovec material is consistent with clinical process material. One-year data from all Cohort 1 patients (n=20) will provide valuable information on safety/efficacy of delandistrogene moxeparovec.

### Disclosures:

CZ receives research support from and serves on an advisory board for Biogen, and was a paid consultant for Optum. CP participates on an advisory board and is a consultant for Biogen, Sarepta Therapeutics, AveXis/Novartis Gene Therapies, Genentech/Roche and Scholar Rock; serves as a speaker for Biogen; is PI of studies sponsored by AveXis/Novartis Gene Therapies, AMO, Astellas, Biogen, CSL Behring, Fibrogen, PTC, Pfizer, Sarepta Therapeutics, and Scholar Rock. CM reports grants from Capricor, Catabasis, Edgewise, Epirium Bio, Italfarmaco, Pfizer, PTC Therapeutics, Santhera Pharmaceuticals, Sarepta Therapeutics; and other from Capricor, Catabasis, PTC therapeutics, Santhera Pharmaceuticals, and Sarepta Therapeutics. SM, SW, ED, SL, JM, DAG, RAP and RS are employees of Sarepta Therapeutics and may have stock options. MG, CR and CW are employees of F. Hoffmann-La Roche Ltd and have nothing to disclose. LRR-K is an employee of Sarepta Therapeutics, has received grant support from Sarepta Therapeutics and the Parent Project Muscular Dystrophy, and financial consideration from Sarepta Therapeutics and Myonex Therapeutics. LRR-K is a co-inventor of AAVrh74.MHCK7.micro-dys technology. JRM has received study funding from Sarepta Therapeutics and has a service agreement with Sarepta Therapeutics to provide training on ongoing studies. JRM is a co-inventor of AAVrh74.MHCK7.micro-dys technology.



Abstract #557

## Oro-Bulbar Involvement in patients with Spinal muscular atrophy treated with Nusinersen

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**Introduction** Nusinersen improves motor and respiratory function in spinal muscular atrophy (SMA). Less is known on oro-bulbar involvement (OBI).

**Objectives** To identify OBI assessments in SMA and to evaluate chewing and swallowing 1y post-nusinersen.

**Methods** Two-year multicentre prospective study. SMAII and III underwent tongue and facial muscle strength (Iowa Oral Performance Instrument, IOPI) and chewing and swallowing (Test of Masticating and Swallowing Solids, TOMASS) assessments.

Nusinersen-treated were compared with age-SMA-type matched naïve patients at baseline. Treated patients were followed for 1 year.

**Results** 63 patients were included, 42 naïve (median age 32.7 years), 21 treated (median age 28.5 years). Baseline IOPI, TOMASS were similar in both groups.

Nusinersen treatment >1y was associated with improved chewing (SMAII) and swallowing (SMAIII). Time from disease onset to treatment was inversely correlated with chewing (r-0.4) and swallowing (r-0.6).

**Conclusions** TOMASS detects changes in OBI in SMA. Early and longer nusinersen treatment duration (>1year) was associated with reduced decline in oro-bulbar function.

Abstract #558

## One-year ENDEAVOR data (ambulatory, ≥4- to <8-year-olds): Phase 1b trial of delandistrogene moxeparvovec in Duchenne muscular dystrophy (DMD)

C. Zaidman,<sup>1</sup> C. Proud,<sup>2</sup> C. McDonald,<sup>3</sup> S. Mason,<sup>4</sup> M. Guridi,<sup>5</sup> S. Wang,<sup>4</sup> C. Reid,<sup>6</sup> E. Darton,<sup>4</sup>

C. Wandel,<sup>5</sup> S. Lewis,<sup>4</sup> J. Malhotra,<sup>4</sup> D.A. Griffin,<sup>4,7</sup> R.A. Potter,<sup>4</sup> R. Salazar,<sup>4\*</sup> L.R. Rodino-Klapac,<sup>4</sup> J.R. Mendell<sup>7,8</sup>

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\*Presenting on behalf of the authors

**Introduction:** Delandistrogene moxeparvovec (SRP-9001) is an investigational gene transfer therapy being studied in DMD.

**Objectives:** ENDEAVOR (NCT04626674) is a two-part, open-label, Phase 1b study assessing expression/safety of commercially representative delandistrogene moxeparvovec material in four cohorts of patients with DMD.

**Methods:** Participants received a single intravenous dose ( $1.33 \times 10^{14}$  vg/kg, linear qPCR) of delandistrogene moxeparvovec. The primary outcome measure is change in micro-dystrophin protein expression from baseline to Week 12 (Part 1). Secondary outcome measures include safety (over 260 weeks).

**Results:** Data from the first 11 patients (Cohort 1; ≥4- to <8-year-old ambulatory boys) demonstrated micro-dystrophin protein expression at Week 12. We present 1-year safety and functional data and 12-week expression data from all Cohort 1 patients (n=20).

**Conclusion:** Data suggest that safety of commercially representative delandistrogene moxeparvovec material is consistent with clinical process material. One-year data from all Cohort 1 patients (n=20) will provide valuable information on safety/efficacy of delandistrogene moxeparvovec.

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Abstract #560

## Phase 1/2a trial of delandistrogene moxeparvovec in patients with Duchenne muscular dystrophy (DMD): 4-year update

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\*Presenting on behalf of the authors

**Introduction:** Delandistrogene moxeparvovec (SRP-9001) is an investigational gene transfer therapy being studied in DMD.

**Objectives:** Study 101 (NCT03375164) is a Phase 1/2a, single-dose, open-label study assessing safety of delandistrogene moxeparvovec in DMD.

**Methods:** Four ambulatory patients with DMD (4–7 years old) were given an intravenous dose ( $2.0 \times 10^{14}$  vg/kg, supercoiled qPCR; linear plasmid standard equivalent of  $1.33 \times 10^{14}$  vg/kg) of delandistrogene moxeparvovec. The primary outcome measure is safety. Efficacy outcome measures include change in the North Star Ambulatory Assessment (NSAA).

**Results:** Previously, delandistrogene moxeparvovec demonstrated an acceptable long-term safety profile 3 years post-treatment. No serious adverse events (AEs), study discontinuations, or AEs associated with clinically relevant complement activation were reported. All patients demonstrated clinically meaningful improvement on the NSAA (mean change [standard deviation] from baseline to Year 3: +7.5 points [3.42]). We present long-term (4-year) safety/functional data.

**Conclusion:** The response following treatment provides proof-of-concept for continuation of delandistrogene moxeparvovec clinical trials.

### Disclosures:

JRM has received study funding from Sarepta Therapeutics and has a service agreement with Sarepta Therapeutics to provide training on ongoing studies. In addition, he is a co-inventor of AAVrh74.MHCK7.micro-dys technology. ZS has received grant support from Sarepta Therapeutics and the Parent Project Muscular Dystrophy. KJL has received an institutional grant from Sarepta Therapeutics. LPL reports receiving salary support from Sarepta Therapeutics through Nationwide Children's Hospital to support training and quality control activities for their ongoing clinical trials and licensing fees for natural history data. NFR reports receiving salary support from Sarepta Therapeutics for Clinical Evaluator training for ongoing and upcoming clinical trials. MAI has nothing to disclose. LNA reports receiving salary support from Sarepta Therapeutics through Nationwide Children's Hospital to support training and quality control activities for their ongoing clinical trials. SL, RAP, DAG, MH, LH, SM, ED and DT are employees of Sarepta Therapeutics and may have stock options. KC and RS have nothing to disclose. LRR-K is an employee of Sarepta Therapeutics, has received grant support from Sarepta Therapeutics and the Parent Project Muscular Dystrophy, as well as financial consideration from Sarepta Therapeutics and Myonex Therapeutics (now acquired by Sarepta Therapeutics). In addition, she is a co-inventor of AAVrh74.MHCK7.micro-dys technology.

Abstract #562

## Integrated analyses of data from clinical trials of delandistrogene moxeparvec in Duchenne muscular dystrophy (DMD)

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\*Presenting on behalf of the authors

**Introduction:** Delandistrogene moxeparvec (SRP-9001) is an investigational gene transfer therapy being studied in DMD.

**Objectives:** To analyse 1-year functional data from ambulatory patients ( $\geq 4$  to  $\leq 8$  years old) with DMD who received a dose ( $1.33 \times 10^{14}$  vg/kg by linear qPCR) of delandistrogene moxeparvec in clinical studies. These data were compared with a propensity score-weighted external comparator (EC) cohort (n=103) comprised of patients with DMD from other studies.

**Methods:** The dataset included patients from Study 101 (Phase 1/2a; NCT03375164), Study 102 (Phase 2; NCT03769116), and ENDEAVOR (Phase 1b; NCT04626674). The primary endpoint is 1-year change from baseline in the North Star Ambulatory Assessment.

**Results:** Functional data from 53 patients (Study 101, n=4; Study 102, n=29; and ENDEAVOR, n=20, Cohort 1) will be compared with the EC cohort. Safety data from all cohorts (Studies 101, 102 and ENDEAVOR) will be presented.

**Conclusion:** These analyses will provide valuable information on safety/efficacy of delandistrogene moxeparvec.

### Disclosures:

CZ receives research support from and serves on an advisory board for Biogen, and was a paid consultant for Optum. PBS reports being a consultant/independent contractor (AveXis, Biogen, Cytokinetics, and Sarepta Therapeutics) and receiving grants/research support (AveXis, Biogen, Cytokinetics, Ionis Pharmaceuticals, Sanofi Genzyme and Sarepta Therapeutics). CP participates on an advisory board and is a consultant for Biogen, Sarepta Therapeutics, AveXis/Novartis Gene Therapies, Genentech/Roche and Scholar Rock; serves as a speaker for Biogen; is PI of studies sponsored by AveXis/Novartis Gene Therapies, AMO, Astellas, Biogen, CSL Behring, Fibrogen, PTC, Pfizer, Sarepta Therapeutics, and Scholar Rock. CM reports grants from Capricor, Catabasis, Edgewise, Epirium Bio, Italfarmaco, Pfizer, PTC Therapeutics, Santhera Pharmaceuticals, Sarepta Therapeutics; and other from Capricor, Catabasis, PTC therapeutics, Santhera Pharmaceuticals, and Sarepta Therapeutics. JWD reports grants from AMO, Audentes, Avidity, Biogen, Cytokinetics, Ionis Pharmaceuticals, Novartis Gene Therapies, Roche Pharmaceuticals, Sanofi-Genzyme, Sarepta Therapeutics, Scholar Rock. JWD participates on advisory boards and is consultant for Affinia Therapeutics, AMO Pharmaceuticals, Astellas Gene Therapies, Audentes Therapeutics, Avidity Therapeutics, Biogen, Cytokinetics, Epirium Bio, Ionis Pharmaceuticals, Kate Therapeutics, Novartis, Novartis Gene Therapies, Pfizer, Roche/Genentech Pharmaceuticals, Sarepta Therapeutics, Scholar Rock, Shift Therapeutics, Vertex. JWD participated in the PepGen Scientific Advisory Board (2021). JWD was a paid advisor to the Muscular Dystrophy Association and an unpaid advisor to Myotonic Dystrophy Foundation, CureSMA, SMA Foundation, Parents Project Muscular Dystrophy, Foundation Building Strength for Nemaline Myopathy, Cure CMD and Solve FSHD. JWD holds patents licensed to Athena Diagnostics for genetic testing of myotonic dystrophy type 2 (US patent 7442782) and spinocerebellar ataxia type 5 (US patent 7527931). SM, LH, LY, ED, JR, JM, TS and RS are employees of Sarepta Therapeutics and may have stock options. MG, CR and CW are employees of F. Hoffmann-La Roche Ltd and have nothing to disclose. LRR-K is an employee of Sarepta Therapeutics, has received grant support from Sarepta Therapeutics and the Parent Project Muscular Dystrophy, and financial consideration from Sarepta Therapeutics and Myonex Therapeutics. LRR-K is a co-inventor of AAVrh74.MHCK7.micro-dys technology. JRM has received study funding from Sarepta Therapeutics and has a service agreement with Sarepta Therapeutics to provide training on ongoing studies. JRM is a co-inventor of AAVrh74.MHCK7.micro-dys technology.

Abstract #564

## Preliminary Results from MLB-01-003: An Open Label Phase 2 Study of BBP-418 in Patients with Limb-girdle Muscular Dystrophy Type 2I (LGMD2I)

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**Introduction:** BBP-418 (ribitol) is an oral substrate supplementation intended to saturate the FKRP enzyme driving increased glycosylation of  $\alpha$ DG, potentially ameliorating the root cause of LGMD2I.

**Objectives:** The study is intended to explore the safety, tolerability and efficacy of BBP-418 in patients with LGMD2I.

**Methods:** Study involved three open-label ascending dose cohorts treated for 3 months with BBP-418. Thereafter, all patients received 12g BID (weight adjusted) for 3 additional months.

**Results:** 14 patients (aged 12-53, 8/14 homozygous for the L276I mutation) were enrolled. After 90 days, participants showed a mean +0.14 (43%) increase in  $\alpha$ DG glycosylation. Creatine kinase (CK) decreased an average of 64% at day 180, 36% to below 400 U/L. BBP-418 was well-tolerated with no observed treatment-related serious AEs or dose-limiting toxicity. Updated data will be provided.

**Conclusions:** Preliminary data suggests a positive effect on  $\alpha$ DG glycosylation and CK. A global, double-blind placebo-controlled Phase 3 study is planned.

Abstract #565

## Providing a sustainable, accessible cough and secretion management service for patients with Neuromuscular Disease throughout the COVID-19 pandemic

**Introduction:** In 2018, we set up an interdisciplinary cough and secretion management service for patients with neuromuscular disease. The aim was to improve the quality of life for those experiencing challenges with secretion management secondary to progressive cough or swallowing difficulties.

Here we show how the service adapted to meet patient needs during the pandemic.

**Method:** Data was collected retrospectively from clinic appointments April 2020 - October 2021.

**Results:** 166 appointments were conducted via face-to-face (n=34), video call (n=63), telephone call (n=63) and text exchange (n=2). Two did not attend.

Set-up of cough augmentation was possible via video consultation when pre-assessment and couriering of equipment was in place prior to the appointment. Virtual monitoring of peak cough flow was possible via electronic records.

**Conclusion:** The clinic is now a hybrid face to face and virtual clinic. This ensures accessible, effective and sustainable treatment.

Abstract #568

## Comparison of open- and closed-state sodium channel blockers in the treatment of myotonia

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**Introduction:** Myotonia Congenita patients suffer from debilitating stiffness. A subthreshold, non-inactivating, sodium persistent inward current (NaP), plays a central role in triggering myotonia. The current treatment for MC is mexiletine, an open-state Na<sup>+</sup> channel blocker, which is only partially effective and has significant side effects. Mu-conotoxin GIIIA (uCTX) is a potent closed-state Na<sup>+</sup> channel blocker.

**Objectives:** Our objective was to (1) compare each drug's ability to reduce NaP amplitude and (2) compare the use-dependent blocking of the Na<sup>+</sup> current needed to trigger action potentials (NaF).

**Methods:** We utilized current clamp and voltage clamp of single muscle fibers from a mouse model of Myotonia Congenita.

**Results:** uCTX was significantly better than mexiletine in treating myotonia. uCTX selectively blocked NaP and spared NaF, whereas Mexiletine caused a much greater use-dependent block of NaF.

**Conclusions:** Our findings suggest that state-dependent blocking of Nav1.4 is a predictor of hypoexcitability as a side effect.

Abstract #569

## Comparison of change in ability to perform timed function tests (TFTs) in nonsense mutation Duchenne muscular dystrophy (nmDMD) patients receiving ataluren: Strategic Targeting of Registries and International Database of Excellence (STRIDE) Registry vs phase 3 clinical trial

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**Introduction:** STRIDE is an ongoing registry providing real-world data on ataluren use in nmDMD patients.

**Objective:** We investigated if ataluren-treated nmDMD patients in STRIDE and a phase-3 clinical trial (Study 20) performed similarly in TFTs.

**Methods:** TFTs were assessed over 48 weeks for STRIDE and Study 020 patients.

**Results:** Ataluren-treated patients from STRIDE and Study 020 experienced smaller mean increases in time (s) to perform TFTs vs Study 020 placebo-allocated patients: 1.run/walk 10m [95% CI]: STRIDE 1.3 [0.6, 2.0], n=113; ataluren 020, 2.3 [1.3, 3.3], n=109; placebo, 3.5 [2.3, 4.7], n=110; 2.climb four stairs: STRIDE, 0.4 [-0.3, 1.0], n=73; ataluren 020, 2.7 [1.6, 3.7], n=105; placebo, 4.5 [3.0, 5.9], n=103; 3.descend four stairs: STRIDE, 0.3 [-0.1, 0.8], n=59; ataluren 020, 2.2 [1.1, 3.2], n=106; placebo, 4.0 [2.4, 5.5], n=100; 4.stand from supine STRIDE, 1.7 [0.6, 2.8], n=93; ataluren 020, 3.8 [2.7, 5.0], n=101; placebo, 3.9 [2.5, 5.3], n=96.

**Conclusion:** Ataluren delays decline in TFT performance in nmDMD patients vs placebo.



Abstract #571

## Associations Between Daily Deflazacort or Prednisone and Ages at Disease Progression Milestones Among Patients with Duchenne Muscular Dystrophy (DMD)

Craig McDonald<sup>1</sup>, Audrey Powell<sup>2</sup>, Nicholas Mastrandrea<sup>2</sup>, Efthimia Leonardi<sup>2</sup>, James Signorovitch<sup>3</sup>, Jessica Marden<sup>3</sup>, Molly Frean<sup>3</sup>, Henry Lane<sup>3</sup>, Adina Zhang<sup>3</sup>, Ha Nguyen<sup>3</sup>

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<sup>3</sup>Analysis Group, Inc., Boston, Massachusetts

**INTRODUCTION:** Corticosteroids are the standard of care for DMD.

**OBJECTIVE:** Compare ages at disease progression milestones between patients on daily prednisone and deflazacort.

**METHODS:** DMD patients were identified from two natural history studies. Associations between daily steroid treatment, deflazacort or prednisone, and disease progression milestones were assessed.

**RESULTS:** 463 patients (mean age 9.86 years; n=288 deflazacort; n=175 prednisone) were identified. Deflazacort patients experienced a delay in timed rise from floor (RFF) $\geq$ 10 seconds and RFF $\geq$ 5 seconds of 0.88 years (log-rank  $p<0.01$ ) and 0.94 years ( $p<0.05$ ), respectively. Delays in progression were also observed for inability to RFF (+1.61 years,  $p<0.001$ ) and inability to complete 4-stair climb (+1.87 years;  $p<0.01$ ) for patients receiving deflazacort vs. prednisone. Median age at loss of ambulation was older for deflazacort patients (15.92 vs. 14.89 years;  $p<0.001$ ).

**CONCLUSION:** Use of daily deflazacort was associated with delayed progression of multiple ambulatory milestones in patients with DMD.

Abstract #572

## Associations between deflazacort vs prednisone/prednisolone and disease progression markers in subgroups of patients with Duchenne muscular dystrophy (DMD)

Craig McDonald<sup>1</sup>, Audrey Powell<sup>2</sup>, Nicholas Mastrandrea<sup>2</sup>, Efthimia Leonardi<sup>2</sup>, James Signorovitch<sup>3</sup>, Jessica Marden<sup>3</sup>, Henry Lane<sup>3</sup>, Adina Zhang<sup>3</sup>, Ha Nguyen<sup>3</sup>

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**INTRODUCTION:** Corticosteroids are the standard of care for DMD.

**OBJECTIVE:** Compare outcomes in DMD by steroid type stratified by baseline age, ambulatory function, and steroid duration.

**METHODS:** Mean changes in 6WMD and other ambulatory outcomes were compared between patients from placebo arms of 4 DMD trials receiving daily deflazacort vs. daily prednisone,

**RESULTS:** Of 328 patients, 231 received daily steroids (n=127 deflazacort; n=104 prednisone). Deflazacort was associated with preservation of 35.4 meters of 6MWD over 48 weeks vs prednisone (P<0.01). Differences between deflazacort vs. prednisone were most pronounced among boys with the following baseline characteristics: aged ≥8 years (+44.5m, P<0.01), rise time ≥5 seconds (+41.3m, P<0.01) and steroid duration >3 years (+57.5m, P<0.01).

**CONCLUSION:** Benefits of daily deflazacort vs daily prednisone for preserving ambulatory function in DMD were most evident among patients who were older, had been on steroids longer, or were at a more progressed disease stage.

Abstract #573

## Associations between steroid treatment and clinical outcomes among non-ambulatory patients with Duchenne Muscular Dystrophy (DMD)

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**INTRODUCTION:** Corticosteroids are the standard of care for DMD.

**OBJECTIVE:** Compare outcomes by steroid treatment among non-ambulatory (NA) DMD patients. **METHODS:** NA DMD patients were identified from an observational study of DMD disease progression (PRO-DMD-01). Associations between steroid treatment (prednisone, deflazacort, or no steroids) were assessed.

**RESULTS:** 86 NA patients (mean age 13.4 years; n=40 deflazacort; n=29 prednisone; n=17 no steroids) were included. Relative to no steroids, both steroids were associated with delays in median age at FVC%-predicted<60% (+0.9 [prednisone]; +2.3 [deflazacort]; log-rank p<0.01). Median ages at LVEF<55% were numerically prolonged, but non-significant (+2.7 [prednisone]; +0.8 [deflazacort]; p=0.65). While median ages at loss of hand-to-mouth function were not consistently reached, higher proportions of steroid patients maintained function at age 15 (85%-deflazacort; 83%-prednisone; 78%-no steroids; p<0.001).

**CONCLUSION:** Steroid use after loss of ambulation was associated with delayed progression of important pulmonary, cardiac and functional deficits in DMD.

Abstract #576

## Assessment of Nusinersen Effect in Adult SMA Patients by Different Tools

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**Introduction:** Clinical data of nusinersen in adults is sparse and needs alternative tools other than HFMSE.

**Objectives:** To show the efficacy of nusinersen by different tools in adult SMA patients.

**Methods:** The outcome was assessed by HFMSE, MRC-SS, ALSFRS-R and 6-MWT at five different time points.

**Results:** Thirty-two patients were analyzed. Twenty-three patients improved by HFMSE at least 3-points after loading doses. There was a significant HFMSE increase in type 3 at each time point, whereas type 2 patients benefited from loading doses and subsequently stay stable. Motor improvement was positively correlated with baseline scores. There was a correlation between ALSFRS-R and HFMSE scores. Even ambulatory patients who could not show a 3-points increase by HFMSE, had more than 30m improvement by 6-MWT. Overall, 78% of patients have responded to treatment according to HFMSE or 6-MWT.

**Conclusions:** ALSFRS-R and 6-MWT may be alternative tools to monitor nusinersen effect.

Abstract #606

## Efficacy of Efgartigimod in Clinical Practice: A Southwestern United States Perspective

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**INTRODUCTION:** Efgartigimod alfa-fcab is the first-in-class FcRn antagonist approved for treatment of acetylcholine receptor antibody-positive generalized myasthenia gravis (AChR+ gMG). Patients receive an initial 4-infusion treatment cycle with subsequent variability in treatment cycles.

**OBJECTIVE:** Describe clinical response to first treatment cycle in AChR+ gMG patients across four academic centers in Southwestern United States.

**METHODS:** Retrospective case series. Inclusion criteria: Patients with AChR+ gMG, completed first treatment cycle, and documented Myasthenia Gravis Activities of Daily Living (MG-ADL) score pre- and post-treatment cycle. Information regarding MG history, MG treatment(s) immediately prior to efgartigimod start, MG-ADL and other MG-specific outcome measures, laboratory data and adverse events will be discussed.

**RESULTS:** Twenty-two patients have completed at least one treatment cycle at our centers. Data collection and analyses are pending IRB approvals at each site.

**CONCLUSIONS:** Our experience suggests clinical improvement trends may not mirror findings of the pivotal trial.

Abstract #608

## Results from STARFiSH: The Study of Testosterone and rHGH in FSHD

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**Introduction:** Testosterone combined with recombinant human growth hormone (rHGH) (combination therapy) synergistically improves respiratory function, lean body mass, protein synthesis, strength, and aerobic endurance in healthy adult populations.

**Objectives:** To determine the safety and tolerability of daily rHGH combined with biweekly testosterone injections in ambulatory men with FSHD.

**Methods:** Subjects received 24-weeks of combination therapy followed by a 12-week washout period. We collected safety and pharmacokinetics data and recorded changes in body composition, functional status, and disease-burden (FSHD-HI).

**Results:** Nineteen participants completed the study with no participants experiencing a serious adverse event. At 24 weeks, six minute walk distance increased by 37.3 meters ( $p=0.0007$ ), lean body mass improved by 2.2 kg ( $p<0.0001$ ), and total disease burden (FSHD-HI) decreased by 19% ( $p=0.04$ ).

**Conclusions:** Combination therapy was safe and well-tolerated and may improve function, muscle mass, and disease burden in FSHD. Placebo-controlled trials are needed to further investigate this therapeutic approach.

Abstract #612

## Exon skipping: The molecular mechanism underlying KIF5A-linked ALS pathogenesis?

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Single nucleotide variants in the cargo-binding domain of KIF5A, a neuronal motor protein involved in transport along microtubules, have been linked to ALS. Specifically, the variants are clustered near exon 27 splice-site junctions. To determine potential RNA splicing defects, we performed multiplexed digital PCR to quantify KIF5A mRNAs in HEK293 cells and calculated exon 27 incorporation rates for each variant. We showed that 5' splice-site (5'ss) variants selectively result in exon 27 exclusion. We further confirmed this result in CRISPR-edited human iPSCs differentiated into motor neurons. In a mouse model of one 5'ss variant, we observed a decrease in Kif5a protein expression in addition to RNA mis-splicing, implicating disrupted transcription and translation in KIF5A-linked ALS pathogenesis. We hypothesize that 5'ss variants in KIF5A selectively disrupt consensus splice sequences where crucial ribonuclear proteins – such as U1 RNP – bind, leading to exon exclusion from RNA, altered protein, and eventually ALS.

Abstract #613

## A Qualitative Patient Experience Study of Eteplirsen Treatment for Duchenne Muscular Dystrophy

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**Introduction:** Eteplirsen is indicated for patients with Duchenne muscular dystrophy (DMD) with exon 51 skip-amenable mutations.

**Objectives:** Explore changes that eteplirsen-treated patients experienced in health-related quality of life (HRQoL), physical functioning, and activities of daily living (ADLs).

**Methods:** Fifteen caregivers of males with DMD were interviewed.

**Results:** Caregivers of ambulatory children reported improvements or maintenance since eteplirsen initiation in walking (n=7/9), running (n=6/9), and using stairs (n=4/9). Half of caregivers (n=7/15) reported improvements or maintenance in fine-motor movements; 1 caregiver (non-ambulatory) reported a continued decline. Improvements or maintenance in ADLs were reported in the total sample, as well as in fatigue (n=9/15), muscle weakness (n=7/15), and pain (n=6/15). Caregivers perceived maintenance as a positive outcome (n=6/9). Improvements generally occurred within 6 months post-eteplirsen initiation.

**Conclusions:** Most caregivers observed improvements or maintenance in aspects of their child's HRQoL, physical functioning, or ADLs since eteplirsen initiation.

**STUDY SUPPORT:** This study was funded by Sarepta Therapeutics, Inc.

**DISCLOSURES:** This study was funded by Sarepta Therapeutics, Inc. **CM, IS, and JI** are employees of Sarepta Therapeutics, Inc., and may own stock/options in the company. **CJ, HK, and SM** are employees of and own stock in Clarivate. Clarivate provides consultancy to various pharmaceutical and biotech companies, including Sarepta. **CT-R** reports consulting fees (Avexis, Biogen, Sarepta Therapeutics, Inc.) and site investigator for clinical trials: Avexis, Biogen, Cytokinetics, Genzyme, Pfizer, PTC, Roche, Sarepta, Scholar Rock. Previously presented at the Virtual ISPOR Europe 2021, November 30–December 3, 2021, and the Academy of Managed Care & Specialty Pharmacy (AMCP) Annual Meeting, March 29–April 1, 2022; McCormick Place Convention Center; Chicago, IL.



Abstract #614

## Safety, $\beta$ -Sarcoglycan Expression, and Functional Outcomes From Systemic Gene Transfer of rAAVrh74.MHCK7.hSGCB in LGMD2E/R4

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**Introduction:** Limb-girdle muscular dystrophy type 2E/R4 (LGMD2E/R4) is caused by mutations in the  $\beta$ -sarcoglycan gene.

**Objectives:** Report results from the phase 1/2 trial (NCT03652259) evaluating SRP-9003, a self-complementary rAAVrh74.MHCK7.hSGCB construct designed to restore SGCB protein production in patients with LGMD2E/R4.

**Methods:** Patients received single-dose of SRP-9003 IV infusion: Cohort 1 (n=3),  $1.85 \times 10^{13}$  vg/kg; Cohort 2 (n=3),  $7.41 \times 10^{13}$  vg/kg. Endpoints included safety, SGCB protein expression, and timed function tests.

**Results:** We report Year 3 (Y3; Cohort 1, n=3) and Year 2 (Y2; Cohort 2, n=2) results. SRP-9003 was well tolerated; adverse events occurred early and were manageable. Immunofluorescence showed robust SGCB expression post treatment maintained to Y2 in both cohorts. Improvements at or over baseline were demonstrated in timed function tests, which were generally sustained at Y3 in Cohort 1 and Y2 in Cohort 2.

**Conclusions:** These data suggest sustained efficacy of SRP-9003 therapy, supporting advancement of the clinical development program.

**FUNDING:** This study was funded by Sarepta Therapeutics, Inc.

**DISCLOSURES:** LRRK, ERP, SL, DAG, ASM, SN, and XL are or have been employees of Sarepta Therapeutics, Inc, and may own stock in the company. LNA and LPL received fees from Sarepta Therapeutics, Inc, for licensure of the LGMD natural history data set. JRM received financial support from Sarepta Therapeutics, Inc, for the travel to meetings to present any products sponsored by Sarepta. BS, KJL, KC, NFR, and MAI have no conflicts to disclose. Product is investigational only. Previously presented at the Muscular Dystrophy Association Clinical & Scientific Conference, March 13–16, 2022, Nashville, TN, the 2022 Academy of Managed Care & Specialty Pharmacy (AMCP) Annual Meeting, March 29–April 1, 2022, Chicago, IL, and the 14th Congress of the European Paediatric Neurology Society, 28 April–2 May 2022, Glasgow, Scotland, UK.

Abstract #618

## Switching from alglucosidase alfa to avalglucosidase alfa: Baseline data from the Pompe Registry

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**Introduction:** Avalglucosidase alfa has received marketing authorization in several countries for Pompe disease.

**Objectives:** To characterize Pompe Registry patients who switched to avalglucosidase alfa.

**Methods:** Eligible participants had  $\geq 1$  alglucosidase alfa record immediately preceding switch to avalglucosidase alfa. Demographics, treatment duration/dose, and respiratory, ambulatory, and biomarker measures are summarized at switch.

**Results:** Through 01 April 2022, 41 participants (1[2.4%] IOPD/40[97.6%] LOPD; 37[90.2%] USA/4[9.8%] Europe; 21[51.2%] male) switched at a mean age of 49.0 (range 7.3–83.0) years; 29 (70.7%) had  $\geq 5$  years of alglucosidase alfa. The most common dose was 14–27 mg/kg/2 weeks for both alglucosidase alfa pre-switch (72.5%) and avalglucosidase alfa post-switch (78.0%). Baseline parameters (mean $\pm$ SD) were 56.2 $\pm$ 22.39% for FVC(Upright) %predicted, 353.0 $\pm$ 159.47 meters for 6MWD, 11.7 $\pm$ 25.48 mmol/mol urine hexose tetrasaccharide, and 596.8 $\pm$ 460.36 U/L serum creatine kinase.

**Conclusions:** Pompe Registry post-switch patient data will support future studies of avalglucosidase alfa respiratory, ambulatory, and biomarker effectiveness in the real-world setting.

Funding: Sanofi

Type of study: Industry-sponsored

Abstract #620

## LONG-TERM SAFETY, TOLERABILITY, AND EFFICACY OF EFGARTIGIMOD IN PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS: INTERIM RESULTS OF THE ADAPT+ STUDY

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**Introduction:** Efgartigimod is a human IgG1 antibody Fc-fragment that reduces pathogenic IgG autoantibody levels through neonatal Fc receptor blockade. Patients completing the phase 3 ADAPT study could enroll in the ADAPT+ long-term extension study.

**Objective:** To evaluate long-term safety and efficacy of efgartigimod.

**Methods:** Efgartigimod (10 mg/kg IV) was administered in cycles of once-weekly infusions for 4 weeks, with subsequent cycles initiated based on clinical evaluation.

**Results:** The most common adverse events were headache, nasopharyngitis, and diarrhea, which were mostly mild/moderate and occurred at frequency similar to ADAPT. Consistent improvements in MG-ADL and QMG (mean[SE] decrease at week 3 of cycles 1-5: -5.5(0.34) and -4.7(0.44), respectively) scores were observed during each cycle, mirroring repeatable reductions in total IgG and anti-AChR autoantibody levels.

**Conclusion:** These analyses suggest long-term efgartigimod treatment results in consistent reductions in IgG antibody levels and repeatable improvement in function and strength, with no new safety signals identified.

## DISCLOSURES

**RM** has received consulting fees/honoraria or support for meeting participation from Alexion Pharmaceuticals, argenx BV, Ra Pharmaceuticals, Biomarin, Catalyst, UCB, TEVA, Merck, Roche, and Biogen.

**VB** has received research support from CSL, Grifols, UCB, Bionevia, Shire, and Octapharma.

**TV** has served as a speaker for Alexion, argenx, CSL Behring, and Allergan/Abbvie. He performed consulting work for argenx, Alexion, and UCB, and participated in trials in MG sponsored by Alexion, argenx, Ra/UCB, Horizon/Viela Bio, Regeneron, Janssen/Momenta, Cartesians Therapeutics, and Sanofi.

**CK** served as a deputy editor for *Neurology* and as a consultant for Acceleron Pharma, Inc, Akcea Therapeutics, Alnylam Pharmaceuticals, Inc, argenx, Biogen, CSL Behring, and Sanofi Genzyme. Dr Karam has received personal compensation for speaking engagements from Akcea Therapeutics, Alnylam Pharmaceuticals, Inc, CSL Behring, and Sanofi Genzyme and research/grant support from Akcea Therapeutics and Sanofi Genzyme.

**SP** reports following conflicts of interest, all outside this work: receiving lecture honoraria from Pfizer, Teva Actavis, Berlin Chemie Menarini, Mylan, Worwag, Adoc, and Salveo; research grants from Kedrion and Octapharma; consultant fees from argenx and Mylan; and travel grants from Octapharma, Kedrion, Teva Actavis, Sanofi Genzyme, Pfizer, Roche, Adoc, and Berlin Chemie Menarini; and reports no other conflicts of interest outside or related to this work.

**JLDB** has served as a consultant for argenx, Alexion Pharmaceuticals, CSL, UCB Pharma, Alnylam, and Orion Pharma.

**HM** has served as a consultant for Alexion Pharmaceuticals, argenx, and UCB. He received speaker honoraria from Japan Blood Products Organization and Chugai Pharmaceutical, and received research support from the Ministry of Health, Labour and Welfare of Japan.

**AM** received speaker honoraria from Alexion, argenx, Grifols, and Hormosan; honoraria from Alexion, UCB, Jansen, and Vitaccess for consulting services; and financial research support from Octapharma and Alexion. He is chairperson of the medical advisory board of the German Myasthenia Gravis Society.

**SB** reports research grants from AB Science, Alexion, Amylyx, argenx, Healey ALS Center-MGH, Janssen, Sanofi, and UCB Pharma and honoraria for consulting or speaking from Alexion, Alnylam, argenx, CSL Behring, Grifols, Janssen, Mitsubishi Pharma, Octapharma, Pfizer, and Takeda.

**MP** has served as a medical advisor or consultant for CSL Behring, Momenta, Alexion Pharmaceuticals, argenx BV, Zwijnaarde, Belgium, Catalyst Pharmaceuticals, and Terumo BCT.

**AG, PU, BVH, and CT** are employees of argenx.

**KU** has served as a paid consultant for argenx, Ra Pharma, UCB Pharma, Janssen Pharma, Viela Bio, Chugai Pharma, and Mitsubishi Tanabe Pharma and has received speaker honoraria from argenx, Alexion Pharmaceuticals, and the Japan Blood Products Organization.

**JV** receives financial support from the Target to B consortium and Prinses Beatrix Spierfonds; has been involved in trials or consultancies for argenx, Alexion, and NMD Pharma; and is coinventor on patent applications based on MuSK-related research. The LUMC received royalties from IBL and funding from argenx for MG research. All reimbursements were received by the LUMC. The author is a member of the European Reference Network for Rare Neuromuscular Diseases.

**JFH** has received research support (paid to his institution) from Alexion Pharmaceuticals, Inc, argenx BV, Cartesian Therapeutics, the Centers for Disease Control and Prevention, Myasthenia Gravis Foundation of America, Muscular Dystrophy Association, National Institutes of Health (including the National Institute of Neurological Disorders and Stroke and the National Institute of Arthritis and Musculoskeletal and Skin Diseases), Patient-Centered Outcomes Research Institute, Ra Pharmaceuticals Inc (now UCB), and Takeda Pharmaceuticals; honoraria from Alexion Pharmaceuticals, Inc, argenx BV, Immunovant, Inc, Ra Pharmaceuticals Inc (now UCB), Regeneron Pharmaceuticals Inc, Sanofi US, and Viela Bio, Inc (now Horizon Therapeutics plc); and nonfinancial support from Alexion Pharmaceuticals, Inc, argenx BV, Ra Pharmaceuticals Inc (now UCB), and Toleranzia AB.

Abstract #622

## Treatment of active idiopathic inflammatory myositis by inhibiting FcRn: Pre-registration report of ALKIVIA, a phase 2/3 trial with efgartigimod

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**Background:** Idiopathic inflammatory myositis (IIM) is a potentially IgG-mediated group of diseases that targets muscle, skin, and other organs. Efgartigimod (EFG), an engineered Fc fragment that inhibits activity of the neonatal Fc receptor, will be studied as a therapy for IIM in a Phase 2/3 randomized, double-blind, placebo-controlled ALKIVIA trial.

**Objective:** To evaluate the efficacy and safety of EFG PH20 subcutaneous (SC) treatment compared with placebo in IIM, in addition to standard-of-care therapy.

**Methods:** ALKIVIA includes two independent stages – a proof-of-concept (24-week) Phase 2 and a confirmatory (52-week) Phase 3 stage. Randomized participants will receive EFG PH20 1000 mg or placebo PH20 SC weekly, added to standard-of-care. Immune-mediated necrotizing myopathy, dermatomyositis, or polymyositis (including antisynthetase syndrome) subtypes will be included in the study.

**Results:** The primary endpoint is total improvement score at weeks 24 (Phase 2) and 52 (Phase 3).

### Conclusion:

ALKIVIA will evaluate three IIM subtypes that are potentially IgG-mediated.

### Disclosures

<b>Rohit Aggarwal</b>	<b>Consultant:</b> argenx
<b>Anthony A. Amato</b>	<b>Medical Advisory Boards / Consultant:</b> Abcuro, argenx, Ra Pharmaceuticals, Horizon Therapeutics, OnoPharma, Alexion, EMD Serono, Takeda, Johnson & Johnson (COVID-19 vaccination program) CDC.
<b>Despoina Papadopoulou</b>	Employee of argenx
<b>Bas van der Woning</b>	Employee of argenx
<b>Paul Duncombe</b>	Contractor to argenx
<b>Ingrid E. Lundberg</b>	<b>Consultant:</b> Corbus Pharmaceuticals; Research grants: AstraZeneca; <b>Advisory boards:</b> AstraZeneca, Bristol Myers Squibb, Corbus Pharmaceutical, EMD Serono Research & Development Institute, argenx, Octapharma, Kezaa, Janssen, Pfizer <b>Stock shares:</b> Roche, Novartis

Abstract #633

## The potential for remote aerobic exercise monitoring in people with neuromuscular disease – an example from experience with Parkinson disease

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**Purpose:** Regular aerobic exercise (AE) may alter the progression of neuromuscular disease (NMD)<sup>1</sup>. In-home virtual platforms may facilitate AE and allow monitoring for researchers and clinicians. As an example of potential feasibility in NMD, we present our data from in-home monitoring of AE behavior in people with Parkinson Disease (PwPD).

**Participants:** 81 PwPD [52(64%) male, age 64.±8.4 yrs; mild to moderate PD.

**Methods:** Goal AE dosage was cycling >20min, 3x/week x 12-months with virtual coaching. Successful monitoring of AE behavior was defined as the recording of summary exercise data.

**Results:** Over 9,100 exercise sessions were recorded. Ride duration ranged from 5->60 minutes. Participants completed 92.84% of the prescribed 150 rides (mean/SD 129.26±53.36).

**Conclusion:** Over a 1-year period, virtual AE monitoring was successfully implemented in a chronic neurologic disease sample. These results demonstrate potential feasibility for use in long-term (>6 mo) studies of exercise effects on individuals with NMD.

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Abstract #637

Evaluating the Efficacy and Safety of Tofersen in Adults with ALS and a *SOD1* Mutation:  
Results from the Phase 3 VALOR Trial and Open-Label Extension

**Authors:** A. Chiò, T.M. Miller\*, M.E. Cudkowicz\*\*, A. Genge\*\*\*, P.J. Shaw\*\*\*\*, G. Sobue\*\*\*\*\*, T. Cochrane\*\*\*\*\*,  
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Fradette,\*\*\*\*\* on behalf of The VALOR and OLE Working Group (Turin, Italy; St. Louis, MO\*; Boston, MA\*; Montreal,  
QC, Canada\*\*; Sheffield, UK\*\*\*; Aichi, Japan\*\*\*\*; Cambridge, MA\*\*\*\*\*; Maidenhead, UK\*\*\*\*\*)

**Presenting author:**

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**Abstract:**

**Introduction:** Tofersen (BIIB067) is an investigational drug for amyotrophic lateral sclerosis associated with mutations in the *SOD1* gene (*SOD1*-ALS).

**Objectives:** The Phase 3 trial (VALOR) and its ongoing open-label extension (OLE) evaluated efficacy and safety of tofersen.

**Methods:** 108 adults were randomized in VALOR 2:1 to intrathecal tofersen 100 mg or placebo; 95 subsequently enrolled in the OLE. By January-2022, all participants had opportunity for 12 months of follow-up from VALOR baseline.

**Results:** Tofersen produced sustained reduction of total CSF *SOD1* protein and neurofilament levels. Early tofersen initiation resulted in less decline across clinical and patient-reported measures compared with delayed initiation. Preliminary data suggest a reduction in risk of death and death or permanent ventilation. Most adverse events were mild/moderate. Serious neurologic events, including myelitis, aseptic meningitis, and papilloedema, were observed.

**Conclusions:** Longer-term integrated data from VALOR and its OLE suggest meaningful biological and clinical disease-modifying effects of tofersen.

Abstract #655

## Development and evaluation of virtual pilates group for people with channelopathies

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**Background:** Muscle ion channelopathies are rare conditions where weakness, paralysis and/or muscle stiffness (myotonia) can be caused either by movement or following rest after exercise. People with channelopathies may be able to move normally between episodes or when warmed up, making it difficult for others to be able to understand the challenges related to exercise and activity.

Pilates is an exercise approach that focuses on controlled, repetitive movements, supporting individuals to optimise stability and strength especially around the core muscles and pelvis. This approach has been well received at patient engagement events, as well as YouTube videos developed for people with Neuromuscular conditions.

People with a channelopathy attending a specialist clinic expressed an interest in joining Pilates groups, but had found local groups inaccessible as the pace, and set up of classes often aggravated symptoms causing pain and/or weakness.

With increased isolation and new options for remote healthcare options following Covid-19 restrictions, there was an opportunity to trial a video Pilates group for people with channelopathies.

### **Aims:**

1. To develop and evaluate a video pilates class for people with paramyotonia congenita (PMC)
2. To develop and evaluate a video pilates class for people with Andersen Tawil syndrome (ATS)

**Methods/Materials:** individual pre group assessments allowed participants to identify priorities, and to select individual outcome measures or targets. Group sessions were designed around individual group members feedback, with evaluation and reflection at the end of each session which then informed the next session.

Groups consisted of six 60 minute sessions. Questionnaires were completed after the course of 6 sessions.

**Results:** Participants of the PMC group completed all sessions. 2 of 3 from the ATS group completed all sessions.

**Conclusion:** Participants participated in all sessions, increasing repetitions, difficulty of and numbers of exercises over the 6 sessions. Sessions were structured to allow individuals to exercise without developing pain or stiffness or weakness, focusing on a maximum of 2 to 4 repetitions for the PMC group.

Informal peer support and motivation were also reported to be beneficial by participants.

Results of the ATS group will be presented once analysed.



## Stratification of NMD and Outcome

Abstract #593 Platform Presenter

### Clinical trial readiness and validation of onsite and remote evaluation in valosin containing protein-associated multisystem proteinopathy

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**Introduction/Objective:** The purpose of our study was to validate functional and patient reported clinical outcome assessments (COA) in patients with valosin containing protein-associated multisystem proteinopathy (VCP-MSP), a rare multisystemic disorder. Disease onset and presentation is heterogeneous, highlighting the need for a prospective clinical trial readiness study to inform future clinical trial design.

**Methods:** Thirty-two subjects have enrolled to-date (mean age: 53.1 years (range: 28-73)). A battery of COA were completed both in a clinic setting and remotely in the patient's home.

**Results:** COA performance was correlated with disease duration and genotype but not with age at visit highlighting the variability in the relationship between genotype and phenotype in VCP-MSP. Test-retest reliability was excellent (ICC $\geq$ 0.8; P<0.001). Performance of most COA was the same across remote and onsite environments.

**Conclusions:** Cohort level feasibility and cross-sectional performance of all COA, sensitivity to change and meaningful change on included assessments over 1-year will also be presented.

Abstract #545 Flash Presenter

## Motor Outcomes to Validate Evaluations in Facioscapulohumeral muscular dystrophy (MOVE FSHD): Protocol for an observational study.

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**Introduction:** The MOVE FSHD study aims to determine the predictive value of clinical and motor assessments, patient-reported outcomes, imaging, and tissue biomarkers on disease progression in FSHD.

**Objectives:** Evaluate 450 FSHD participants over three years with 200 participating in an MRI and muscle biopsy sub-study to validate FSHD evaluations.

**Methods:** Annual visits collect FSHD history, physical examination, patient reported outcomes, strength, timed functional tasks, and respiratory parameters. Sub-study participants will have additional biomarkers collected, including whole-body MRI at Baseline and 12-month visits with muscle biopsy occurring at Baseline and (n=40) at 4-month visits.

**Results:** MOVE FSHD study has over 175 participants across 12 US sites who have completed their Baseline visit and has begun enrolling sub-study participants.

**Conclusions:** MOVE FSHD addresses barriers to clinical trials by validating motor, clinical, and patient reported outcomes, as well as potential biomarkers. The data from MOVE FSHD can also improve our understanding of FSHD and directly impact patient care.

**Funding:** Grants from FSHD Society, Friends of FSH Research, FSHD Canada, and Avidity Biosciences.

**References:** Statland JM, Tawil R. Facioscapulohumeral Muscular Dystrophy. *Continuum (Minneapolis, Minn)*. 2016;22(6, Muscle and Neuromuscular Junction Disorders):1916-31. Epub 2016/12/07. doi: 10.1212/CON.0000000000000399. PubMed PMID: 27922500; PMCID: PMC5898965.

Abstract #590 Flash Presenter

## Towards digital monitoring of Amyotrophic Lateral Sclerosis (ALS) patients: a deep learning-based application to assess the evolution of dysarthria via the analysis of multimedia data

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Emanuele Frontoni is with the Department of Political Sciences, Communication, and International Relations of Università Degli Studi di Macerata (Macerata, Italy), with AIDAPT S.r.l (Ancona, Italy) and NeMo Lab (Milano, Italy)

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**INTRODUCTION:** Dysarthria is among the onset symptoms of bulbar ALS and, although its evolution correlates with other bulbar signs' decline, it is still a poorly characterized condition in literature<sup>1</sup>.

**OBJECTIVE:** Based on Dysarthria Robertson's Profile (DRP), this work's aim is identifying new indices for assessing dysarthria progression from multimedia data analysis acquired via a remotely-usable digital tool based on a web-application (app) for smartphones.

**METHODS:** The app guides bulbar-onset ALS patients in performing DRP's verbal and motor tasks while recording audio and video through the smartphone's microphone and camera. Deep-learning algorithms process the acquired data and quantify patients' performance.

**RESULTS:** We delivered the app to 12 patients and compared the per-task app-outcome with the respective DRP-score. As a sample of result, app-outcomes show a correspondence with clinician's DRP-scores when assessing fatigability in diadochokinesis tasks.

**CONCLUSIONS:** The tool may support clinicians in early identification of dysarthria's progress enabling them to timely identify changes in disease trajectory.

<sup>1</sup> Green, Jordan R., et al. Bulbar and speech motor assessment in ALS: Challenges and future directions (2013).

Abstract #504

## Muscle Structure, Function, and Gait Patterns in Distal Hereditary Motor Neuropathy and the Effect of Carbon fiber Ankle Foot Orthosis on Gait

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**Introduction:** Distal Hereditary Motor Neuropathy (dHMN) is an inherited neuromuscular disorder characterised by distal weakness. It is a disabling condition and eventually many patients need aids to walk. Research is needed to understand the muscle impairments that lead to altered gait patterns, and to develop interventions to correct walking gait conservatively. The preliminary data presented here focuses on relationships between intramuscular fat infiltration, muscle strength and gait. We also explored the effect of bilateral carbon fibre ankle foot orthoses (AFO) on gait of people with DHMN.

### Methods:

Participants: Eight people with dHMN.

Outcome measures: Intramuscular fat measured by MRI using modified Mercuri muscle grading scale. Isokinetic and isometric ankle muscle strength measured by a Humac Norm Testing & Rehabilitation System. Spatiotemporal parameters of gait measured by 3D gait analysis.

Rehabilitation Interventions: Carbon fiber Ankle foot orthosis, bilateral.

Statistical analysis: The collected data was analysed to explore the relationship between Intramuscular fat infiltration and muscle function using Spearman test, and to investigate effect of bilateral carbon fibre ankle foot orthoses on gait using paired T-test.

### Results:

- Summary of participants characteristics and study preliminary results are given in table1.
- MRI T1-weighted cross-sectional scan at the calves' level showed involvement of calves' muscles mostly at the posterior compartment (planter flexors) (table1).
- The stride length has a moderate to strong correlation with the Soleus Muscle fat infiltration; 0.601(P= 0.1153) and 0.715 (P= 0.0461) for the right and left side respectively (table2). However, the correlation with other planter flexor muscles was weak to very weak (<0.5). Correlation of stride length with planter flexors isometric torque values was higher than the isokinetic.
- The gait significantly improved with using AFO in speed (P=0.0266). Step length (P=0.0032), stride length (P=0.0031), and the stance phase duration (P=0.0395). However, this improvement was shown on the right side only and this could be due to the small sample, but we also experienced some visibility issues of the left side and the lab settings (table3).
- 

### Conclusions:

We present a dHMN cohort showing greater plantar flexor muscle weakness. This was associated with reduced ankle torque and stride length. Variation existed between cases, however, with differences in ankle strength and MRI findings, indicating that this is not a homogenous group of diseases. The study preliminary results suggest that carbon fibre ankle foot orthoses can compensate for calf weakness and improve gait of people with DHMN. Results also showed that 3D gait analysis is a valuable tool for research to measure gait spatiotemporal parameters.

Table1: Summary of participants characteristics and study results		R	L
Demographics	Numbers	8	
	Gender (Male/Female)	(5/3)	
	Age; mean years; range	58 (44/75)	
	Genetic diagnosis (HSPB1/unknown)	(4/4)	
	CMTES; mean (SD)	5.25(2.8)	
	Walk-12 questionnaire; mean (SD)	32(10.8)	
Manual muscle testing	DF MRC; mode; range	4- (1-5)	4+ (1-5)
	PF MRC; mode; range	4+ (1-5)	4+ (1-5)
Dynamometry	DF isokinetic mean (SD), N/m	14(8.2)	19.25(7.6)
	PF isokinetic mean (SD), N/m	22.1(23.6)	18.4(14.7)
	DF isometric 10° mean (SD), N/m	15.9(19.9)	16.7(18.6)
	DF isometric 30° mean (SD), N/m	19.5(17.8)	23.6(20)
	PF isometric 10° mean (SD), N/m	34(23.8)	32.7(15.9)
Calf MRI: Modified Mercuri's scale for Muscle grading	Anterior Tibial Muscle; mode; range	1 (0-3)	1 (0-3)
	Extensor Digitorum Longus; mode; range	2a (0-3)	1 (0-3)
	Extensor Hallucis Longus; mode; range	2a (0-3)	1 (0-3)
	Long Fibular Muscle; mode; range	1 (0-4)	2a (0-4)
	Medial Gastrocnemius; mode; range	3 (2a-4)	2b (2a-4)
	Lateral Gastrocnemius; mode; range	1(0-3)	1 (1-3)
Gait Parameters	Soleus Muscle; mode; range	2a (2a-4)	3 (1-4)
	Speed; mean (SD), m/s	1.1(0.2)	1.1(0.2)
	Stride Length; mean (SD), m	1.2(0.2)	1.3(0.2)
	Stride Time; mean (SD), s	1.1(0.06)	1.1(0.05)
	Strides/Minute; mean (SD)	53(3.3)	52.4(2.4)
	Step Length; mean (SD), m	0.6(0.1)	0.6(0.1)
	Step Time; mean (SD), s	0.6(0.03)	0.6(0.02)
	Steps/Minute; mean (SD)	106.1(6.7)	104.8(4.7)
	Percent Stance; mean (SD), %	0.62(0.01)	0.6(0.02)
Gait Parameters with AFO	Speed; mean (SD), m/s	1.2(0.2)	1.2(0.2)
	Stride Length; mean (SD), m	1.3(0.2)	1.3(0.9)
	Stride Time; mean (SD), s	1.1(0.1)	1.1(0.09)
	Strides/Minute; mean (SD)	52.7(3.6)	52.9(4)
	Step Length; mean (SD), m	0.7(0.09)	0.7(0.09)
	Step Time; mean (SD), s	0.6(0.04)	0.6(0.04)
	Steps/Minute; mean (SD)	105.4(7.2)	105.8(8)
	Percent Stance; mean (SD), %	0.6(0.03)	0.6(0.03)

Modified Mercuri's scale: stage 0= normal appearance; stage 1= early moth-eaten appearance, with scattered small areas of increased signal; stage 2a= late moth-eaten appearance, with numerous discrete areas of increased signal with beginning confluence, comprising less than 30% of the volume of the individual muscle; stage 2b=late moth-eaten appearance, with numerous discrete areas of increased signal with beginning confluence, comprising 30 – 60% of the volume of the individual muscle; stage 3= washed-out appearance, fuzzy appearance due to confluent areas of increased signal; stage 4= end stage appearance, muscle replaced increased density connective tissue and fat, with only a rim of fascia and neurovascular structures distinguishable; N; Newtons; m; meters; s, seconds; R, right; L, left; DF, Ankle Dorsiflexion; PF, Ankle plantarflexion; MRC, medical research council scale; SD, standard deviation; CMTES, CMT examination score; HSPB1, Heat-Shock 27-KD Protein 1.

**Table2: Correlation coefficient of Plantarflexion parameters**

	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
Stride Length	0.601	0.715	0.469	0.469	-0.1	-0.17	0.5	0.386	0.476	0.548
PF isokinetic dynamometer	-0.1	0.013	-0.136	0.144	-0.601	-0.106			0.619	-0.024
PF isometric dynamometer	-0.15	0.281	-0.309	-0.086	-0.751	-0.509	0.619	-0.024		
1                      0                      -1 	Soleus Muscle FI		Medial Gastrocnemius FI		Lateral Gastrocnemius FI		PF isokinetic dynamometer		PF isometric dynamometer	

Correlation represented by R values between 0.0 and .030 are very weak, 0.30 to 0.50 are weak, 0.50 and 0.70 are moderate, 0.70 and 0.90 are strong, and 0.90 and 1.00 are very strong. FI, fat infiltration; DF, Ankle Dorsiflexion; PF, Ankle plantarflexion.

**Table3: The effect of AFO on Gait Parameters**

Parameters	Mean difference (±SD)		P- value		95% CI of difference	
	Right	Left	Right	Left	Right	Left
Speed, m/s	0.09154 (0.09252)	0.05463 (0.1618)	0.0266	0.3713	0.01419 to 0.1689	-0.08062 to 0.1899
Stride Length, m	0.1108 (0.07086)	0.05338 (0.1391)	0.0031	0.3138	0.05151 to 0.1700	-0.06294 to 0.1697
Stride Time, s	0.007500 (0.03872)	-0.006042 (0.05850)	0.6008	0.7787	-0.02487 to 0.03987	-0.05495 to 0.04287
Strides/Minute	-0.3397 (1.8169)	0.4825 (2.7257)	0.6133	0.6319	-1.8587 to 1.1792	-1.7962 to 2.7613
Step Length, m	0.05517 (0.03546)	0.02683 (0.06948)	0.0032	0.3108	0.02552 to 0.08481	-0.03125 to 0.08492
Step Time, s	0.003667 (0.01940)	-0.003125 (0.02927)	0.6095	0.7715	-0.01255 to 0.01989	-0.02760 to 0.02135
Steps/Minute	-0.6792 (3.6338)	0.9650 (5.4517)	0.6134	0.632	-3.7171 to 2.3588	-3.5927 to 5.5228
Percent Stance, %	-0.01825 (0.02043)	-0.02288 (0.02502)	0.0395	0.0362	-0.03533 to -0.001167	-0.04379 to -0.00198

Difference is significant when the P-Value is less than 0.05 (p<0.05). m; meters; s, seconds; SD, standard deviation; CI; confidence interval.

Abstract #509

### vCMTES: a validated virtual evaluation for Charcot-Marie-Tooth patients

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**Introduction:** COVID-19 pandemic highlighted the need for reliable scales for remote evaluations of Charcot Marie Tooth (CMT) disease patients unable to travel to clinics because of their disabilities, distance, financial concerns or other reasons.

**Objective:** To demonstrate the validity and reliability of vCMTES

**Methods:** We modified the CMT Examination Score (CMTESv2) replacing the pinprick and vibration items with light touch and position sense, which can be performed by the patient on his own or with assistance remotely. We developed a standardized protocol. We then evaluated patients in person and remotely.

**Results:** Sixty-four patients with CMT were evaluated with CMTESv2 and vCMTES. CMTESv2 correlates strongly with the vCMTES in person and virtually. Test-retest analysis showed good results.

**Conclusions:** All the statistical analyses showed that the vCMTES is valid and reliable as a clinical outcome assessment for CMT. Further studies are needed to test responsiveness to change and progression in different subtypes.

Abstract #513:

## Description of Motor Function Test and Parent Report of Gross Motor Abilities in Congenital Myotonic Dystrophy.

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**Introduction:** Congenital Myotonic Dystrophy (CDM) is a multi-systemic neuromuscular disorder with known cognitive and physical impairments. There is concern that these cognitive impairments impact individual's ability to reliability and accurately complete motor function tests (MFT).

**Objective:** Understand if motor performance measured by MFTs, is similar to caregiver's report of motor performance in the community.

**Methods:** Participants (n=29, age: 3-14 years) completed MFTs- four stair climb, 10m run, rise from floor and six-minute walk. Participants were allowed exceptions to standardized administration due to cognition and attention difficulties. Caregivers completed the gross motor domain of the Vineland Adaptive Behavior Scales (VABS) via clinical interview.

**Results:** The majority (93%) of participants were rated to have low to moderately- low adaptive gross motor skills by their caregivers and performed lower than age matched peers on MFTs.

**Conclusions:** Caregiver's rating of participants with CDM motor skills agree with performance on MFTs.



Abstract #523

## Evolving the multidisciplinary approach to whole genome sequencing analysis enhances precision genetic diagnostics

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**Introduction:** Diagnostic whole genome sequencing (WGS) is increasingly used in NMDs, though standard analysis may overlook diagnoses.

**Objectives:** We aimed to improve the WGS diagnostic rate by establishing an enhanced personalised approach to analysis.

**Methods:** 102 patients with suspected mitochondrial disease underwent WGS. Undiagnosed cases were reviewed by a clinician and bioinformatician enabling bespoke informatic approaches, co-ordinated phenotypic validation (e.g., pathology and radiology), and functional work.

**Results:** A ~two-fold increase in diagnostic rate was achieved (from 16.6 % to 31.3%) with strong candidate disease-causing variants in an additional 3.9% of patients. There were management implications for all new diagnoses including two patients becoming eligible for drug trials.

**Conclusions:** We demonstrate a new standardised model of care that supports neuromuscular clinicians to maximise the potential benefits from genomics. This research was made possible through access to the data and findings generated by the 100,000 Genomes Project.

Abstract #527

## Balance Confidence in Individuals with Charcot-Marie-Tooth

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**Introduction:** Balance and function impairment is common in individuals with Charcot Marie Tooth disease (CMT).

**Objectives:** The aim of this study was to evaluate the balance confidence, fall frequency, and perceived effect of AFOs on balance in individuals with CMT who use AFOs.

**Methods:** The Activities Specific Balance Confidence Scale (ABC) was distributed by email to individuals with CMT, through the Inherited Neuropathy Consortium Contact Registry.

**Results:** 306 individuals participated in this study. Participants reported decreased balance confidence across a range of activities. Many participants reported daily (14.1% of participants) or weekly (37.6% of participants) falls and 77.8% of participants indicated their AFOs improved their balance.

**Conclusions:** Results from this study will help to focus future studies to refine AFO design and prescription to better improve balance, reduce falls, and meet the needs of individuals with CMT.

Abstract #532

## High Frequency Remote Data Collection is Feasible and can Provide Novel Insights into Idiopathic Inflammatory Myopathy Disease Trajectory – Implications for Clinical Trials and Personalised Patient Care

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**Background:** Technological advances of wearables and ubiquity of smartphones provides the opportunity for remote collection of high-frequency data from patients with chronic muscle diseases, such as the idiopathic inflammatory myopathies (IIM).

**Objective:** To assess feasibility/acceptability of collecting daily symptom data and continuous gait pattern data in an IIM cohort.

### Methods:

Adult IIM patients were recruited to the study in 2019. Participants were asked to:

1. Complete daily patient-reported outcome measurements (PROMs) via a specially designed smartphone-based app for 91 days each (Table 1).
2. Continuously wear a single thigh-worn accelerometer sensor throughout the 91 day period (Figure 1).

**Results:** 21 participants submitted 22,880 individual PROMs (88% of potential total) and 42,308 hours of sensor data throughout the study (93% of potential). Individual patient data indicates ability to identify the start of a flare (Figure 2).

**Discussion:** Remotely collected high frequency data collection is feasible and facilitates insights into disease trajectory.

Table 1 - Question sets related to disease activity and impact, and their frequencies

Domain	Question stem	Answer scale	Answer anchors
<b>Daily data collection</b>			
<b>Global activity</b>	Considering all of the ways it affects you, how active do you feel your myositis is today?	VAS	“Not active” (0); “Very active” (100)
<b>Pain</b>	What is your overall level of pain today?	VAS	“No pain” (0); “Extreme pain” (100)
<b>Pain</b>	What is your level of pain due to myositis today?	VAS	“No pain” (0); “Extreme pain” (100)
<b>Fatigue</b>	How much fatigue do you feel today?	VAS	“No fatigue” (0); “Very severe fatigue” (100)
<b>Sleep</b>	How refreshed did you feel when you woke up for the day?	5 point Likert scale	“Not at all rested” “Slightly rested” “Somewhat rested” “Well-rested” “Very well-rested”
<b>Sleep</b>	How would you rate the quality of your sleep last night?	5 point Likert scale	“Very poor” “Poor” “Fair” “Good” “Very good”
<b>Weakness</b>	How weak do you feel today?	VAS	
<b>Mood</b>	How would you rate your mood today?	5 point Likert scale	“Poor” to “Excellent”
<b>Function</b>	Are you able to wash and dress yourself today?	Ordinal with checkbox	“Unable to do” “With some difficulty” “With much difficulty” “Without any difficulty”
<b>Function</b>	Are you able to walk outdoors on flat ground today?	Ordinal with checkbox	“Unable to do” “With some difficulty” “With much difficulty” “Without any difficulty”
<b>Function</b>	Are you able to walk up five steps today?	Ordinal with checkbox	“Unable to do” “With some difficulty” “With much difficulty” “Without any difficulty”
<b>Weekly data collection</b>			
<b>Flare occurrence</b>	Have you experienced a flare of myositis in the last seven days?	Dichotomous	Yes; no
<b>Function</b>	Have you been able to carry shopping bags in the last seven days?	Ordinal with checkbox	“Unable to do” “With some difficulty” “With much difficulty” “Without any difficulty”

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<b>Exercise</b>	Have you been able to exercise in the last seven days?	Ordinal with checkbox	“Unable to do” “With some difficulty” “With much difficulty” “Without any difficulty”
<b>Social interaction</b>	Have you been able to socialise in the last seven days?	Ordinal with checkbox	“Unable to do” “With some difficulty” “With much difficulty” “Without any difficulty”
<b>Function</b>	Have you been able to reach and get down a 5 pound object (such as a bag of sugar) from just above your head in the last seven days?	Ordinal with checkbox	“Unable to do” “With some difficulty” “With much difficulty” “Without any difficulty”
<b>Function</b>	Have you been able to bend down to pick up clothing from the floor in the last seven days?	Ordinal with checkbox	“Unable to do” “With some difficulty” “With much difficulty” “Without any difficulty”
<b>Employment status</b>	Are you currently employed (working for pay)?	Dichotomous	Yes; no
<b>Effect of myositis on employment</b>	Has your ability to work been affected by myositis in the last seven days?	Dichotomous	Yes; no
<b>Hours of employment missed due to myositis</b>	During the past seven days, how many hours did you miss from work because of problems associated with your myositis?	Numerical	
<b>Hours missed due to other reasons</b>	During the past seven days, how many hours did you miss from work because of any other reason, such as vacation, holidays, time off to participate in this study?	Numerical	
<b>Hours worked</b>	During the past seven days, how many hours did you actually work?	Numerical	
<b>Degree myositis affected work productivity</b>	During the past seven days, how much did your myositis affect your productivity while you were working?	VAS	Myositis had no effect on work (0); Myositis completely prevented me from working (100)
<b>Monthly data collection</b>			
<b>Function</b>	Health Assessment Questionnaire. Validated questionnaire comprising 23 item assessing physical function	Overall score of 0-3	

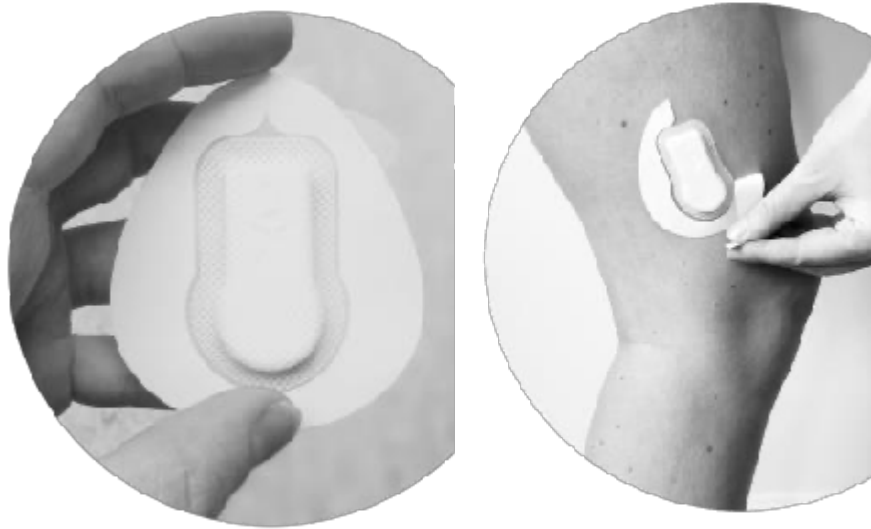


Figure 1 – Pictures of wearable sensor employed in study

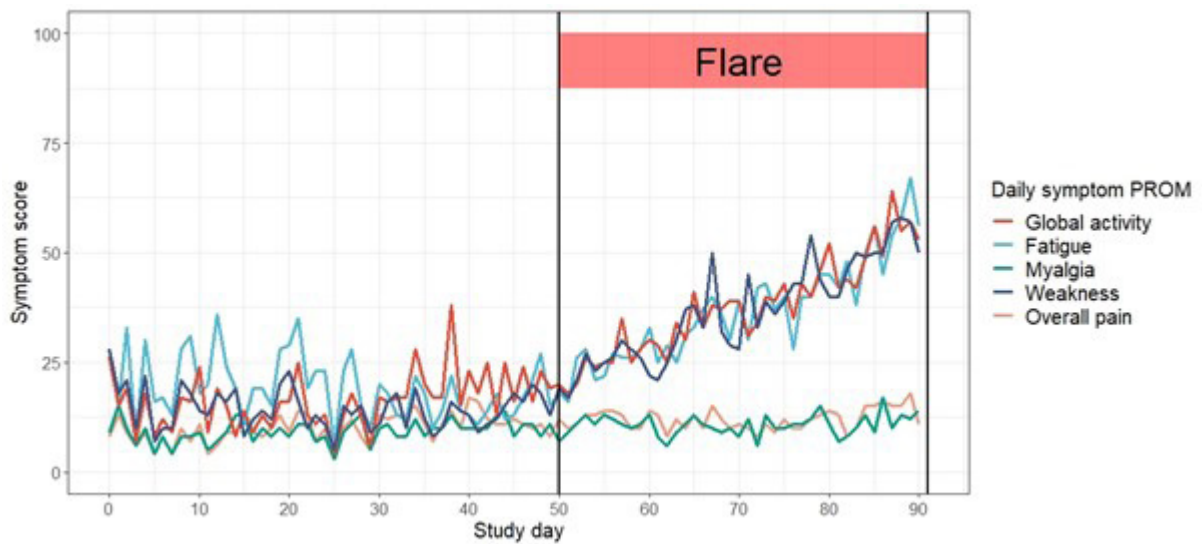


Figure 2 – Individual participant PROM data demonstrating ability to identify the start of a flare (study day 50) via increasing symptom scores (global activity, myalgia, weakness)

Abstract #533

## Assessment of muscle mass measurements by dual-energy X-ray absorptiometry (DEXA) as a correlate for muscle strength and function in facioscapulohumeral muscular dystrophy (FSHD)

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and the ReSolve Investigators of the FSHD CTRN.

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**Introduction:** FSHD is a progressive disease of skeletal muscle. DEXA is a widely available, cost-effective, and sensitive measure of whole body and regional lean tissue mass.

**Objectives:** Investigate the association between lean tissue mass measurements (composed of mainly muscle) and clinical outcomes assessments (COAs) in FSHD patients.

**Methods:** We obtained DEXA scans and COAs (i.e., 10-meter-walk-run) in 160 patients with FSHD at the baseline visit of the ReSolve study, a prospective, longitudinal, observational multisite study (NCT03458832).

**Results:** There was moderate correlation between arm strength measured by quantitative muscle testing and lean tissue mass of both upper extremities ( $\rho = 0.46-0.49$ ); moderate correlation between leg strength and lean tissue mass of each lower extremity ( $\rho = 0.61$ ); and moderate correlation between ambulatory COAs and lean tissue mass of lower extremities ( $\rho = 0.44-0.61$ ).

**Conclusions:** DEXA lean tissue mass may be a biomarker in FSHD clinical trials.

Abstract #535

## Morphological and quantitative imaging biomarkers obtained with high-field MRI in sciatic nerves of patients with CMT1A and controls

R.Sadjadi\*, B.Sveinsson\* (Boston,MA\*)

**Introduction:** There has been growing interest in developing more sensitive biomarkers to evaluate disease progression in peripheral nerve diseases such as Charcot-Marie-Tooth (CMT) disease.

**Objectives:** We explored combine morphological and quantitative imaging using 7T MRI in patients with CMT1A patients and healthy controls.

**Methods:** We used Double-Echo in Steady-State (DESS) 7T MRI sequence to assess T2 relaxation, apparent diffusion coefficient (ADC), and fat fraction (FF), in the lower right thigh of 6 patients and 6 age-matched controls. We obtained quantitative measurement from individual nerve fascicles of proximal and distal tibial and peroneal nerves.

**Results:** In addition to individual fascicle visualization, we get better quantitative assessment of sciatic nerve in patients and healthy controls. Nerve fascicles were significantly larger and had larger variability in diffusion and T2 measurement.

**Conclusions:** The study provides feasibility and further insight in the assessment of peripheral nerves as potential biomarkers.



Abstract #538

## Understanding falls in FSHD

Enrico Bugiardini<sup>1</sup>, Katy Eichinger<sup>2</sup>, Michael G Hanna<sup>1</sup>, Gita Ramdharry<sup>1</sup>, Michael McDermott<sup>2</sup>, Kiley Higgs<sup>3</sup>, Michaela Walker<sup>3</sup>, Leann Lewis<sup>2</sup>, Bill Martens<sup>2</sup>, Doris Leung<sup>4</sup>, Sabrina Sacconi<sup>5</sup>, Karlien Mul<sup>6</sup>, Valeria Sansone<sup>7</sup>, Elena Carraro<sup>7</sup>, Leo Wang<sup>8</sup>, Perry Shieh<sup>9</sup>, Bakri Elsheikh<sup>10</sup>, Samantha LoRusso<sup>10</sup>, Russell Butterfield<sup>11</sup>, Nicholas Johnson<sup>12</sup>, Chiara Frisoni<sup>7</sup>, Rabi Tawil<sup>2</sup>, Jeffrey Statland<sup>3</sup> and ReSolve Investigators of the FSHD CTRN.

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<sup>12</sup>Virginia Commonwealth University, VA, USA

**Background:** Patients with neuromuscular disease are at a risk of falls.

**Objective:** To assess prevalence and consequences of falls in a multicentre observational study in FSHD (ReSolve).

**Methods:** We administered a fall survey weekly for 12 weeks (Fsu) and a retrospective fall questionnaire (Fhx). Based on survey falls count, patients were classified as non-fallers, infrequent (n=1) or recurrent fallers (n>1). Patient reported outcomes (FSHD-HI and PROMIS57), manual muscle testing (MMT) and Motor Function Measurement (MFM) were compared between groups.

**Results:** Prevalence of falls was high (52% in Fhx, n=97; 36% in Fsu, n=132 respectively). Infrequent and recurrent fallers are weaker in proximal lower limbs and had a higher disease burden and motor impairments compared to non-fallers (FSHD-HI mean score 37.47, 41.15, 25.54 range 0-100; MFM 58.97, 53.85, 82.05, range 0-100; p <0.05).

**Conclusions:** Prevalence of falls is high in FSHD patients. Fallers are weaker and have lower quality of life compared to non-fallers.

Abstract #541

## Co-creating a multi-sensory balance programme for people living with Charcot-Marie Tooth Disease

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**Introduction:** People with Charcot-Marie-Tooth disease (CMT) experience poorer balance than the general population. Multi-sensory balance rehabilitation is effective in people with other conditions, and early studies have shown promising results in CMT. Co-design strategies can ensure that interventions address real-world problems and are tailored to the target group.

**Methods:** A series of co-creation workshops involving six people with CMT, facilitated by physiotherapists, a patient expert, and an artist/designer. Experience-based co-design methods will be used to explore priorities and preferences for a selection for balance exercises, design of a digital and paper-based resource, and a strategy for dissemination to the international CMT community.

**Results:** The results of this co-design project will be disseminated at the 2022 Muscle Study Group Annual Scientific Meeting.

**Conclusion:** Output from this project will stand alone as a tangible resource for the CMT community, but the findings will also be integrated into a larger future exercise trial.

Abstract #561

## Longitudinal analysis of PUL 2.0 domains in ambulant and non-ambulant Duchenne patients: how do they change in relation to functional ability?

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**Introduction:** PUL is a functional scale assessing upper limb function in both ambulant and non ambulant DMD patients. As the scale is increasingly used in clinical trials, it is becoming crucial to understand if the progression in the different domains is related to the overall functional abilities.

**Objectives:** To establish the patterns of 24-month PUL total and domain changes in different functional groups subdivided by ambulatory status and time since loss ambulation (LOA).

**Methods:** Data were collected from 14 tertiary Italian centers, the PUL 2.0 was used to assess upper limb function.

**Results:** Two-hundred-seventy-two patients had at least one pair of assessments at 24 months, for a total of 812 paired assessments. There were different pattern of changes in the individual domains in relation to different functional abilities.

**Conclusions:** Patterns of changes should be considered at the time of designing clinical trials for stratification, inclusion criteria or for their interpretation.

Abstract #567

## Validity of remote evaluation of the North Star Ambulatory Assessment in patients with Duchenne muscular dystrophy (DMD)

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\*Presenting on behalf of the authors

**Introduction:** In ongoing delandistrogene moxeparvovec (investigational gene transfer therapy) studies, remote functional assessments were initiated during the COVID-19 pandemic, in accordance with FDA guidance.

**Objectives:** To evaluate the reliability of remote functional assessments versus in-person assessments for patients with DMD.

**Methods:** The reproducibility of remote North Star Ambulatory Assessment (NSAA) and timed function tests were assessed against in-person scores using pre-specified statistical analyses—including intraclass correlation coefficient (ICC), Pearson, Spearman and Bland-Altman analyses.

**Results:** Results from 21 patients with DMD in Studies 101/102 found strong correlations between remote and in-person NSAA scores (ICC=0.96 [95% confidence interval; CI 0.91–0.98]; Pearson=0.96 [95% CI 0.90–0.98]; Spearman=0.96 [95% CI 0.90–0.98]), with no statistical or clinical differences attained remotely versus in person.

**Conclusions:** Findings suggest that remote functional assessment of patients with DMD is not statistically different from in-person assessment and has comparable clinical meaningfulness, validating its use in delandistrogene moxeparvovec trials.

**Disclosures:** LPL reports receiving salary support from Sarepta Therapeutics through Nationwide Children's Hospital to support training and quality control activities for ongoing clinical trials and licensing fees for natural history data. LNA reports receiving salary support from Sarepta Therapeutics through Nationwide Children's Hospital to support training and quality control activities for their ongoing clinical trials. MAI reports no conflicts of interest. NFR reports receiving salary support from Sarepta Therapeutics for Clinical Evaluator training for ongoing and upcoming clinical trials. KG is an employee of Eli Lilly and was previously an employee of Sarepta Therapeutics, and may have stock options. LH, LY and SW are employees of Sarepta Therapeutics and may have stock options. JRM has received study funding from Sarepta Therapeutics and has a service agreement with Sarepta Therapeutics to provide training on ongoing studies. JRM is a co-inventor of AAVrh74.MHCK7.micro-dys technology.

Abstract #570

## Motor unit compensation in adults with spinal muscular atrophy varies by functional status

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**Introduction:** Motor unit (MU) enlargement via collateral sprouting is a mechanism by which the MU pool can compensate for motor neuron loss. However, MU compensatory mechanisms across the functional spectrum remain unexplored.

**Objective:** To investigate relationships between MU characteristics and disease severity in adults with SMA.

**Methods:** Adults with SMA on nusinersen and healthy controls were enrolled. MUs were decomposed from multi-electrode surface recordings during a 30-second maximum contraction of the abductor digiti minimi. MU characteristics were compared by ambulatory status and correlated to Revised Upper Limb Module (RULM) score.

**Results:** The MU action potential amplitude and firing rates of ambulatory adults with SMA were significantly greater than non-ambulatory adults with SMA and healthy controls. Moderate to strong correlations exist between these MU characteristics and RULM score.

**Conclusions:** There is differential capacity for MU compensation across the functional spectrum. This has implications for expected treatment effectiveness and long-term functional outcomes.

Abstract #591

## Evaluating the expression of spontaneous movements in infants with neuromuscular conditions using Prechtl's General Movements Assessment

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**Introduction:** Prechtl's General Movements Assessment (GMA) uses visual analysis to evaluate infants' spontaneous movements. Developed for early identification of cerebral palsy, little is understood about the expression of general movements (GMs) in infants with neuromuscular disorders (NMD).

**Objective:** We seek to describe GMs in infants birth to 6 months of age with NMD.

**Methods:** Fourteen infants have been enrolled to date (spinal muscular atrophy [SMA], N=7; Duchenne muscular dystrophy [DMD], N=3; and others, N=4). Each infant's GMs were evaluated using the GMA global categorization and detailed scoring forms.

**Results:** Four (29%) were evaluated as having normal movement patterns; of those, 2 were post-treatment SMA. There was a moderate correlation between other clinical outcome assessments and the GMA detailed scoring. Further exploration into the influence of disease-modifying treatments on the expression of GMs will be presented.

**Conclusions:** These preliminary results suggest many infants with NMD express movement abnormalities from birth.

Abstract #592

The bolus journey behind a horizontal smile. A clinical-functional evaluation of dysphagia in facioscapulohumeral muscular dystrophy (FSHD).

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**Introduction:** the assumption of deglutition-sparing in FSHD has been challenged, but thorough explorations are lacking.

**Objectives:** to detect, estimate incidence, and characterize swallowing patterns and dysfunction in FSHD.

**Methods:** the FSHD Evaluation Scale, the EAT10 questionnaire, and the Three-oz Water Swallow test were administered to 43 FSHD patients. Dysphagic subjects were assessed by IOPI Medical LLC, videofluoroscopy, esophageal barium transit, and double-contrast esophagography. Dysphagia severity was scored by the DOS-Scale.

**Results:** DOSS scores and tongue strength among the 15 mild dysphagic patients were correlated with the EAT10-assessed symptoms, disease's duration and severity. Lip dysfunction was associated with tongue asymmetric weakness, leading to altered oral management. Pharyngeal and esophageal transit impairment were also detected and often associated with Zenker diverticulum, hiatal hernia and gastroesophageal reflux.

**Conclusions:** a generally mild but progressive dysphagia is clinically detectable and often radiographically confirmed in FSHD, related not only to the oral bolus management but often to pharyngeal and esophageal motility disorders.

Abstract #600

## Correlating Fatigue Severity Scale to objective measures of disease progression in Kennedy's Disease.

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**Introduction:** Kennedy's disease (KD) or X-linked spinal and bulbar muscular atrophy (SBMA) is a rare inherited adult-onset neuromuscular disorder. In our dedicated service, we undertake assessments to evaluate markers of muscle damage and muscle weakness progression. Fatigue is very common in people living with KD.

**Objective/aim:** To correlate mean values in Fatigue Severity Scale (FSS) to other functional and biological indicators of disease progression such as CPK and Creatinine levels, 6 minutes' walk test, adult myopathy assessment tool and patient reported functional rating scales.

**Methods:** Using a custom code in "R", we have run correlations between FSS and other validated measures of disease progression in 60 participants.

**Results:** Correlation between mean values of FSS and indicators of disease progression in SBMA were statistically significant

**Conclusion:** Fatigue is an important feature in KD impacting quality of life. We suggest using FFS as an outcome measure in upcoming interventional trials in KD.



Abstract #601

## Descriptive Analysis Of Promis Mobility And Upper Extremity Scales In Patients With Duchenne Muscular Dystrophy (Dmd): Implications For Assessing Physical Functioning From The Patient Perspective

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**INTRODUCTION:** PROMIS Mobility and Upper Extremity (UE) questionnaires were administered to DMD patients and caregiver proxies attending Nationwide Children's Hospital.

**OBJECTIVE:** Examine psychometric properties of generic PROMIS Mobility and UE to establish suitability for assessing physical functioning in DMD and determine need for further customization.

**METHODS:** 170 and 279 complete records of PROMIS Mobility and UE questionnaires, respectively, filled in by caregivers of DMD patients aged 4-27 years were used to assess item performance (ceiling/floor effect), internal consistency reliability (ICR), and item correlations.

**RESULTS:** Item ceiling effects were observed in PROMIS Mobility, primarily in youngest ambulatory subgroup (4-7) whilst floor effects were noted in the oldest (13-17). Item ceiling effects were prevalent in PROMIS UE across all ages. ICR was excellent for both domains. Item correlations revealed some item redundancy within domains.

**CONCLUSIONS:** Results suggest both scales have good potential for assessing physical functioning in DMD but require further work.

Disclosures: LL, NR, LA and MI are employees of the Nationwide Children's Hospital, Columbus, OH, USA, and have provided the data for this study. CLR is an independent biostatistician who received funding from Sarepta to help with the analysis. IA and KG are employees of Sarepta.

Abstract #602

## Pilot Assessment of Pain in Adults with Spinal Muscular Atrophy (PAIN in SMA)

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**Introduction:** There is limited data on pain in adults with spinal muscular atrophy (SMA).

**Objectives:** To evaluate the frequency, characteristics, severity, and therapy used for pain and explore its association with functional status.

**Methods:** We conducted a cross-sectional study using the Brief Pain Inventory, Fatigue Severity Scale, and SMA-specific motor function measures.

**Results:** We analyzed data from twenty patients (12 women and 8 men; median age 37.5). Fifteen (75%) reported pain related to SMA. Pain location varied and was frequently (55%) described as aching. The majority used NSAIDs and acetaminophen—only two used opioids. Ten patients (50%) reported significant fatigue. We found no significant association of pain with fatigue score, ambulatory status, disease duration, SMA type, SMN2 copy number, or motor function measures.

**Conclusions:** Our study demonstrates a high frequency of pain in adults with SMA and highlights pain as a significant issue that warrants detailed evaluation and investigation.

Abstract #603

## Is Sustained Phonation Time related to Forced Vital Capacity in Individuals with Amyotrophic Lateral Sclerosis?

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**Introduction:** Respiratory failure is the leading cause of death in individuals with Amyotrophic Lateral Sclerosis (ALS). Sustained Phonation Time (PT) may be a potential identifier of changes in respiratory capacity.

**Objectives:** Examine the relationship between PT with Forced Vital Capacity (FVC).

**Methods:** Individuals with ALS completed three sustained phonations trials (hold an “ah”--seconds) and FVC (liters) measurements. A regression analysis was performed to determine the relationship between their best PT and their FVC.

**Results:** Twenty-nine individuals (10 females, age M=69.1 (SD=11.7)) (M ALSFRS=35.6 (SD=8.2)) resulted in a variance,  $R^2$  of 0.39, ( $p$ -value, < 0.001) meaning the variation in measured PT accounted for 39% of the variation in measured FVC; suggesting a moderate relationship between PT and FVC.

**Conclusions:** These preliminary results suggest that PT could be a clinical tool to understand FVC and potential decline in respiratory capacity. We will be increasing our sample size to examine this possibility.

Abstract #604

## Validation of the Toronto Cramp Impact Index (TCII)

Hans Katzberg, Sara Al Najjar, Meg Mendoza, Lorne Zinman, Agessandro Abrao, Hemant Shah, David Cherney, Vera Bril, Carolina Barnett Tapia.

**Introduction:** Although cramp frequency has been used traditionally to assess cramp severity, a more comprehensive outcome measure is needed.

**Objectives:** To validate a novel patient reported outcome, the 16-item Toronto Cramp Impact Index (TCII).

**Methods:** Cramp frequency, location, intensity, duration, as well as muscle pain, stiffness, quality of life, sleep quality and sleepiness parameters were collected on each patient. A subgroup of patients had the TCII repeated at 2 weeks to assess intra-rater reliability.

**Results:** Preliminary review of 86 patients with idiopathic and secondary cramps were included. Mean number of cramps/week was 10, mean severity 6.8/10 and mean duration 6.7 minutes. There was significant and moderate correlation between the TCII and all associated cramp characteristics and associated parameters. Intra-rater reliability (n=61) was moderate the total TCII score (Cohen's kappa = 0.55).

**Conclusions:** The TCII shows promise as a patient centred, reliable and comprehensive way to assess muscle cramps (final results expected at the MSG meeting).

Abstract #605

Associations between speech-language difficulties, speech delay, *DMD* genotype, and motor function performance in corticosteroid-naïve boys with DMD.

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We tested the hypothesis that care-giver reported neurodevelopmental symptoms and distal *DMD* mutations are prognostic of worse motor function performance in DMD. We analyzed care-giver-assessed speech-language difficulties (SLD), age at speaking in full sentences, *DMD* mutation location, six-minute walk distance (6MWD), North Star Ambulatory Assessment (NSAA) total score and timed motor function tests from 196 corticosteroid-naïve boys with DMD. Boys with reported SLD walked 25.8 fewer meters on average than those without SLD on 6MWD but did not demonstrate statistically significant results in the NSAA total score or other timed motor function tests. Boys with distal *DMD* mutations walked 20 fewer meters on 6MWD and were slower on timed-motor-function tests. The difference in mean 6MWD between those with and without SLD was independent of *DMD* mutation location, and the difference in mean 6MWD between *DMD* genotypes was independent of SLD. Distal *DMD* genotype is associated with worse baseline motor function.

Abstract #611

## Wearable Sensors Detect Changes in Timed Up and Go Performance after Nerve Tumor Excision

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**Background and Purpose:** Individuals with neuromuscular disorders experience postural instability during turning tasks placing them at high risk for falls. Functional tests often rely on overall performance to quantify postural stability. This study sought to determine if wearable sensors could detect changes in turning task performance following nerve tumor excision.

**Methods:** 10 patients (50% female, age= 40.2±13.1) performed Timed Up and Go (TUG) tests pre- and post-vestibular schwannoma excision. T-tests were used to compare pre- and post-surgical TUG performance.

**Results:** Wearable sensors detected significant pre to post surgery differences in peak turning velocity (p=0.007) and turn duration (p=0.006). TUG total time did not differ significantly between assessments.

**Conclusion:** Wearable sensors used during turning tasks detected differences in TUG performance not apparent by overall task time. Similarly, quantification of turning tasks with wearable sensors in individuals with neuromuscular disorders may allow quantification of fall risk and more sensitive assessment of performance changes associated with rehabilitation.

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Abstract #615

## Patient Reported Upper Extremity Function is Associated with Measures of Strength and Function in Individuals with Facioscapulohumeral Muscular Dystrophy (FSHD)

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**Introduction:** Measuring clinically relevant upper extremity function is challenging in FSHD studies. The Upper Extremity Functional Index (UEFI) is a patient reported outcome measure assessing the difficulty performing daily tasks such as grooming/dressing and household activities.

**Objective:** To examine the relationship between the UEFI and measures of strength and function in individuals with FSHD.

**Methods:** Individuals with FSHD participating in the ReSolve study completed the UEFI, measures of strength and measures function including donning/doffing a coat and measures of reachable workspace.

**Results:** Participants (n=251) were 56% male with a mean age of 50 years. Participants had a UEFI score of 54.60 (range 4-80). UEFI score was moderately correlated with donning/doffing coat ( $\rho=0.45$ ;  $p<0.001$ ), reachable workspace ( $\rho=0.44$  (R) and 0.49 (L);  $p<0.001$ ), and strength ( $\rho=0.55$ ;  $p<0.001$ ).

**Conclusions:** The UEFI is correlated with measures of strength and function, supporting the clinical relevance of using these outcome measures in future FSHD clinical trials.

NINDS U01 grant U01NS101944; MDA clinical research network grant #573783; FSH Society grant # 52016; Friends of FSH Research grant; CTSA grant from NCATS (# UL1TR000001, and UL1RR024160); Fulcrum Therapeutics; and a grant from AFM (SS).

Abstract #617

## Muscular activity monitoring with an artificial intelligence-based wearable sensor in facioscapulohumeral muscular dystrophy: A pilot study

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**Introduction.** As the field anticipates more facioscapulohumeral muscular dystrophy (FSHD) clinical trials, there is an acute need for reliable/quantitative clinical outcome measurements to monitor FSHD.

**Objectives.** To assess an innovative clinical outcome assessment using an artificial intelligence (A.I.)-based wearable device for tracking shoulder joint kinematics and muscle activity in FSHD subjects.

**Methods.** A flexible experimental wireless apparatus comprising a triaxial accelerometer and four surface electromyography sensors (over bilateral trapezius, infraspinatus, biceps, and deltoid muscle regions) was employed on 4 adult FSHD and 4 healthy control subjects.

**Results.** The device reliably showed range of motion (ROM) measures in all activities tested (shoulder abduction, elbow flexion, shoulder external and internal rotations) with 3 trials in each performance. There was also a significant difference between the detected ROM and muscular activity between control and FSHD subjects ( $P < 0.05$ ).

**Conclusions.** Our pilot data demonstrated a potential utility of an A.I.-based wearable sensor in monitoring FSHD.



Abstract #626

## Construct validity of the 10-meter walk and modified time up and go tests in inclusion body myositis: an observational cross-sectional study

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**Introduction:** There is a lack of validated outcome measures to assess the effect of interventions in inclusion body myositis (IBM).

**Objectives:** Our aim was to evaluate the construct validity of the 10-meter walk (10MW) and modified time up and go (mTUG) tests in IBM.

**Methods:** Observational cross-sectional study. The construct validity of the 10MW (4 versions: normal and fast pace, each one measured in seconds and in steps) and mTUG was tested at baseline using Spearman correlation with other strength and disability outcome measures (MMT, QMT and IBMFRS).

**Results:** Among 58 patients, 69% were male, with mean (SD) age and disease duration of 66.3 (9.6) and 7.4 (4.0) years, respectively. Moderate to strong correlations between 10MW/mTUG and other outcome measures were found.

**Conclusions:** The 10MW and mTUG proved to be valid in IBM. Their potential to evaluate the impact of IBM and its treatment on functioning should be further evaluated.

Abstract #628

Evaluation Cognitive Function, Cerebral Structure and Functional Connectivity in Children with Congenital (CDM) and Childhood-Onset Myotonic Dystrophy Type 1 (chDMI)

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**Introduction:** Cognitive function (CF) is significantly impaired in children with CDM/chDMI.

**Objective:** Identify key cerebral structural and functional connectivity (FC) factors predictive of CF deficits in CDM/chDMI.

**Methods:** Thirty participants with CDM/chDMI and controls completed neuropsychological, structural and resting state functional MRI (rsfMRI) evaluations. A 3T scanner, DPARSEFA toolbox and SPM8 were used for image collection and processing. Group differences in brain structure and FC were examined. Regression analysis was used to identify relationships between neuropsychological measures and MRI/rsfMRI.

**Results:** Preliminary data revealed significant differences in brain structure and FC in CDM/chDMI; greater connectivity between the cingulate cortex (CC) and prefrontal brain regions (PBR) in CDM; strong associations between CF and CC-PBR connectivity in CDM.

**Conclusion:** Our results are consistent with previous reports of prefrontal white matter changes in DMI and suggest that anomalous prefrontal development plays a key role in the cognitive deficits in CDM/chDMI.

Abstract #630

## Application of muscle MRI in Complex Upper Extremity Neuropathies

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**Introduction:** Complex upper extremity neuropathies can have varied clinical presentation. Physical examination and detailed history are often not sufficient to make a conclusive diagnosis. While nerve conduction studies with electromyography (NCS/EMG) can be valuable, the yield is often limited when there is underlying confounding pathology. In such cases magnetic resonance imaging (MRI) of muscles can be helpful.

**Objective:** To report a series of patients in whom MRI upper extremity assisted in diagnosis.

**Case Presentations:** To date four cases were identified where EMG/NCS was inconclusive, and muscle MRI helped in diagnosing posterior interosseous nerve syndrome, proximal median neuropathy, multifocal motor neuropathy, and malignant infiltration of the axillary nerve bundle.

**Results:** This study illustrates how muscle MRI can identify certain pattern of muscle involvement and complement EMG findings in complex upper extremity neuropathy cases.

**Conclusion:** MRI of the upper extremities can provide complimentary information to EMG and help making a correct diagnosis.

Abstract #653

## Validation of the Inclusion Body Myositis Functional Rating Scale (IBMFRS): Results from 2 studies.

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**Introduction:** The IBMFRS is a Clinician Reported Outcome measure that assesses a patient's ability and independence in completing 10 functional activities. There is limited information about IBMFRS psychometric properties.

**Objective:** Our aim was to investigate IBMFRS content validity, inter- and intra-rater reliability, responsiveness, and what constitutes a meaningful change in IBMFRS scores.

**Methods:** Two prospective studies provided data for both validity (content and construct) and reliability evaluation of the IBMFRS. Evaluation of responsiveness and derivation of a meaningful change threshold was also conducted.

**Results:** Data show that the IBMFRS is content valid based on both patient and clinician feedback with the key functional limitations captured. Additionally, the IBMFRS has strong construct validity (convergent and known-groups validity), reliability, and responsiveness. Additionally, a meaningful change threshold has been derived.

**Conclusion:** The IBMFRS is a valid and reliable measure for assessing the key functional impacts of IBM.

## Impact and Burden of NMD

Abstract #644 Flash Presenter

### Risk factors for falls and fracture in myositis: A cross-sectional study of 470 patients

Abhiram Bhashyam, MD, PhD<sup>1,2</sup>, Avneet Hans, MD<sup>3</sup>, Manuel Lubinus, PhD<sup>2</sup>, Emily Filmore<sup>2</sup>, Lynn Wilson<sup>2</sup>,  
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America

Introduction: Myositis can lead to marked weakness, predisposing patients to falls/injuries.

Objectives: We investigated risk factors for falls/fractures.

Methods: A survey was sent to members of Myositis Support and Understanding inquiring about falls and fractures. Ordinal logistic regression was performed.

Results: In a cross-sectional study of 470 participants with myositis, 80% reported having at least one fall since their initial diagnosis. 57% of participants fell at least once in the past year and 121 falls resulted in a fracture (32%). Mobility aids were used by 57% of participants. Fall risk was highest for IBM (OR 2.5,  $p=0.002$ ) or PM (OR 2.0,  $p=0.037$ ) compared to DM, and for those using mobility aids (OR 3.1,  $p<0.001$ ). Only 47% of participants reported being prescribed fracture prevention. Only 52% of participants on >1 month of steroids were prescribed calcium/vitamin D.

Conclusions: Fall and fracture prevention efforts should be emphasized in myositis.

Abstract #471

## Neuromuscular Manifestations Associated With COVID-19

Billie Hsieh, Ashley Smith, Xiaojin Li, Kristin Brown, Suur Biliciler, Thy Nguyen

**Introduction:** Both central and peripheral nervous system (PNS) manifestations of COVID-19 have been reported. A Chinese retrospective case series, on 214 hospitalized COVID-19 patients, found that 8.9% presented with peripheral nerve disease and 7% had muscular injuries. Other studies looking at the prevalence of PNS manifestations are limited and have significantly lower numbers.

**Objectives:** Determine neuromuscular manifestation incidence in COVID-19 patients from the longitudinal electronic health record database Optum.

**Design/Methods:** The COVID-19 data is sourced from more than 700 hospitals and 7000 clinics in the US. Patients with numerous neuromuscular diagnoses were identified based on ICD-10 coding. Examples include carpal tunnel syndrome, radial nerve lesion, sciatic nerve lesion, myasthenia gravis, acute transverse myelitis, Bell's palsy, and trigeminal neuralgia.

**Results:** We reviewed a total of 598,847 patients with positive COVID-19 PCR and/or diagnosis coding. Neuromuscular complications must have been within 45 days of diagnosis to be included. Incidence of similar neuromuscular complaints was evaluated in 3,001,153 controls without COVID-19. Critical illness neuropathy was found in 35,782 COVID-positive patients and 6,281 of those without. Retrospective study limitations include temporal relationship to COVID-19 does not necessarily indicate causality and inability to confirm the coding by record review or EMG/NCS.

**Conclusions:** Incidence of neuromuscular disorders is generally lower or equivalent in COVID-19 patients than in the general population, except for critical illness neuropathy and myopathy. This finding may be explained by more COVID-19 patients being in the intensive care unit and bedbound for longer periods. It is worth noting that a small case series of COVID-related critical illness neuropathy and myopathy patients showed no histopathological or clinical differences compared to non-COVID patients. To our knowledge, this report includes an analysis of neuromuscular manifestations in one of the largest cohorts of COVID-19 patients. This can assist with risk-benefit discussions regarding treatment initiation, etiology of diagnoses, and counseling for COVID-19 questions.

Abstract #510

## Myalgia and fatigue as “LONG COVID” Symptoms: a 1-year follow up

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### ABSTRACT

**Introduction:** COVID-19 is a syndrome caused by SARS-CoV-2 virus and the main manifestation is interstitial pneumonia. However, many neurological and also neuromuscular manifestations were described as associated to SARS-CoV-2 infection. Multiorgan symptoms after COVID-19 are being reported by increasing numbers of patients, lately grouped in a syndrome called “long COVID”. However, the long-term health consequences of COVID-19 remain largely unclear.

**Methods:** We enrolled 124 patients hospitalized between March and May 2020 for SARS-COV-2. We established a 6 and 12 months follow-up. For each patient cognitive tests, scales for depression and anxiety and a specific Fatigue Severity Scale (FSS) were performed.

**Results :** Twenty-five patients (19.8%) died during hospitalization. Eighty-seven (70%) patients were male and mean age was 67.3 years. During hospitalization 38.5 % of patients complain of myalgia. Patients with reported myalgia had higher CK ( 534 U/L vs 93 U/L,  $p<0.001$ ) and LDH levels (363 U/L vs 303 U/L) and they needed more often oxygen therapy (78% vs 42%,  $p<0.001$ ) and non-invasive ventilation ( 20% vs 5%,  $p<0.001$ ).

At 12 months follow up 85 patient were evaluated and 42 % still complain about myalgia while 34% reported fatigue. Mean FSS value were significantly higher in patients who complain about fatigue (40.2 vs 25.5  $p<0.001$ ) and muscle pain (40, 84 vs 26,80,  $p<0.001$ ) compared to who did not.

**Conclusions:** During hospitalization for COVID-19 myalgia was associated with an higher level of CK and LDH, suggesting a possible direct muscle involvement. At 12 months myalgia and fatigue were commonly reported. These manifestation could be the main “long COVID” symptoms at one year follow-up.

**Disclosures:** no disclosures

Abstract #529

## Understanding the Perseverance of the Muscular Dystrophy Community One-Year into the COVID-19 Pandemic

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**Introduction:** We examined the social and health impacts of the coronavirus disease 2019 (COVID-19) pandemic on people with muscular dystrophy (MD).

**Objectives:** Assess the impacts of the pandemic on social factors, muscle disease, and medical care.

**Methods:** Our “COVID-19 Impact Survey” was a de-identified, electronic survey distributed to adults with MD via international registries and advocacy group websites from February 8, 2021 to March 22, 2021.

**Results:** Respondents (n=1243: 49% Facioscapulohumeral Muscular Dystrophy; 43% Myotonic Dystrophy, and 8% Limb-Girdle Muscular Dystrophy) were mostly women and middle-aged (range 18-90 years). COVID-19 infections rates were low (8%); reported recovery times were short. Most reported slight worsening of their dystrophy and moderate stress levels.

**Conclusions:** People with MD managed their stress and overcame obstacles during the COVID-19 pandemic. COVID-19 infection rates and medical complications were similar to the general population. Previously predicted risks for MD patients may need to be reconsidered.



Abstract #530

## The Worldwide Impact of the COVID-19 Pandemic on the Muscular Dystrophy Community by Geographical Region

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**Introduction:** We examined the social and health impacts of the coronavirus disease 2019 (COVID-19) pandemic on people with muscular dystrophy (MD) worldwide.

**Objectives:** Comparing impact of the pandemic by geographical region.

**Methods:** Our “COVID-19 Impact Survey” assessed the pandemic’s effects on social factors, muscle disease, and medical care. The de-identified, electronic survey was distributed to adults with MD via international registries and advocacy group websites from February 8, 2021 to March 22, 2021.

**Results:** Rates of COVID-19 infections, symptoms, and recovery time were similar between geographical regions. The most common challenges due to the pandemic were different between regions: social distancing in Europe (60%), obtaining treatment in Canada (54%) and United Kingdom (48%), and stress management in the United States (41%). Individuals living in the United States reported significantly less stress than other regions.

**Conclusions:** We identified significant differences and similarities of impacts on people with MD between geographical regions.

Abstract #531

## Long-term outcomes of mitochondrial myopathies diagnosed in adulthood

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**Introduction:** Little is known regarding the natural history of mitochondrial myopathies (MM) in adults.

**Objectives:** To describe the clinical spectrum and long-term outcomes of MM diagnosed in adulthood.

**Methods:** Retrospective review of adult patients diagnosed with MM at Mayo Clinic (2005-2021).

**Results:** We identified 94 patients (82 genetically-defined, 12 histopathologically-defined); 48 females. Median age was 31 years at symptom onset and 48 years at diagnosis. Most common presentations included chronic progressive external ophthalmoplegia (37 patients); a nonsyndromic multisystem disorder (24); MELAS (14) and isolated myopathy (13). On muscle biopsy, cytochrome-c oxidase negative fibers were the most common mitochondrial abnormality, representing on average 5.1% of fibers. Progression of muscle weakness was overall slow, with a decline of 0.05 point/year in the summated strength score. Median overall survival was 10.9 years from diagnosis and 33.5 years from symptom onset.

**Conclusions:** MM are characterized by slowly progressive muscle weakness and probably limited longevity.

Abstract #540

## A qualitative exploration of self-management in people living with a neuromuscular condition

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**Introduction:** Self-management support (SMS) is now widely accepted as a fundamental component of high-quality personalised care. Qualitative data can provide valuable insights into the ways we conceptualise patients' experiences and can influence service design and delivery. However, there is a paucity of data exploring SMS in people with neuromuscular diseases (NMD).

**Methods:** Semi-structured interviews explored the perspectives of 28 individuals with NMD on their perspectives, preferences, and priorities for SMS. Reflexive thematic analysis was used to code data and identify key domains and themes.

**Results:** Three overarching themes were identified, linking into two fundamental questions: “*what keeps me going*” and “*what holds me back*”. The overarching themes were ‘*support systems*’, ‘*adapting to change*’, and ‘*it’s not just physical*’.

**Conclusion:** Qualitative data reflecting the perspectives of people with NMD on SMS is lacking. The findings from this study provide insight into the way that SMS is enacted in this population.

Abstract #543

**Introduction:** The International Centre for Genomic Medicine in Neuromuscular Diseases (ICGNMD) launched in 2019. It is a 5-year initiative to improve health outcomes in neuromuscular diseases (NMDs) globally and spans 14 centres in Brazil, India, Turkey, South Africa, the UK, and Zambia.

**Objectives:**

1. Deliver research/capacity-building in genomic medicine
2. Facilitate NMD patient access to genetic diagnoses
3. Assemble deeply phenotyped/genotyped NMD cohorts
4. Grow clinical capacity in NMDs by training a clinical academics

**Methods:** Participants are consented and details entered into a secure database. Cross-site meetings determine best genetic testing options, Samples are analysed locally or at UCL, London. Results are discussed at cross-site MDT meetings.

**Results:** After 3 years, 4,718 participants (2855 probands) have been recruited, with a balance of paediatric/adult muscle/nerve/mitochondrial disorders.

**Conclusions:** Genetic results are emerging at scale; these will seed international collaborations and underpin research concerning the global genetic architecture and aetiology of NMDs.



Abstract #547

## Co-designing a strategy to engage people with neuromuscular diseases from racially minoritized backgrounds in research

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**Introduction:** There is evidence of poor representation people from racially minoritized backgrounds with neuromuscular diseases (NMDs) in clinical research. The people best placed to develop the strategies for engagement are people with these demographics.

**Objectives:** We used public engagement workshops to co-design a recruitment strategy in partnership with people living with NMDs from racially minoritized backgrounds.

**Methods:** We invited people to three workshops using video conferencing. Workshop 1: Exchange of experiences and ideas; Workshop 2: Bringing ideas together for a strategy and action points; Workshop 3: Agreeing the final strategy.

**Results:** Workshop 1 highlighted key challenges, such Knowledge, Personal Choice, Trust and Shame. Ideas were developed around Communication and will be expanded in workshop 2 to create a recruitment strategy.

**Conclusion:** The first step of the process has concluded. We will launch the final strategy to research colleagues to facilitate greater diversity in trial cohorts at our institution.

Abstract #577

## Investigating “scarcity theory” in DMD

H. Karra\*, A. Hanif\*, M. Ridder\*, E. Boone\*, M. Thangarajh\* (\*Richmond, VA)

Recent lived experiences have raised awareness regarding socioeconomic determinants of health. The “scarcity theory” identified by economists postulates that financial scarcity affects decision-making due to consumption of cognitive resources, leaving the individual with narrow cognitive control. We investigated the hypothesis that mothers of DMD patients from a lower socioeconomic status had lower cognitive capacity than mothers from a higher socioeconomic status. We used the psychometrically-sound NIH Toolbox Cognition Battery to obtain crystallized and fluid intelligence scores. We correlated these scores to self-reported annual income. Our results show that mothers of DMD patients who reported an annual income of less than US 50,000 scored an average of 25 points lower in fluid intelligence scores compared to mothers who reported an annual income of more than USD 150,000 (p-value of 0.02). Our preliminary findings underscore the importance of recognizing socioeconomic determinants of health in DMD.

Abstract #586

## Exploring the impact of balance impairments and falls in people with Charcot Marie Tooth disease

M.M. Dudzic, L.E. Lee, M.M. Reilly, G.M. Ramdharry (London, UK)

**Introduction:** Balance confidence in people Charcot Marie Tooth disease (CMT) is reduced. More exploration is needed to understand how this influences everyday activities, physical and psychological well-being.

**Objectives:** This qualitative work aims to gain further insight and understanding into the experience of living with balance impairments in people with CMT1A.

**Methods:** Participants underwent semi-structured interviews. Questions focussed on the impact of balance impairments on daily life. Interviews were transcribed and coded using thematic analysis.

**Results:** 13 people participated. Themes included (1) *Living with CMT*; (2) *Emotional Issues related to balance*; (3) *Physical Issues*; (4) *Strategies to avoid falls*. The ability to cope with the changing nature of the condition is important. People with CMT adapt and identify strategies which work for them, though some feel more able to do this than others

**Conclusions:** Clinicians can use this information when supporting patients to self-manage their condition.

Abstract #598

## Longitudinal study of cognitive function in DMD: is it really stable?

Anna Capasso\*, Gianpaolo Cicala\*, Daniela Chieffo\*\*\*, Martina Ricci\*, Claudia Brogna\*\*, Giorgia Coratti\*\*, Federica Moriconi\*\*\*, Monia Pellizzari\*\*\*, Costanza Cutrona\*, Eugenio Mercuri\*\* (\*Centro Clinico Nemo, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome; \*\*Pediatric Neurology, Università Cattolica del Sacro Cuore, Rome, Italy; \*\*\* Psychology Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome)

**Introduction:** So far cognitive abilities in DMD have been reported to be stable over time

**Objectives:** To evaluate the consistency of longitudinal cognitive findings in DMD boys and their relation to behavioural patterns.

**Methods:** Data were collected from 2010 to 2021 using the Weschler scales (cognitive), CBCL and clinical observation (behaviour). Patients were subdivided depending on IQ level, behavioural disorders, brain dystrophin involvement.

**Results:** Seventy patients had at least two assessments. Concordant results were found in 63% of the paired assessment. Discrepancy were mostly observed in patients with abnormal CBCL and/or attention deficits.

**Conclusions:** Changes in IQ may occur in DMD boys and these are more likely to be associated to behavioral or attention deficits than to the involvement of Dp140 and 71 or to IQ level.



Abstract #596

## Long term follow-up of scoliosis progression in type II SMA patients.

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**Introduction:** Scoliosis is one of the most common and feared complications in type II SMA.

**Objectives:** The aim of this study is to retrospectively evaluate the onset and the progression of scoliosis in a large cohort of untreated type II patients, in relation to different variables.

**Methods:** Data were collected between 2007 and 2022 from 3 tertiary Italian centers. Cobb angle measurement method was standardized among centers. The model was adjusted by age, sex, Cobb, HFMSE values at baseline, and SMA function.

**Results:** Eighty-four SMA II patients were enrolled. The mean annual rate of increase in Cobb angle was 5.22 (95%CI: 4.22-6.23). Age and Cobb value at baseline were identified as modifiers of scoliosis progression.

**Conclusions:** the available data in untreated patients will be of help to determine possible differences in treated patients.

Abstract #607

## Frequency of SMA cases and treatment accessibility in Zambia

M.M. Kapapa, D. Bearden \*, S. Somwe \*\*, M. Mweemba \*\*\*, M.P. Kvalsund \*\*\*\* (Lusaka, ZM; New York, USA\*; Lusaka, ZM\*\*; Lusaka, ZM\*\*\*; New York, USA\*\*\*\*)

**Introduction:** Known to be the most common genetic cause of morbidity and mortality, SMA affects approximately 1 in 12,000 live births with a prevalence of approximately 1-2 per 100 000 persons.

**Objective:** Determine the proportion and accessibility of SMA treatments in Zambia.

**Methods:** Participants were evaluated by a neurologist prior to study entry. Diagnosis was based on available clinical data.

**Results:** SMA accounted for 20% of the total NMDs being seen with females slightly more affected than males. Mean age of onset was 1.7 months and mean diagnostic age 3.6 months. 73% of the patients had access to physiotherapy while 27% to medical care.

**Conclusion:** SMA was the highest in frequency of NMDs. The current cohort of SMA has access to physiotherapy but their motor function as well as their life span could be better improved with access to the current therapeutics.

Abstract #619

## Quality of Life Survey Assessing Accessibility for Patients with Spinal Muscular Atrophy

Kelsee Parry, Tate Keough, Sarah Moldt, Emily Woolsey

**Introduction:** While there has been disease-stopping advancement in SMA, loss of ambulation shows gaps in accessibility.

**Objective:** Community-wide accessibility is a barrier for persons' with SMA (pwSMA), and participants feel this is not being properly addressed.

**Methods:** An open-ended QOL survey was used to identify pain points with accessibility, such as the want for longer transition periods in schools, difficulty with social activities and job searches, and frustrated caregivers.

**Conclusions:**

Overall data suggest our patients feel some needs are met, but there is still much room for improvement. With better awareness, schools and the community could contribute to accessibility, resources, and awareness of community challenges to improve QoL for pwSMA. This especially pertains to patients approaching adulthood (majority of surveyed patients) and losing public school services.

Abstract #621

## Pain impacts quality of life, psychological disorders and exercise in a large international cohort of patients with facioscapulohumeral muscular dystrophy

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**Introduction:** Facioscapulohumeral muscular dystrophy (FSHD) is one of the most common forms of muscular dystrophy affecting more than 870,000 patients worldwide.

**Objectives:** Discover the impacts of pain, a significant cause of morbidity, in people with FSHD.

**Methods:** We analyzed data from a large international observational study run by the FSHD Clinical Trial Research Network which included patient reported data, motor assessments, and quality of life measurements.

**Results:** We included 219 patients in the analysis. 182 patients (83%) reported pain most commonly in the lower back and shoulders. We uncovered differences in pain management between the US and EU. Univariate analysis found a statistically significant association between the presence of pain and quality of life, psychological problems and resistance exercise rates.

**Conclusions:** Taken together, these data point to the importance of further characterizing pain in FSHD patients and to develop methods for assessing pain in FSHD clinical trials.

Abstract #639

## Impact of Socioeconomic and Insurance Status on Time to Myositis Diagnosis

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Introduction: Socioeconomic factors may impact time to myositis diagnosis.

Objectives: We investigated the impact of socioeconomic and insurance status on time to diagnosis and creatine kinase (CK) normalization.

Methods: Primary outcomes, time to diagnosis and CK normalization, were analyzed using Cox regression. Secondary outcomes, including probability of MRI femur and muscle biopsy completion, were analyzed using logistic regression.

Results: 189 patients were included. Charity and Medicare/Medicaid status were associated with 4.58-fold ( $p=0.0009$ ) and 4.6-fold ( $p=0.006$ ) increase in probability of being diagnosed 200 days after first elevated CK, respectively. Females had a 66% decreased probability of being diagnosed after the first elevated CK within the first 40 days ( $p=0.0003$ ). Median household income, race, and ethnicity showed no significant difference in time to diagnosis and CK normalization. No factors impacted the probability of MRI femur or muscle biopsy completion.

Conclusions: Differences in insurance type and sex may impact time to myositis diagnosis.

Abstract #643

## Risk factors for delayed diagnosis of myositis: A cross-sectional study of 470 patients

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Introduction: Myositis can be difficult to diagnosis leading to delayed diagnosis and increased morbidity.

Objectives: We aimed to investigate the risk factors for delayed diagnosis.

Methods: A survey was sent to members of Myositis Support and Understanding inquiring about circumstances around diagnosis. Multivariate linear regression was performed.

Results: In a cross-sectional study of 470 participants with myositis, the average time to diagnosis was 28.1 months (range: 0-120 months), 33.8% of participants traveled >50 miles to a center of excellence and 64% of participants saw >2 providers before a diagnosis was made. Variables associated with longer time to diagnosis were seeing >2 providers (coefficient=32, p<0.001), being uninsured (coefficient=52, p=0.003), having inclusion body myositis (coefficient=54, p<0.001), or having income <\$20,000/year (coefficient=42, p=0.005).

Conclusions: To obtain faster diagnosis, uninsured and poorer patients are likely to require social support, and those with suspected myositis, especially IBM, should be referred to myositis specialists.

Abstract #645

## Risk factors for financial burden in myositis: A cross-sectional study of 470 patients

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**Introduction:** Myositis requires multidisciplinary care, which may increase financial burden, an unknown dimension in myositis.

**Objectives:** We investigated risk factors for financial burden in myositis.

**Methods:** A survey was sent to members of Myositis Support and Understanding to assess financial burden using two validated measures: Financial Worry Score and Financial Burden Composite Score (FBCS). Multivariate linear regression was performed.

**Results:** In a cross-sectional study of 470 participants with myositis, high financial worry was endorsed by 202 participants (43%) and moderate FBCS (avg±std dev. 1.8±1.9). Factors associated with high financial worry/burden were annual income <\$75,000 (OR 2.4-5.1, p<0.001) and being on disability (OR 1.98, p=0.023). Medicare was the only protective factor for decreased likelihood for high financial worry/burden (OR 0.4, p=0.008).

**Conclusions:** Financial worry/FBCS in myositis are like that in cancer and orthopedic trauma. Policy changes should allow myositis patients to enroll in Medicare earlier than the 24-month waiting period.

## Mechanisms of Disease and Less Common Disease

Abstract #554 Platform presenter

Neuromuscular junction transmission failure is a translationally-relevant mechanism of sarcopenia

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**Introduction:** Sarcopenia, loss of muscle strength and size, contributes to loss of physical function in older adults. Improving physical function in older adults is an urgent need to reduce healthcare costs and improve quality of life. Mixed data exists regarding altered form and function of the neuromuscular junction (NMJ) transmission during aging.

**Objective:** We aimed to investigate NMJ transmission failure as a potential mechanism of age-related weakness.

**Methods:** We applied stimulated single fiber electromyography as an in vivo measure of NMJ transmission that can be applied across species.

**Results:** We show for the first time that NMJ transmission failure is a conserved feature in aged rodent models and older adults with clinically-meaningful weakness. Severity of NMJ deficits is associated with indices of muscle strength in both rodents and humans.

**Conclusions:** Our findings provide direct evidence for NMJ dysfunction as a mechanism of sarcopenia and target for therapeutic development.



Abstract #563 Platform Presenter

## Survival Motor Neuron Protein: Addressing Therapeutic Concerns of Sensorimotor Toxicity

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**Introduction:** Spinal Muscular Atrophy (SMA) is a motoneuron disease caused by homozygous loss of *SMN1*, and consequentially, low Survival Motor Neuron protein (SMN) levels. scAAV9-mediated *SMN1* gene therapy is routinely used to treat SMA patients. A recent report raised concern of sensorimotor toxicity via protein aggregation in scAAV9-SMN-treated wildtype mice, implying caution is warranted with the clinical therapy; yet, neither promoter nor dose tested matched the clinical construct.

**Objective:** Determine whether scAAV9-SMN therapy induces sensorimotor toxicity/SMN aggregation when utilizing the clinically-relevant construct.

**Methods:** Using the clinically-relevant promoter, dose, and mouse model, we assessed the toxicity potential of scAAV9-mediated SMN delivery in wildtype mice.

**Results:** We found no functional, behavioral, or electrophysiological evidence of toxicity, nor SMN aggregation, following scAAV9-SMN treatment.

**Conclusions:** Our data support that clinically-relevant scAAV9-mediated SMN delivery is not expected to cause sensorimotor toxicity and argues against the call for concern/alteration to the current clinical therapy paradigm.

Abstract #580 Platform presenter

## Bridging the preclinical-clinical gap: reverse translation of muscle velocity recovery cycles allows in vivo assessment of skeletal muscle excitability in mice and humans.

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Transgenic mice with Hypokalaemic periodic paralysis have no spontaneous attacks of weakness whilst recessive Myotonia Congenita mice exhibit muscle atrophy rather than the hypertrophy seen in humans. This suggests a species' difference in muscle excitability.

Muscle Velocity Recovery Cycles (MVRCs) use post-impulse changes in conduction velocity as an indirect measure of excitability. We reverse translated MVRCs to allow mouse-human skeletal muscle excitability comparison.

Whilst human MVRCs (n=26) have two phases of increased conduction velocity known as early and late supernormality, mouse MVRCs only have one. Instead of late supernormality mice exhibit late *sub*normality (reduced velocity). Subnormality has never been seen in human MVRCs. The subnormal phase in mice was converted to supernormality by intraperitoneal injection of 30mg/kg 9-Anthracene Carboxylic Acid a CIC-1 blocker.

MVRCs are a valuable new tool to compare in vivo muscle membrane properties between species and will allow further dissection of the molecular mechanisms regulating muscle excitability.

Abstract #499 Platform presenter

## Symptom Onset In Maternally *versus* Paternally Inherited Myotonic Dystrophy type 2.

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**Introduction:** Myotonic dystrophy type 2 (DM2) is likely underdiagnosed and there is no definitive evidence of genetic anticipation or congenital form in this muscular dystrophy.

**Objective:** To investigate phenotypic differences with focus on symptom onset and type of symptoms in maternally- and paternally- inherited DM2 patients.

**Methods:** We reviewed the chart of 70 genetically confirmed DM2 patients and collected information about phenotype and parental inheritance when available.

**Results:** 26 DM2 patients (from 18 families) were identified as having maternal (14 patients) or paternal inheritance (12 patients). 13 out of 14 maternally inherited DM2 patients developed symptoms by third decade of life. Within paternally inherited DM2 group; none developed symptoms before third decade of life, six developed symptoms during third decade of life or later, and six remained asymptomatic by at least third decade of life.

**Conclusions:** An earlier symptom onset was observed in maternally inherited DM2 patients in this cohort.

Abstract #506 Platform presenter

## A comparison of in silico predictive tools to robust in vivo functional characterisation of CLCN1 genetic variants in skeletal muscle channelopathies.

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Accurate determination of the pathogenicity of missense genetic variants of uncertain significance is a huge challenge for implementing genetic data in clinical practice. In silico predictive tools are increasingly used to score variants' pathogenicity. However, their value in clinical settings is often unclear since they have usually not been validated against robust functional assays. We compare nine in silico predictive tools with detailed cell-based electrophysiology for 126 *CLCN1* variants we discovered in patients with the skeletal muscle channelopathy myotonia congenita. We found poor accuracy for most predictive tests. The highest accuracy was with Mutation Taster (84.58%) and REVEL (ROC 0.89). However, both scores have poor specificity. EVE has better specificity while maintaining good AUC and sensitivity. Combined methods based on concordance, improved performance but still lacked specificity. Tools with better specificity are urgently required. This is a wider issue and a huge challenge for effective clinical implementation of genetic data.

Abstract #517 flash presentation

## Unmasking anti-HMGCR myopathy: the hurdles of a prompt recognition

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**INTRODUCTION.** Anti-HMGCR (3-hydroxy-3-methylglutaryl coenzyme A reductase) is an immune-mediated necrotizing myopathy induced by statin. Atypical presentations hinder recognition and prompt treatment. We present two cases with either atypical clinical or pathological features.

**CASE REPORT.** First patient was found with asymptomatic high CK (~10000IU/L) at age of 45. Biopsy showed minimal changes without significant inflammation. She then developed slowly progressive proximal weakness and diagnosed as limb girdle muscular dystrophy. Genetic investigations resulted negative. Twelve years later, she had severe proximal weakness and muscle MRI showed diffuse fatty infiltration and disproportionate high STIR signal. HMGCR antibodies resulted positive. Immunosuppressive therapy stopped progression with a partial improvement of symptoms.

Second patient developed slowly progressive upper and lower proximal weakness with high CK (~4000IU/L); muscle biopsy revealed a lymphocyte infiltrate with angiocentric distribution suggestive for vasculitis. Clinical reassessment prompted testing of HMGCR antibodies that resulted positive.

Anti-HMGCR myopathy can present with slowly progressive myopathy and atypical pathology.

Abstract #518 Platform Presenter

## Caveolae-Associated Protein (cavin)-4 autoantibodies in immune mediated rippling muscle disease (iRMD)

**Importance:** iRMD is a rare autoimmune myopathy characterized by electrically silent abnormal muscle excitability and mosaic caveolin-3 sarcolemmal expression.

**Objective:** To identify a novel autoantibody biomarker of iRMD.

**Methods:** Archived sera from iRMD patients were evaluated for a common biomarker using phage immunoprecipitation sequencing (PhIP-Seq). Patients' muscle biopsies were also evaluated for putative autoantigen expression.

**Results:** PhIP-Seq identified peptides corresponding to different regions of the cavin-4 in iRMD sera. Eight of ten iRMD patients were positive for cavin-4 IgG by immunofluorescent cell-based-assay. Healthy and disease controls were cavin-4 IgG seronegative. Muscle biopsy was performed in 7/8 cavin-4 IgG seropositive patients; 6/6 muscle specimens revealed a mosaic pattern of sarcolemmal cavin-4 immunoreactivity, matching caveolin-3 expression. Three of 6 seropositive patients who received immunotherapy had resolution of symptoms; one had mild improvement and two had no change.

**Conclusion:** Cavin-4 IgG is a novel and specific serological autoantibody biomarker of iRMD.

Abstract #476

## Skeletal Muscle Channelopathies: A UK Prevalence Study

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**Introduction:** Skeletal muscle channelopathies are a group of skeletal muscle disorders caused by variations in genes that encode for ion channels. The last UK prevalence study found the minimum point prevalence of skeletal muscle channelopathies to be 1.12/100,000 in 2011. Since then, there has been an implementation of Next Generation Sequencing in the National Hospital for Neurology and Neurosurgery and increased research into variants associated with skeletal muscle channelopathies.

**Objectives:** To provide an up-to-date and accurate minimum point prevalence of genetically defined Myotonia Congenita (MC), Sodium Channel Myopathy (SCM), Paramyotonia Congenita (PMC), Hyperkalemic Periodic Paralysis, Hypokalemic Periodic Paralysis and Anderson-Tawil Syndrome (ATS). It also looks at the different variants associated with the conditions and the mode of inheritance.

**Methods/Materials:** Analysis of 4241 patients on the National Channelopathy database was undertaken, looking at the variants of CLCN1, SCN4A, CACNA1 and KCNJ2.

**Results:** The point prevalence of all Skeletal Muscle Channelopathies is 2.04/100,000 population. The minimum point prevalence of MC is 1.13/100,000, of SCN4A variants which encode for PMC and SCM is 0.37/100,000, of periodic paralysis is 0.44/100,000 and of ATS is 0.1/100,000.

**Conclusion:** There has been an overall increase in point prevalence in skeletal muscle channelopathies, with the biggest increase found to be in MC. This can be attributed to an increased implementation in NGS for patients and relatives presenting to channelopathy services. Despite there being an increase in total number of variants, a small number account for a large proportion of patients with the condition.

Abstract #491

## Proposal for the functional assessment of acute inflammatory neuropathy (FAAIN) in Guillain-Barré syndrome

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**Introduction:** Guillain Barré syndrome (GBS) functional assessment is necessary in clinical practice, research and clinical trials. Existing instruments are not sensitive to change and are not applicable to the current GBS clinical spectrum.

**Objectives:** To construct a functional assessment for acute inflammatory neuropathies (FAAINGBS), inclusive for current GBS spectrum.

**Methods:** FAAIN-GBS was made up of two subscales (extension and intensity). Its structure and interpretation were defined. It was validated using data from medical record of 167 GBS patients admitted to the Institute of Neurology and Neurosurgery.

**Results:** FAAIN-GBS was constructed. Internal consistency was acceptable (Cronbach 0.745). Spearman correlation between FAAIN-GBS and Hughes scale was 0.463. Sensitivity was 0.714 and specificity, 0.986. AUROC was 0.93.

**Conclusion:** FAAIN-GBS was constructed and a first step of validation was made, showing good internal consistency and validity. New prospective studies will be necessary to perfect this instrument that could be useful in neurological practice.



Abstract #501

## Creatine Kinase (CK), Mitochondrial CK, and Macro-CK.

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**Introduction:** Testing for serum creatine kinase (CK) activity level is a routine practice when evaluating patients with muscle weakness. Whereas serum CK is well-known and often used in clinical practice, mitochondrial CK (Mt-CK) and macro-CKs are not.

**Objectives:** To understand origin, structure, function, tissue expression, and potential clinical applications of Mt-CK and macro-CKs.

**Methods:** We reviewed PubMed medical literature about Mt-CK and macro-CKs and their significance in health and disease.

**Results:** Macro-CK type 1 has been found in the serum of patients with autoimmune disorders such as myositis and in healthy subjects. Macro-CK type 2 is a Mt-CK oligomer that has been associated with malignancies. In biopsied skeletal muscle, electron-dense intramitochondrial deposits of Mt-CK resembling the appearance of “parking lot” has been reported as a feature of mitochondrial cytopathies.

**Conclusions:** Existing data in literature suggest that Mt-CK and macro-CKs may be clinically useful when evaluating patients with neuromuscular diseases (myopathies).

Abstract #511

## Dominant Cardioskeletal Titinopathies Reflect Distinct Mechanisms of Disease

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**Introduction:** We identified novel dominant skeletal/cardioskeletal titinopathies segregating in families with single truncating, splice-site or deletion *TTN* variants.

**Objective:** To investigate mechanism of disease.

**Methods:** Tibialis anterior biopsies were studied via Western blot, RNASeq, EM, and muscle fiber mechanic studies in 9 cases, 7 controls, and one disease control.

**Results:** Western blot revealed normal full-length and truncated titin in the deletion case (exons 346-362), but only normal titin in the truncating and splice-site cases. *TTN* transcript levels were reduced in the truncating and deletion cases and in the HMERF control, but normal in the splice-site cases. Skipping of exons 347-361 was observed in the deletion case. Reduction of *RBM* transcripts and differential splicing of known gene targets was observed in 3 cases with the c.44816-1G>A splice variant.

**Conclusions:** Dominant truncating, splice-site or deletion *variants appear* to result in distinct disease mechanisms in skeletal titinopathies, including dominant negative modes of action.

Abstract #512

## Characterising the molecular consequences of LMNA-related congenital muscular dystrophy in patient myoblasts

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Mutations in LMNA, encoding lamin A/C, can cause congenital muscular dystrophy (L-CMD), but the downstream molecular mechanisms that give rise to L-CMD are not fully understood. Using quantitative western blotting and immunofluorescence microscopy, we show that myoblasts from three individuals with L-CMD have abnormal nuclear morphology and mislocalised emerin, whilst the expression levels of lamin A/C and emerin are comparable to myoblasts from health controls. Quantitative proteomics analysis revealed differential expression of 124 and 228 proteins in L-CMD myoblasts and myotubes, respectively, compared to controls. Ingenuity pathway analysis revealed enriched canonical pathways associated with the differentially expressed proteins including synaptogenesis signalling and necroptosis signalling pathways in L-CMD myoblasts, and Huntington's disease signalling, xenobiotic metabolism signalling and insulin secretion signalling pathways in L-CMD myotubes. The proteins and molecular pathways identified here shed light on the downstream molecular consequences of L-CMD and may represent targets for future development of therapies.

Abstract #514

## A Novel Approach to Treating Myotonia Congenita

**Introduction:** Myotonia Congenita (MC) is an inherited disease affecting the skeletal muscle chloride channel. Patients with MC suffer from debilitating involuntary muscle stiffness. Myotonia can be triggered through voluntary movement or percussion. It is still unknown if the two mechanisms are distinct.

**Objective:** To determine the mechanism causing percussion myotonia with the goal of improving treatment for MC.

**Methods:** In vitro and in vivo electrophysiology experiments were performed on both genetic and pharmacologic mouse model of MC.

**Results:** We examined the role of transient receptor potential vanilloid 4 (TRPV4) in myotonia. Percussion myotonia was markedly suppressed in TRPV4-KO muscles and in muscles treated with selective TRPV4 channel inhibitors. Inhibition of TRPV4 did not alter intrinsic muscle excitability and it reduced the severity of myotonia by 80% in vivo.

**Conclusion:** These results suggest two distinct mechanisms generate myotonia and block of TRPV4 offers a new therapeutic option for MC.

Abstract #519

## A stable human Schwann cell model of Charcot-Marie-Tooth disease type 1A

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Charcot-Marie-Tooth disease type 1A (CMT1A) is a hereditary condition affecting the insulating myelin sheath surrounding peripheral nerves, resulting in muscle weakness and wasting and loss of sensation. CMT1A is caused by duplication of the *PMP22* gene which leads to overexpression of peripheral myelin protein 22 in Schwann cells, leading to myelin sheath defects and axonal loss. The reduction in levels of PMP22 is therefore a promising approach for potential therapies. To study this, we have established a stably transfected, clonal, immortalized human Schwann cell line with high over-expressed levels of cytoplasmic PMP22 fusion protein. Plasma membranes were often irregular and spindly in the PMP22 transfectants but generally had a smooth appearance in control transfectant cells. Ongoing work aims to identify drugs and interaction partners in these cells which may have potential to regulate the expression levels or stability of PMP22 as an approach to therapy.

Abstract #525

## Unlocking the potential of oligonucleotide therapeutic candidates for Duchenne muscular dystrophy through enhanced delivery.

Ashling Holland, Sonia Bracegirdle, Sam Ching, Jaya Goyal, Smita Gunnoo, Calum Irwin, Rachel Johnson, Jane Larkindale, Pallavi Lonkar, James McArthur, Michelle Mellion, Niels Svenstrup, Caroline Godfrey, PepGen Inc.

**Introduction:** PepGen's Enhanced Delivery Oligonucleotide (EDO) technology is engineered to optimize tissue penetration, cellular uptake and nuclear delivery of oligonucleotide therapeutic candidates, potentially enhancing therapeutic activity. PGN-EDO51 is designed to treat individuals with Duchenne muscular dystrophy (DMD) amenable to exon 51 skipping.

**Objectives:** Evaluate the potential of PGN-EDO51 in *mdx* mouse and non-human primates (NHP).

**Methods:** Single administration in *mdx* mice (0, 30, 60 mg/kg) and single/repeat administration in NHP (0, 10, 20, 30, 40, 60 mg/kg).

**Results:** PGN-EDO23 (murine analogue of PGN-EDO51), induced 90.4%, 99.7% 80.6% and 25.7% of normal dystrophin levels in the quadriceps, biceps, diaphragm, and heart of the *mdx* mouse respectively. NHPs showed broad biodistribution, with significant levels in skeletal, smooth, and cardiac muscle and central nervous system. Repeat administrations demonstrated accumulation of exon skipping. No significant toxicology was observed.

**Conclusions:** PGN-EDO51 was generally well tolerated through clinically relevant doses and is currently being evaluated in a Phase I healthy volunteer study.

Abstract #526

## Unlocking the potential of oligonucleotide therapeutic candidates for myotonic dystrophy through enhanced delivery.

Ashling Holland, Sonia Bracegirdle, Sam Ching, Jaya Goyal, Smita Gunnoo, Calum Irwin, Rachel Johnson, Jane Larkindale, Pallavi Lonkar, James McArthur, Michelle Mellion, Niels Svenstrup, Caroline Godfrey, PepGen Inc.

**Introduction:** PepGen's Enhanced Delivery Oligonucleotide (EDO) technology is engineered to optimize tissue penetration, cellular uptake and nuclear delivery of oligonucleotide therapeutic candidates. The EDO platform achieves robust delivery of oligonucleotides to skeletal, smooth and cardiac muscle and central nervous system in non-human primates (NHPs). PGN-EDODMI is designed to deliver a PMO into muscle cells that binds to the pathogenic CUG repeat expansion present in the *DMPK* mRNA, reducing the ability of the repeats to sequester MBNL1, thereby correcting splicing and reducing disease symptoms.

**Objectives:** Evaluate potential of PGN-EDODMI to treat the underlying cause of DMI.

**Methods:** Single dose administration in DMI cellular model (2,600 CTG repeats) and HSA<sup>LR</sup> murine model.

**Results:** Dose dependent correction of mis-splicing was observed in both models. Cellular model showed reduction in toxic foci. The HSA<sup>LR</sup> murine model showed sustained correction of mis-splicing and complete amelioration of myotonia. No significant toxicology was observed at clinically relevant doses.

**Conclusions:** These results support further development of PGN-EDODMI as a disease-modifying treatment for DMI.

Abstract #528

## Development of a diagnostic framework for vestibular causes of dizziness and unsteadiness in patients with mitochondrial disease – a Delphi consensus

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**Introduction:** Vestibular dysfunction is prevalent in adults with mitochondrial disease (MD) (Holmes et al. 2018). A consensus method was employed to identify statements for a diagnostic framework to facilitate identification of vestibular dysfunction in MD.

**Methods:** A three-round, modified electronic Delphi approach was used. Round one developed the statements from evidence-based literature. Statements were emailed to neuro-otologists of the European Academy of Neurology to obtain their level of agreement with the statements being in the framework. Consensus was defined when  $\geq 75\%$  of the responses were in the lower or higher tertile (Boukdedid et al., 2011).

**Results:** Twelve statements were emailed in round two, five reached consensus, four were removed and three were reworded. One reached consensus in round three.

**Conclusion:** Six questions were identified to ask patients with MD reporting dizziness and unsteadiness. These are included in a diagnostic framework being validated in an observational cohort study design.



Abstract #536

## Evaluation of face mobility in spinal muscular atrophy: exploiting a face tracking approach

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**Introduction:** Weakness in the oro-facial district may affect several functions. Quantitative assessments and oro-facial response to current therapies are scanty in Spinal Muscular Atrophy (SMA).

**Objectives:** To quantitatively evaluate face mobility in SMA.

**Methods:** Subjects were asked to perform different tasks (eg. frown, close your eyes, smile, kiss, inflate your cheeks) while frontal face videos were acquired prior to acquisition of a neutral face expression. Face mobility index (FMI), an easy-to-interpret index based on a face tracking algorithm that exploits Facial Action Coding System, was calculated.

**Results:** 23 adults (33.30±13.06 years) and 13 kids (9.46±3.55 years) with SMA and 10 age-matched healthy controls were recruited. FMI detected a significant difference in the 'smile' task in children and in the 'kiss' task in adults compared to controls.

**Conclusions:** FMI seems to be an interesting non-invasive measure of face mobility in SMA. Follow-up data in patients on nusinersen are on-going to explore the potential effects of treatment in the facial district.

Abstract #537

## Neurophysiological study of facial nerve and Motor Unit Number Index (MUNIX) of orbicularis muscle in spinal muscular atrophy (SMA)

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**INTRODUCTION.** Orobulbar involvement in SMA is frequent but quantitative assessment still relies on exploratory measures. MUNIX studies have shown correlation with disease severity but its application has been limited to limb muscles.

**OBJECTIVES.** To explore MUNIX of the orbicularis oculi and facial nerve in SMA.

**METHODS.** MUNIX of the orbicularis muscle and facial nerve responses (measured as compound motor action potential, CMAP), was cross-sectional recorded in SMA patients and compared to healthy controls (HCs).

**RESULTS.** 36 SMA (20 SMA2;16 SMA3) patients and 27 HCs (comparable in age and gender) have been recruited. In the SMA cohort median CMAP amplitude and MUNIX scores were 1.5 mV and 20.8 respectively. Mean CMAP amplitude and MUNIX scores were significantly lower in SMA patients compared to controls and correlated to functional status (SMA2 vs SMA3) and Active Maximum Mouth Opening.

**CONCLUSIONS.** Follow-up analysis to monitor facial muscle strength is ongoing to explore the potential benefit of nusinersen over time in facial muscles.

Abstract #546

## A case of myotonic dystrophy type 1 associated with Parkinson disease

**Introduction:** Myotonic dystrophy type 1 (DMI) is a genetic disorder that caused muscle dystrophy and myotonia in combination with multisystemic involvement. Coexistent parkinsonism symptoms are very uncommon and since 1996 only six cases are reported.

**Case Report:** A 62-year-old male presented with complaints of a 6 years of worsening dysphagia and balance disorder and subsequently a bilateral foot dorsiflexion deficit. Hospitalized in March 2022 for further worsening of dysphagia and weight loss; on examination the patient showed moderate bilater bradykinesia, biliteral limb rigidity and slowing gait with reduced arm swing.

**Methods and results:** Electromyographic exam and DAT-Scan were carried out. EMG confirmed the diagnostic suspicion of DMI while DAT imaging demonstrated presynaptic dopaminergic deficit in bilateral putamen. Then we started levodopa treatment without benefit.

**Conclusion:** These data are similar to those reported in literature; the association of DMI and parkinsonism may not be coincidental. Poor-levodopa response is a common aspect in all DMI reported cases.

Abstract #549

## Proteomic profiling of fibroblasts differentiates patients with severe, intermediate and mild spinal muscular atrophy

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Most research characterising the molecular consequences of spinal muscular atrophy (SMA) have focused on SMA I. Here, quantitative proteomic profiling of skin fibroblasts from severe (SMA I), intermediate (SMA II), and mild (SMA III) patients, compared to controls, found limited overlap of differentially expressed proteins across each SMA type. Nevertheless, enriched canonical pathways common to all types included mTOR signalling, regulation of eIF2 and eIF4 signalling, and protein ubiquitination. BioLayout expression clustering identified proteins that discriminate or correlate with severity, from which PYGB (SMA I), RAB3B (SMA II), and IMP1 and STAT1 (SMA III) were selected and verified. Transfection of SMA II fibroblasts with an SMN-construct enhancing its expression confirmed RAB3B expression is SMN-dependent. Combined, this four-protein panel may be useful for stratifying patients in clinical trials or for therapeutic monitoring. The proteins and pathways identified pave the way for studies to optimise therapies for SMA patients of differing severities.

Abstract #550

## Dysregulation of intermediate filament proteins associated with cardiac pathology in two mouse models of differing Spinal Muscular Atrophy (SMA) severity

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Using quantitative proteomics analysis, we previously detected widespread molecular defects in heart tissue from the Taiwanese mouse model of severe spinal muscular atrophy. Using the same approach, we now report significant perturbation of the heart proteome in the *Smn*<sup>2B/-</sup> milder SMA mouse model. In *Smn*<sup>2B/-</sup> hearts, 277 proteins were significantly dysregulated compared to controls with 50 similarly dysregulated in Taiwanese hearts. Bioinformatics analysis found many of the dysregulated proteins to be associated with cardiovascular development and function. Similarly, to Taiwanese mice, lamin A/C was increased in *Smn*<sup>2B/-</sup> hearts whilst desmin was reduced in both. Lentiviral-mediated SMN restoration restored desmin levels in *Smn*<sup>2B/-</sup> hearts to control levels whereas lamin A/C remained elevated. Intermediate filament proteins have key roles in cardiac function and their dysregulation may explain cardiac impairment in SMA. Cardiac pathology may need considering in long-term care of SMA patients, as current treatments may not fully rescue SMA peripheral pathology.

Abstract #551

## Hypercapnic respiratory failure in a patient with rheumatoid arthritis and systemic sclerosis overlap caused by hydroxychloroquine-induced toxic myopathy

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Hydroxychloroquine (HCQ) and chloroquine (CQ) have been commonly used agents in the prevention of malaria and the treatment of a variety of systemic inflammatory disorders since the 1950s. Off-target effects due to accumulation of HCQ/CQ in lysosomes include myopathy. We describe a 51-year-old female with rheumatoid arthritis and systemic sclerosis overlap complicated by type 1 pulmonary arterial hypertension treated with a combination of methotrexate, etanercept, and hydroxychloroquine who developed acute hypercapnic respiratory failure and inability to wean from the ventilator despite aggressive pulmonary management. Diagnostic workup yielded evidence of a proximal myopathy, atrophic diaphragms, near-absent phrenic nerve responses, and non-specific chronic myopathic changes on muscle biopsy. Electron microscopy ultimately revealed evidence of abnormal autophagy with accumulation of curvilinear material associated with hydroxychloroquine drug toxicity. After discontinuation, she gradually weaned from positive pressure ventilation and regained strength. This case demonstrated the value of ultrastructural examination differentiating HCQ toxicity from overlap myositis.

Abstract #566

## Detection of alpha-dystroglycan glycation in muscle biopsies using a multiplexed western blot method

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**Introduction:** Limb-girdle Muscular Dystrophy (LGMD) Type 2I is an autosomal recessive disease caused by partial loss of function mutations in fukutin-related protein (FKRP) leading to hypo-glycosylation of alpha dystroglycan ( $\alpha$ DG).

**Objectives:** Develop a method for evaluating the extent of glycosylation of  $\alpha$ DG in muscle biopsies from patients with LGMD2I.

**Methods:** A multiplex western blot (WB) was developed to assess glycosylation of  $\alpha$ DG by detecting both total  $\alpha$ DG and glycosylated  $\alpha$ DG. This generates a ratio of  $\alpha$ DG-glycan to total  $\alpha$ DG that estimates glycosylation.

**Results:** Two compatible antibodies were identified. Specificity was assessed using DAG1 HEK293T knockout cell lysates. Signal linearity was evaluated using control tibialis anterior (TA). This WB method will assess muscle biopsies in participants of our LGMD2I natural history study.

**Conclusions:** A multiplexed WB has the potential to inform on the extent of  $\alpha$ DG glycosylation in LGMD2I patients and to assess cellular response to a therapeutic intervention.

Abstract #574

The Tragic Couple:  
Adult Onset Desmin-Related Myopathy and Multiple Sclerosis

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**Introduction:** Mutations of *DES* gene, which encodes an intermediate filament called desmin, mostly causes myofibrillar myopathy.

**Case report:** We report a patient with desmin-related myopathy and multiple sclerosis (MS) simultaneously.

**Methods:** A 26-year-old male was admitted with progressive proximal weakness. He had no family history of myopathy. Decrease in right-sided visual acuity and mild sensory impairment were noted besides limb weakness. Brain MRI was compatible with primary demyelinating disease. High serum creatine kinase, and myopathic changes in electromyography were detected. Muscle biopsy showed myopathic features consisted of cytoarchitectural abnormalities and mild increase in connective tissue.

**Results:** New generation DNA sequencing revealed homozygous splice site mutation c.1289-2A>G in *DES* gene, which has been reported once before.

**Conclusion:** Although central nervous system involvement can be present in various muscle disorders, the co-occurrence of MS and myopathy is very rare. In our knowledge, this is the first case with desmin-related myopathy and MS.



Abstract #575

## Evaluation of the Biodistribution, Efficacy, and Side-Effect Profile of Deflazacort, Prednisone/Prednisolone and Vamorolone in a Duchenne Muscular Dystrophy (DMD) Mouse Model

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**Introduction:** Corticosteroids are the standard of care for DMD.

**Objective:** Compare the biodistribution, efficacy and side-effects of deflazacort, prednisone/prednisolone, and vamorolone in adult mdx mice.

**Methods:** All 3 corticosteroids were evaluated using biologically equivalent doses that were compared at clinically relevant exposures.

**Results:** Deflazacort had a lower brain:plasma ratio(0.05) than vamorolone(0.55). D. All three corticosteroids inhibited NF-kB inflammatory cytokines associated with the beneficial effects of corticosteroids, and induced genes associated with drug side-effects.

Prednisone/prednisolone and vamorolone had a greater extent of altered gene expression in mdx mouse brain (4914 and 4730 genes) vs deflazacort (329 genes, highest dose). Mice treated with deflazacort showed greater improvement in grip strength vs prednisone/prednisolone or vamorolone (67%, 27%, and 0%, respectively). Vamorolone and prednisone/prednisolone induced greater depression than deflazacort in corticosteroid-induced depression tests in these same mice.

**Conclusion:** Deflazacort was most effective in increasing muscle strength, with the least potential for behavioural side-effects.

Abstract #578

## Clinical Improvement Mirrored Antibody Reduction in Myasthenia Gravis

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**Introduction:** The relationship of anti-acetylcholine receptor (AChR) antibody levels to treatment response remains unclear in seropositive myasthenia gravis (MG) patients.

**Objective:** To examine whether changes in AChR antibody level ( $\Delta$ Ab) correlate with clinical response in subjects in the Thymectomy in Myasthenia Gravis Trial (MGTX).

**Methods:** Post-hoc analysis of the MGTX antibody level dataset at baseline, 12, 24, 36 months. Changes in Myasthenia Gravis Activities of Daily Living ( $\Delta$ MG-ADL) and Quantitative Myasthenia Gravis ( $\Delta$ QMG) scores compared to  $\Delta$ Ab between the thymectomy+prednisone versus prednisone only groups. Statistical methods included bivariate linear regression, Spearman correlation and Mann-Whitney test.

**Results:** Data from 86/126 enrolled subjects, including outliers, was analyzed. Correlation with  $\Delta$ MG-ADL was statistically significant at 12 and 24 months (P 0.0397 and 0.0008 respectively).  $\Delta$ QMG and  $\Delta$ Ab directly correlated at all 3 timepoints [P= 0.0032, P= 0.0031, P=0.0005, respectively].

**Conclusion:** Reductions in AChR antibody level generally correlated, in both treatment arms, with improvement in QMG and MG-ADL scores.

Abstract #581

## Spectrum of multisystem proteinopathies: single center experience

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**Introduction:** Multisystem proteinopathies (MSPs) are genetically heterogenous disorders sharing the common pathomechanism of RNA granule function defect leading to protein aggregation.

**Objectives/Methods:** To study the MSP spectrum in patients evaluated at Mayo Clinic (2010-2022) by reviewing clinical and laboratory findings.

**Results:** Among 25 patients (22 families), *VCP*-MSP was the most common (68%) followed by *SQSTM1+TIAI*-MSP (20%). *HNRNPAl*-, *MATR3*-, and *TFG*-MSP, each accounted for single cases. Myopathy occurred in 92%: mean age-onset was 53 and phenotype was limb-girdle (12/15 *VCP*-MSP), distal or scapulo-distal (other MSPs). Rimmed vacuoles were present in 85% of muscle biopsies. Motor neuron phenotype was rare (2 *VCP*-MSP; 1 *TFG*-MSP). Frontotemporal dementia and Paget's disease of bone each occurred in 12% of patients. Within 12-year follow-up, 72% required a gait-aid 9 years (median; range 1-21) after disease-onset; 24% developed restrictive lung disease; none had cardiomyopathy.

**Conclusion:** Rimmed-vacuolar myopathy was the most common presentation in our MSP cohort.

Abstract #583

## Characterization of Inclusion Body myositis (IBM) population, single center study

**Introduction:** IBM is a slowly progressive myopathy beginning in mid life with no proven treatment.

**Objective:** to characterize the IBM population seen in our Myositis Clinic over the years.

**Methods:** retrospective chart review from 1/2017 until present.

**Results:** Out of 32 patients with IBM, 18 were tested for the NT5c1A antibodies. 72% were positive and 28% were negative. The NT5c1A seropositive patients, dropped in average with 3.3 points IBMFRS per year. The seronegative patients progressed in average with 1.76 points on the IBMFRS per year. The seropositive patients had their disease in average for the past 16 years and 61% are ambulatory and 30 % are non-ambulatory and one died after 40 years of disease. The seronegative patients had their disease in average for the past 11.2 years and all but one are still ambulatory (80%).

**Conclusions:** The seropositive patients seem to decline faster and are more likely to lose ambulation than the seronegative patients.

Abstract #584

## Myasthenia gravis with “frozen globes” responding to Complement inhibitors

**Introduction:** Ocular MG can cause ophthalmoplegia or “frozen globes”. Here we describe a case responding well to eculizumab.

**Case report:** 48 year old with ocular MG AchR + presents with double vision and ptosis. His worst MGFA Score IIB. He has bilateral eye ptosis left worse than right and ophthalmoplegia. He is currently on Mestinon and monthly IVIG. Prior medications include prednisone and Azathioprine. His MRI orbits was negative with no atrophy of the extraocular muscles. While his disease is ocular only, the symptoms are severe and interfere with his quality of life.

**Results:** With eculizumab, in 3 months his MMT cranial muscle score went from 10 to 2 and in 10 months he was asymptomatic.

**Conclusion:** Intrinsic complement regulators are expressed at lower levels at EOM neuromuscular junctions, which would put them at risk for the complement-mediated injury that occurs in MG. Thus complement inhibitors should be used early in ocular MG before progression to atrophy of EOM.

Abstract #588

## Early assessment of infants with SMA identified through newborn screening

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**Introduction:** Neonatal screening for SMA is allowing the identification of patients with mutations in the SMN gene generally considered as presymptomatic.

**Objectives:** The aim of this study was to assess a cohort of infants identified through screening and to compare them to healthy controls. We also aimed to establish if the scores were different in patients who had already signs of SMA.

**Methods:** CHOP INTEND was performed in both SMA patients and healthy controls.

**Results:** A total of 26 (SMA) and 130 (controls) assessments were collected. Of the 26, 18 were from presymptomatic and 8 from symptomatic patients. CHOP INTEND score was different between symptomatic and presymptomatic or controls ( $p < 0.001$ ), while was not different between presymptomatic and healthy controls ( $p > 0.05$ ).

**Conclusions:** The CHOP INTEND is able to identify symptomatic patients identified by neonatal screening.

Abstract #589

## Female carriers for dystrophin gene mutation with various clinical manifestations – case series.

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**Introduction:** Female dystrophin (DMD) gene mutation carriers manifest various disease symptoms. Very little is known about the disease progression resulting in lack of Standards of Care (SOC).

**Objectives:** To review a cohort of symptomatic females with DMD mutation.

**Methods:** A retrospective review of patient medical notes.

**Results:** Thirteen females with DMD gene mutations presented with various sequela including: respiratory (31%) (one started non-invasive ventilation when ambulant), cardiomyopathy (62%), motor function decline and muscle weakness (100%), contractures (54%), falls (38.5%), lower limbs fractures (15%), bulbar involvement (31%) (in 4 ambulant patients), pain (38.5%), fatigue (31%), gastro-intestinal disturbances (15%), cognitive (23%) and psychological (31%) involvement. Four (31%) were treated with long-term corticosteroids of whom three (23%) found them beneficial.

**Conclusions:** Manifesting female DMD gene carriers are clinically heterogeneous, demonstrating similarities to affected males however, progression may differ. Recognising various disease presentations is critical to establishing SOC for management of this patient group.

Abstract #594

## The Importance Of Segregation in the Genetic Diagnosis Of Hereditary Neuropathies

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**Introduction:** Confirming pathogenicity of genetic variants in Charcot-Marie-Tooth (CMT) disease is of vital importance, particularly with the emergence of potential treatments. Segregation studies involving family members play a pivotal role in this.

**Objectives:** To assess the impact of the segregation studies on the diagnostic rate when using family-analysis compared to proband-only analysis for patients with genetic findings.

**Methods:** Blood was requested from relatives of 150 patients, in whom only the proband's DNA was initially available. Segregation of candidate variants was performed where applicable. Variants were reassessed as to the likelihood of their pathogenicity.

**Results:** Out of a total of 59 positive genetic test results 43 (73%) were confirmed pathogenic using segregation and 16 (27%) were confirmed pathogenic through singleton studies.

**Conclusions:** Segregation is crucial in the genetic diagnosis of hereditary neuropathies and remain a major part of the overall assessment of genetic variants in complex hereditary neuropathy clinics.



Abstract #595

## Episodic weakness in patients with mitochondrial DNA MT-ATP6 mutations: the Queen Square experience

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**Introduction:** Episodic muscle weakness has been described in people harbouring mitochondrial DNA (mtDNA) *MT-ATP6* mutations, mimicking periodic paralysis.

**Objectives:** To report the prevalence and clinical/electrophysiological features of episodic limb weakness in patients with mtDNA *MT-ATP6* mutations.

**Methods:** We retrospectively evaluated 19 patients with pathogenic *MT-ATP6* variants attending the Queen Square NHS England Highly Specialised Service for Rare Mitochondrial Disorders, London. Demographic, clinical, and electrophysiological data were collated.

**Results:** Of 19 patients, five (26.3%, two female) reported episodic lower limb weakness. The following *MT-ATP6* mutations were reported: m.9185T>C (n=3); m.8782G>A (n=1); and m.9176T>G (n=1). In all cases but one, a diagnosis of CMT2-like neuropathy was present. Long exercise testing was performed in three cases and resulted negative.

**Conclusions:** *MT-ATP6* mutations should be considered in patients with episodic weakness, normal long exercise testing, and negative pathogenic variants in skeletal muscle channelopathy genes.

Abstract #597

## Clinical heterogeneity in IBM patients

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**Introduction:** IBM is the most common acquired myopathy in individuals over age 50, and currently no therapeutic treatment is available. Clinical heterogeneity may influence treatment responsiveness; however, data regarding heterogeneity in IBM is limited and often conflicting.

**Objectives:** We aimed to identify clinically distinct subgroups within a large IBM cohort, as well as prognostic factors for disease progression.

**Methods:** Clinical, histologic, radiologic, and electrophysiologic data from IBM patients enrolled in a longitudinal cohort at the Johns Hopkins Myositis Center was analyzed. Univariate, multivariate, and graphical analyses were used to identify prognostic factors.

**Results:** 335 IBM patients met the inclusion criteria, with an average age of 58.7 years of disease onset. Average delay of diagnosis was 5.2 years, and in 20% onset was before age 50. Initial misdiagnosis and immunosuppressant treatment were common.

**Conclusion:** the study demonstrated distinct clinical phenotypes, particularly among female and Black patients.

Abstract #599

### New role for dystrophin in neuronal homeostasis

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Abnormal synaptic proteome function is a mediator of cognitive deficits in Duchenne Muscular Dystrophy. Neurons are highly polarized cells with multiple dendrites but a single axon, which underscores a highly regulated trafficking of cellular organelles, with the somatodendritic cargo not permitted to enter the axon. To investigate the mechanisms that regulate neuronal trafficking, we investigated the expression of ankyrin-G, the master regulator of neuronal polarity in CA1 hippocampal neurons of the mdx52 mouse model, using high resolution structural illumination microscopy, proteomics immunohistochemistry, and neuronal modeling. AIS structure and function was abnormal in mdx52 mice. The AIS was abnormal in length and diameter in mdx52 mice. Ankyrin-G colocalized with kinesin KIF5a, the anterograde protein transporter, with higher levels in older mdx52 mice compared to young mdx52 mice suggesting functional compromise of the AIS in neurons. Our data suggests that dystrophin deficiency compromises neuronal homeostasis through ankyrin-G based mechanisms.

Abstract #609

## Atypical cases of Sporadic Inclusion Body Myositis

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**Introduction:** Sporadic inclusion body myositis (sIBM) is classically heralded by weakness in the finger flexors and quadriceps in patients aged over 50. Respiratory and tongue involvement can be seen later but it is unusual to be seen early in the disease. There have been a few reports describing facial weakness as a presenting feature.

**Case Series:** We describe five cases of sIBM with atypical presentations.

**Methods:** The patients had undergone in depth investigations including histopathology, muscle MRI and in some cases advanced neurogenetics.

**Results:** Facial weakness was a presenting feature in two middle-aged patients. Marked tongue involvement and respiratory dysfunction early during the disease was seen in three cases. Two patients developed symptoms in their thirties with one such patient presenting with proximal weakness.

**Conclusions:** Despite the classical archetype described in the literature sIBM can present in a heterogenous fashion. sIBM should be increasingly recognised as a potential differential for early facial weakness and respiratory dysfunction.

Abstract #616

## Swallowing impairment in Myotonic Dystrophy type 1 (DM1): a slowly progressive event

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**Introduction:** Swallowing disorders in DM1 are potentially life-threatening.

**Objectives:** To determine the prevalence and progression of dysphagia and its correlation to neuromotor and self-assessment scales.

**Methods:** We retrospectively reviewed charts from 113 adults with DM1 and recorded clinical-demographic features, fiberoptic endoscopic evaluation of swallowing scores and nutritional status.

**Results:** At baseline 25% of patients had normal swallowing, 69% mild-moderate and 6% severe dysphagia. 4 of 113 had a PEG tube. After 2 years of follow-up (n = 65) over 80% of population was unchanged. From 2 to 4 years 50% of patients progressed from normal swallowing function to mild-to moderate dysphagia and 35% showed swallowing alterations with liquid consistency. 5 of 65 required a PEG tube (9%). BMI was unchanged.

**Conclusions:** Dysphagia is frequent in DM1 but progression seems to be slow. Management needs to be disease-specific and balanced between patients and caregivers perception and the potential to cause morbidity and mortality.

Abstract #625

Characterising sex differences in human skeletal muscle excitability and function.

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Dr Karen Suetterlin (Academic Clinical Lecturer in Neurophysiology at Newcastle University and Clinical Neurophysiology Registrar at the Royal Victoria Infirmary, Newcastle).

**Introduction:** Women are at greater risk of sudden cardiac death from drug-induced and genetic long QT arrhythmia. Sex differences in skeletal muscle excitability are also likely to exist as females with genetic skeletal muscle channelopathies may be asymptomatic carriers and have negative electrodiagnostic tests.

**Aims:** To investigate sex differences in healthy human skeletal muscle membrane properties and ionic homeostasis.

**Methods:** Muscle Velocity Recovery Cycles (MVRCs) and 30Hz frequency ramp EMG of Tibialis Anterior and Rectus Femoris of 70 healthy volunteers (35 males; 35 females; 18-39 years) will be used to assess excitability. Ionic homeostasis will be assessed by comparing continuous and intermittent voluntary contraction using the HandClench relaxometer. A KardiaMobile device will be used to measure QT interval and correlate with MVRC parameters.

**Results:** Early data will be presented at the conference.

**Conclusions:** We hope this study improves the techniques available for diagnosis/monitoring of diseases affecting muscle ion homeostasis.

Abstract #636

## Distal Adermatoglyphia (loss of fingerprints) in a patient with sporadic Inclusion body Myositis

Breanna Tuhlei, Nakul Katyal, Praveen Attele, Erik Ensrud, Richard J. Barohn

**Introduction:** We discuss the first description of partial distal adermatoglyphia in a patient with IBM.

**Case Report:** A 68 year old male presented with distal right hand and both proximal and distal left leg weakness of 5 years duration. Examination showed right hand finger flexion strength of  $\frac{3}{5}$  in digit 2 and 3 and  $\frac{4}{5}$  in digit 1 and 4. Left hip flexion strength was 4+/5. EMG showed myopathic findings in the left psoas and flexor digitorum profundus. NT5C1A antibody was positive. Muscle biopsy showed inflammatory infiltrates with T cell predominance in the endomysium with scanty rimmed vacuoles. The patient was diagnosed with sporadic IBM.

At age 68, his fingers started turning smooth and glossy. Distal fingerprints could not be obtained on the biometric scanner. Examination showed a lack of epidermal ridge pattern on the distal palmar aspect of bilateral fingers.

**Conclusion:** Partial distal adermatoglyphia can be seen in patients with sporadic IBM.

Abstract #638

## POLG mutation causing autosomal dominant progressive external ophthalmoplegia and distal weakness.

Introduction: POLG-related disorders comprise a group of mitochondrial diseases with overlapping phenotypes. In the subtype, autosomal dominant progressive external ophthalmoplegia, the pattern of weakness is traditionally proximal.

Case Report: A 53-year-old female presented with bilateral ptosis and distal upper extremity weakness. At age 40, she developed bilateral ptosis followed by bilateral hand weakness over five years. The patient's sister, paternal aunt and her son have ptosis. Examination revealed bilateral ptosis, symmetric bilateral weakness of finger extension (3/5), wrist extension (4/5), and finger abduction (4/5). EMG showed fibrillation potentials and diffuse chronic neurogenic changes in the upper and lower limb. Sequence analysis revealed a heterozygous mutation in the POLG gene.

Conclusion: We describe an unusual case of POLG mutation presenting as distal weakness



Abstract #641

### TDP-43 loss of function in the skeletal muscle

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TDP-43 is a predominantly nuclear RNA-binding protein that mislocalizes to the cytoplasm in both ALS/FTD and muscular disorders. The concomitant nuclear loss of function leads to impairment of gene expression and splicing, which can be analysed through RNA-sequencing, as successfully done in ALS/FTD brain. There is a lack of characterisation of such mechanisms in muscles. Thus, we developed an IHC-guided RNA-sequencing pipeline that can detect RNA changes in affected tissues, and we are applying it to biopsies from several muscle diseases and healthy controls.

We report on this ongoing effort, and on the importance of impaired RNA processing in muscle diseases.

Abstract #642

## Implementing genome and transcriptome sequencing methods to improve the diagnosis of Mendelian myopathies

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**Introduction:** Fewer than half of individuals with Mendelian (i.e. monogenic) myopathies obtain a molecular diagnosis. Prior work in our group was the first to demonstrate the diagnostic utility of RNA sequencing (RNA-seq) in Mendelian myopathies.

**Objectives:** To improve the diagnostic yield in Mendelian myopathies using a combined platform of whole genome sequencing (WGS) and bulk RNA-seq.

**Methods:** We performed WGS from whole blood, annotating single nucleotide variants, indels, structural variants, short tandem repeat expansions, and mitochondrial variants. In addition we performed RNA-seq from muscle biopsies or cultured fibroblasts, applying autoencoder denoising methods (FRASER, OUTRIDER) paired with a web browser visualization tool to identify gene and splice isoform outliers in a cohort of 172 individuals with suspected Mendelian myopathies.

**Results:** Implementation of these methods 1) improved the diagnostic yield in our cohort by 18%, and 2) validated the transcriptional effect of variants predicted to affect splicing.

**Conclusions:** Low diagnostic yield in Mendelian myopathies can be mitigated by optimization of WGS and RNA-seq methods for variant identification and resolution.

## Academic Registries and Patient Organizations

Abstract #542

### Self-reported postural symptoms predict vestibular dysfunction and falls in patients with multi-sensory impairment

Professor D. Kaski, Dr N. Koochi, S. Holmes, E. Bennet, A. Male, Dr R D S Pitceathly, and Professor M.G. Hanna (London, UK)

**Introduction:** Primary mitochondrial diseases (PMDs) are a genetically heterogeneous group of conditions. Ataxia, neuropathy, myopathy, and vestibular dysfunction (VD) are common manifestations. We investigated the relative contributions of sensory impairment to postural control in patients with MD, using PMDs as a clinical model of multi-sensory impairment.

**Methods:** 130 patients with a confirmed genetic and/or clinicopathological diagnosis of MD attending a specialist clinic in the United Kingdom were included: the presence of ataxia, peripheral neuropathy, myopathy, symptoms of dizziness and imbalance and self-reported falls were reported.

**Results:** 52% of patients with ataxia, and 52% of patients with confirmed VD, reported falls; compared to 38% with neuropathy and 30% with myopathy. 80% of MD patients with confirmed VD reported imbalance, 56% reported dizziness.

**Conclusions:** Dizziness and imbalance are useful self-reported indicators of vestibular dysfunction in patients with multisensory impairment, and highly predictive of falls.

Abstract #552

## Nurse coaching for newly tracheostomized patients at the Nemo Clinical Center: a single center experience

**INTRODUCTION:** Nurse coaching plays a crucial role in coordinating the multidisciplinary team involved in the care of patients with Amyotrophic Lateral Sclerosis (ALS).

**OBJECTIVES:** To describe the holistic approach used at the NEMO Clinical Center to train caregivers of patients with ALS subjected to neotracheostomy.

**MATERIALS AND METHODS:** Charts from caregivers of neotracheostomized patients with ALS discharged to their homes between April 2020 and April 2022 were retrospectively reviewed.

**RESULTS:** 24 people with ALS (average age at tracheostomy: 62.17 years  $\pm$  8.60) and 42 caregivers were recruited. The NC coordinated the multidisciplinary team for each patient. Training consisted of at least 2 frontal lessons and 3 days or more of practical training. The average duration of the training process was 26.29 days  $\pm$  11.76.

**DISCUSSION:** The study highlights the importance of nurse coaching within a multidisciplinary team. The educational reports emphasize the need for training in activities of daily living in patients with a neotracheostomy and not only in specific procedural skills (e.g. endotracheal aspiration technique) usually the only issues addressed.

Abstract #555

## Updated demographics and safety data from patients with nonsense mutation Duchenne muscular dystrophy (nmDMD) receiving ataluren in the Strategic Targeting of Registries and International Database of Excellence (STRIDE) Registry

Francesco Muntoni,<sup>1</sup> Filippo Buccella,<sup>2</sup> Isabelle Desguerre,<sup>3</sup> Janbernd Kirschner,<sup>4</sup> Eugenio Mercuri,<sup>5</sup> Andrés Nascimento Osorio,<sup>6</sup> Már Tulinius,<sup>7</sup> Shelley Johnson,<sup>8</sup> Christian Werner,<sup>9</sup> Allan Kristensen,<sup>8</sup> James Li,<sup>8</sup> Audrey Powell,<sup>8</sup> Nicholas Mastrandrea,<sup>8</sup> Efthimia Leonardi,<sup>8</sup> and Panayiota Trifillis<sup>8</sup>

<sup>1</sup>University College London, Great Ormond Street Institute of Child Health, London, United Kingdom; <sup>2</sup>Parent Project APS, Rome, Italy; <sup>3</sup>Hôpital Necker – Enfants Malades, Paris, France; <sup>4</sup>Medical Center – University of Freiburg, Freiburg, Germany; <sup>5</sup>Department of Pediatric Neurology, Catholic University, Rome, Italy; <sup>6</sup>Hospital Sant Joan de Déu, Unidad de Patología Neuromuscular, Universidad de Barcelona, Barcelona, Spain; <sup>7</sup>Department of Pediatrics, Gothenburg University, Queen Silvia Children's Hospital, Gothenburg, Sweden; <sup>8</sup>PTC Therapeutics Inc., South Plainfield, New Jersey, USA; <sup>9</sup>PTC Therapeutics Germany GmbH, Frankfurt, Germany.

**Introduction:** STRIDE is an ongoing registry providing real-world data on ataluren use in patients with nmDMD.

**Objective:** To describe the demographics of the STRIDE population and the interim safety results, as of January 31, 2021.

**Methods:** Patients' data are collected at the consent date. Patients are followed for  $\geq 5$  years.

**Results:** As of January 31, 2021, 286 boys enrolled in STRIDE in 13 countries and received  $\geq 1$  ataluren dose. Mean ( $\pm$ SD) ataluren exposure was  $1352 \pm 517$  days. Safety outcomes were consistent with the known safety profile of ataluren. Of the 286 boys enrolled, 269 had genetically confirmed nmDMD. Mean ( $\pm$ SD) age at consent date was  $9.9 \pm 3.8$  years. Mean ( $\pm$ SD) age at first symptoms and nmDMD confirmation was  $2.7 \pm 1.7$  years and  $4.9 \pm 2.7$  years, respectively. Median time between first symptoms and nmDMD confirmation was 1.4 years.

**Conclusions:** These data suggest ataluren's safety profile is consistent between clinical trials and clinical practice.

Abstract #559

## Comparing the change in 6-minute walk distance (6MWD) in nonsense mutation Duchenne muscular dystrophy (nmDMD) patients receiving ataluren: Strategic Targeting of Registries and International Database of Excellence (STRIDE) Registry compared with phase 3 clinical trial

Francesco Muntoni,<sup>1</sup> Mar Tulinius,<sup>2</sup> Filippo Buccella,<sup>3</sup> Isabelle Desguerre,<sup>4</sup> Janbernd Kirschner,<sup>5</sup> Andrés Nascimento Osorio,<sup>6</sup> Shelley Johnson,<sup>7</sup> Christian Werner,<sup>8</sup> Allan Kristensen,<sup>7</sup> James Li,<sup>7</sup> Audrey Powell,<sup>7</sup> Nicholas Mastrandrea,<sup>7</sup> Efthimia Leonardi,<sup>7</sup> Panayiota Trifillis,<sup>7</sup> and Eugenio Mercuri<sup>9</sup>

<sup>1</sup>University College London, Great Ormond Street Institute of Child Health, London, United Kingdom; <sup>2</sup>Department of Pediatrics, Gothenburg University, Queen Silvia Children's Hospital, Gothenburg, Sweden; <sup>3</sup>Parent Project APS, Rome, Italy; <sup>4</sup>Hôpital Necker – Enfants Malades, Paris, France; <sup>5</sup>Medical Center – University of Freiburg, Freiburg, Germany; <sup>6</sup>Hospital Sant Joan de Déu, Unidad de Patología Neuromuscular, Universidad de Barcelona, Barcelona, Spain; <sup>7</sup>PTC Therapeutics Inc., South Plainfield, New Jersey, USA; <sup>8</sup>PTC Therapeutics Germany GmbH, Frankfurt, Germany; <sup>9</sup>Department of Pediatric Neurology, Catholic University, Rome, Italy.

**Introduction:** STRIDE is an ongoing registry providing real-world data on ataluren use in patients with nmDMD.

**Objective:** We investigated if ataluren-treated nmDMD patients in real-world practice (STRIDE Registry) experienced a similar decline in 6MWD vs ataluren-treated patients in a phase 3 clinical trial (Study 020).

**Methods:** 6MWD for STRIDE patients (n=42) and Study 020 patients (ataluren [n=45] and placebo [n=50]) was assessed over 48 weeks.

**Results:** Mean (95% CI) first baseline 6MWD assessment for STRIDE patients (349.7 [341.4, 358.0] m, n=42) was comparable to that for patients in Study 020 (ataluren, 356.7 [348.9, 364.5] m, n=47; placebo, 354.5 [346.3, 362.8] m, n=52). Mean (95% CI) decline in 6MWD were: STRIDE patients (-3.5 [-20.9, 13.8] m), ataluren-treated Study 020 patients (-28.3 [-45.1, -11.5] m), placebo-allocated Study 020 patients (-75.5 [-105.7, -45.3] m).

**Conclusion:** In both the real-world and clinical trial setting, ataluren delays motor function decline in nmDMD patients vs placebo.

Abstract #582

## Executing an Exception from Informed Consent (EFIC) Plan

J. Fong, J. Shah, B. Albala, D. Vanblitter, E. Drum, D. Gutierrez, B. Boden-Albala (Irvine, CA)

**Introduction:** Exception from Informed Consent (EFIC) is implemented in emergency studies and allows patients to enroll into clinical trials without the standard informed consent process.

**Objectives:** UC Irvine (UCI) developed and executed an EFIC plan to ensure our local community was informed and had the opportunity to provide feedback.

**Methods:** Community consultation and public disclosure events were implemented. Our clinical trial team worked closely with various UCI employees such as the Center for Clinical Research, Program in Public Health, PR/marketing, and medical doctors.

**Results:** 11 community events were completed including presentations/focus groups, social media messaging, and marketing booths. We spoke with 460 community members and received feedback from 210 members. 17 public disclosure events were completed including posting on websites/social media and mailing/newspaper/radio advertisements. Within 3 months, 1,176,323-people were reached.

**Conclusion:** Community members were made aware of EFIC and gained research knowledge. This plan will be implemented for future UCI clinical trials that require EFIC.

Abstract #623

## Clinical Research Coordinator Shortage and an Approach for an Educational Partnership to Increase Candidates

A. Bartlett, J. Agriesti \*(Columbus, OH) The Ohio State University

Prior to the “Great Resignation” that occurred during COVID-19, the medical field was exploding with clinical research studies and many sites were having a shortage of staffing to administer the trials, which has only increased after COVID. NeuroNEXT Clinical Research managers will be surveyed to understand current employment opportunities at their site, staffing educational details, length of employment, training programs, career path and the perceived impact of shortage of trained staffing on trials. An educational program at Columbus State Community College (CSCC) is being discussed for a partnership to create a clinical research associate’s degree and training opportunity for hire at the medical center. Then as people work in clinical research they could potentially be earning a bachelor’s degree (tuition free) while increasing the workforce and the average time employed.

**NOTE:** The survey is being constructed and response analysis will be complete by August. We have already had a meeting with CSCC and they are interested. Therefore, some of the background work is yet to be done, but we feel this is a timely proposal.



Abstract #627

## TREAT-NMD FSHD Global Registry Network: A Collaboration of Neuromuscular and FSHD Patient Registries

B Porter<sup>1</sup>, N Bennett<sup>1</sup>, R Forbes<sup>2</sup>, E Yiu<sup>2</sup>, M Jagut<sup>3</sup>, M Cosyns<sup>3</sup>, L Mokrá<sup>4</sup>, S Vohánka<sup>4</sup>, A Mahoney<sup>5</sup>, U Werlauff<sup>5</sup>, S Thiele<sup>6</sup>, MC Walter<sup>6</sup>, T Matsumura<sup>7</sup>, H Nakamura<sup>8</sup>, S Setlere<sup>9</sup>, I Micule<sup>9</sup>, M Rodrigues<sup>10</sup>, R Roxburgh<sup>10</sup>, T Golli<sup>11</sup>, D Osredkar<sup>11</sup>, JC Deenen<sup>12</sup>, BG van Engelen<sup>12</sup>, N Bulut<sup>13</sup>, I Gürbüz<sup>13</sup>, S Mergen<sup>14</sup>, H Durmus<sup>14</sup>, H Walker<sup>15</sup>, C Marini-Bettolo<sup>16</sup>, D Allison<sup>1</sup>, C Campbell<sup>17</sup>, M Guglieri<sup>18</sup>, A Ambrosini<sup>19</sup>, R Tupler<sup>20</sup>

*1 TREAT-NMD Services Ltd, Newcastle upon Tyne, UK; 2 Australian Neuromuscular Disease Registry, Royal Children's Hospital and Murdoch Children's Research Institute, Melbourne, Australia; 3 Belgian Neuromuscular Diseases Registry (BNMDR), Belgium; 4 ReaDY Registry, Czech Republic; 5 The Danish National Rehabilitation Centre for NMD, Denmark; 6 German NMD Registry, Friedrich-Baur Institute Dept. of Neurology, Ludwig-Maximilians University Munich, Germany; 7 Department of Neurology, National Hospital Organization Osaka Toneyama Medical Center, Osaka, Japan; 8 Registry of muscular dystrophy (Remudy), National Center of Neurology and Psychiatry, Tokyo, Japan; 9 NMS datu kolekcija, Children's Clinical University Hospital, Latvian Biomedical Research and Study Centre, Latvia; 10 Punaha Io Neurogenetic Research Bank (New Zealand Neuromuscular Disease Registry), Neurology, Auckland DHB and Centre for Brain Research Neurogenetic Research Clinic, University of Auckland, Auckland, New Zealand; 11 Registry of Slovenian Children with NMD, Slovenia; 12 FSHD registratie, Radboud University Medical Center, Nijmegen, the Netherlands; 13 Turkish NMD Registry – KUKAS, Hacettepe University, Ankara, Turkey; 14 Department of Neurology, Istanbul Faculty of Medicine, Istanbul University, Turkey; 15 UK FSHD Patient Registry, John Walton Muscular Dystrophy Research Centre, Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, UK; 16 UK FSHD Patient Registry, John Walton Muscular Dystrophy Research Centre, Translational and Clinical Research Institute, Newcastle University and Newcastle Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK; 17 Department of Paediatrics, Clinical Neurological Sciences & Epidemiology, Western University, London, ON, Canada; 18 John Walton Muscular Dystrophy Research Centre, Translational and Clinical Research Institute, Newcastle University and Newcastle Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK; 19 Fondazione Telethon, Milan, Italy; 20 Department of Biomedical Science, Unimore, Modena, Italy*

**Introduction** TREAT-NMD operates a Global Registry Network (GRN) where member registries collect agreed disease-specific datasets. The FSHD GRN collects data from 21 registries.

**Objective:** Perform a high-level analysis of data collected by the FSHD GRN.

**Method:** An electronic survey requesting demographic/diagnostic data was sent to registries in 2022.

**Results:** Thirteen registry responses provided data on 3,372 FSHD patients (female:1,528; male:1,645; unknown:199). Most patients had FSHD1 (1,747/3163) with fewer FSHD2 (82) cases. However, 42% of patients were of unknown FSHD type. Overall, 1,463 patients received genetic confirmation of FSHD, with FSHD1 cases (1,262/1747;72%) higher than FSHD2 (32/82;39%) or unknown FSHD type (171/1334;13%).

**Conclusions:** TREAT-NMD FSHD GRN represents an international harmonised data resource, which can support clinical trial planning through registry enquiries. Despite most registries being clinician-reported (62%), many patients lacked genetic confirmation or a specific FSHD type diagnosis. Understanding these aspects will be important as they represent clinical trial essential criteria.

Abstract #629

## Engaging Participation in Research in Fascioscapulohumeral Dystrophy (FSHD)

S. Moldt CCRC; M. McIntyre PT, DPT; K. Wong MS, CGC; R. Butterfield MD, PhD  
University of Utah, Utah, Pediatric Neurology

**Introduction/Objectives:** Participant engagement and retention are common barriers to clinical research. With slow progression and limited treatments, patients with FSHD have reported being disengaged from the healthcare system and research. With the majority of recruitment for research taking place in clinic, we are missing a portion of the population who don't routinely seek out healthcare, hurting the generalizability of current studies.

**Methods:** To increase enrollment in our study of genetic modifiers in a historic Utah kindred with FSHD, we implemented a multi-faceted approach to patient/family outreach focused on minimizing participation barriers and engaging patients, including family engagement, community outreach, and education events.

**Results:** With expanded outreach, we enrolled 102 participants to the study including affected and unaffected individuals and obtained DNA sample, self-reported phenotype, and/or clinical evaluations.

**Conclusions:** We implemented multiple recruitment strategies that minimized barriers and increased participation in a population that would otherwise been lost to follow-up, improving the generalizability of studies.

Abstract #631

## Prospective Analysis of Early-Onset Facioscapulohumeral Muscular Dystrophy in the United States

Natalie Katz<sup>1</sup>, Rabi Tawil<sup>1</sup>, Jeffrey Statland<sup>2</sup>

<sup>1</sup>Department of Neurology, University of Rochester Medical Center, Rochester, NY, USA

<sup>2</sup>Department of Neurology, University of Kansas Medical Center, Kansas City, KS, USA

**Introduction:** Early-onset FSHD (EO-FSHD) is associated with a more severe phenotype, faster disease progression, and extra-muscular manifestations. Few studies have described this population in the United States (US).

**Objective:** Understand how the EO-FSHD population in the US differs from adult-onset FSHD.

**Methods:** Prospective data from 578 genetically confirmed FSHD type 1 participants enrolled in the US FSHD National Registry will be used to determine baseline demographics, disease severity, and risk factors contributing to disease progression. EO-FSHD is defined as diagnosed before age 10.

**Results:** As of September 2019, 35 individuals had EO-FSHD (6%); were more likely to be female (74.3%) compared to the overall registry (47.9%); and had a higher frequency of 1-3 D4Z4 repeats (65.7% vs. 10.4%).

**Conclusion:** This represents the largest EO-FSHD cohort to be prospectively described. Additional data on incidence of the need for ambulatory aides and risk factors for disease progression will be presented.

Abstract #634

## Creation of a Scalable Registry and Data Dashboard for Neuromuscular Immune-Related Adverse Events of Immune Checkpoint Inhibitors Using Consensus Disease Definitions

M Eskian, LB Burton, J Hillis, BK Chwalisz, M O'Hare, GS Manzano, S Shalhout, L Zubiri, D Miller, KL Reynolds, AC Guidon (Boston, MA)

**Introduction:** Mis-classification of neuromuscular (NM) immune-related adverse events (irAEs) from immune checkpoint inhibitors (ICIs) has limited care and research. We recently published consensus disease definitions (CDD) for neurologic irAEs.<sup>1</sup>

**Objectives:** To describe 1) development of a Redcap registry for NM irAEs based on CDD and 2) results from application of CDD to a cohort with NM irAEs,

**Methods:** Patients with suspected neurologic irAEs from Massachusetts General Brigham were systematically identified. Diagnoses of irNeuropathy, irNeuromuscular Junction (NMJ) disorders and irMyopathy assigned using CDD. Testing, treatments and outcomes were included. R was used for statistical analyses and data visualizations.

**Results:** Forty-one patients with 53 NM irAEs (23, irMyopathy; 19, irNeuropathy; 11, irNMJ Disorder) are currently included. Median age 73 [37, 91]. Most NM irAEs reached probable-definite certainty (40/53, 75.5%). Updated data will be presented.

**Conclusions:** Study of NM irAE phenotypes and outcomes is feasible using this rigorous, scalable registry based on CDDs.



# Neuromuscular Study Group

ANNUAL SCIENTIFIC MEETING

SEPTEMBER 30 - OCTOBER 2  
HOTEL REGINA PALACE  
STRESA, LAKE MAGGIORE, ITALY



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# Welcome



On behalf of your Neuromuscular Study Group, we would like to welcome each of you to the 23rd Annual Neuromuscular Study Group Meeting. This is an exciting time in neuromuscular research as we continue to grow and adapt.

One of those ways was to update our name to include Neuro. This year, the members along with the Executive Committee settled on the current name, Neuromuscular Study Group (NMSG).

After two years of very successful online meetings, we decided for the meeting to be held in Italy this year. We are pleased that our in-person meeting has received over 200 registrations and an unprecedented 141 abstract submissions. This year we are excited to have so much industry involvement from both Europe and the U.S. Thank you so much to our sponsors for the support. Clearly, an in person meeting in Italy was a great choice.

We held our first online Shark Tank event earlier this year. The Shark Tank session has gained momentum and we will host our 4th Shark Tank event during the meeting with 6 proposals presented. The winner will receive a \$10K grant to use towards their study. Last year's winners will present at the meeting and we look forward to learning how their funded proposals have progressed.

The NMSG continues to fund a Neuromuscular Research 2-year fellowship program, so at any one time we have one Fellow in the first year, and one in the second year. Both our current Fellows will be presenting during the meeting.

As the Co-Chairs of the Neuromuscular Study Group, we would like to thank this year's planning committee for putting together an excellent agenda that covers such a broad range of topics and interests within the neuromuscular field. We also want to thank Liz Paulk, NMSG Administrative Manager, for organizing another successful and large event. The planning committee and Liz all have spent much time planning this international meeting that will appeal to our global audience and advance the field of Neuromuscular medicine.



RICHARD J. BAROHN, M.D.  
*Chair, Neuromuscular Study Group*  
*Executive Vice Chancellor for Health Affairs & Hugh E. and Sarah D. Stephenson Dean, School of Medicine University of Missouri*



PROF MICHAEL G. HANNA, M.D.  
*Co-chair, Neuromuscular Study Group*  
*Director, University College London Institute of Neurology*



## 2022 PLANNING COMMITTEE

### CHAIR

Valeria Sansone, M.D., Ph.D.  
*NEMO Clinical Center*

### CO-CHAIR

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*University of Manchester*

Senda Ajroud-Driss, M.D.  
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*UT Southwestern*

Karissa Gable, M.D.  
*Duke University Medical Center*

Melissa McIntyre, DPT  
*University of Utah*

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*Virginia Commonwealth University*

Mazen Dimachkie, M.D.  
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Miriam Freimer, M.D.  
*The Ohio State University*

Jeffrey Guptill, M.D.  
*Duke University*

Michael Shy, M.D.  
*University of Iowa*





# Information



## THANKS TO:

Amardeep Gill  
*Livestream Director, StreamGuru.net*

Roberto Petruzzelli  
*Word of Mouth*

Hotel Regina Palace

Liz Russo Paulk  
*NMSG Administrative Manager*

Michaela Walker  
*University of Kansas Medical Center*

Amanda Sebok  
*University of Missouri*

Laura Herbelin  
*University of Kansas Medical Center, retired*

Breanna Tuhlei  
*University of Missouri, medical student*

Christine Oldfield  
*University College London*

## WIFI

The NMSG has a special wifi access for NMSG meeting attendees. This network can be used in all the meeting rooms and also the hotel.

Network name: **MSG2022**

Password: **Meeting22**



## GALA

For the Gala dinner on Saturday night we will be taking a very short ferry to Isola dei Pescatori on Lake Maggiore. The location of the ferry will be announced during the meeting as it is dependent on the lake level.

Because of the large number of registrees we will host dinner at two restaurants on the island very close to one another.

After dinner we will have dessert and reception and return by ferry to Stresa.

Dress for the evening is business attire.

All are welcome, guests not attending the scientific sessions may also attend for an additional \$75 per person.

## SPEAKERS/PRESENTERS

Please bring your presentation to Amardeep Gill, our onsite AV expert, in the Lalique general session room the morning of your session so that your slides can be loaded. Our technical staff will assist you with any audio/visual needs you may have. You will not need your own laptop as we have one available.

## POSTERS

The poster exhibition is located in the Azalea Room.

Walk through poster session is  
Friday, September 30th 6:30-8:00pm

Please set up your poster in the Azalea Room on Thursday evening after 8:00pm or first thing on Friday. Posters will be displayed all day and evening on Friday.

Important note: Poster presenters are requested to be beside their poster during the walk though session.

Please remove your poster before Friday evening, start of dinner.

# Agenda

## THURSDAY, SEPTEMBER 29

6:00 - Check-In  
7:30 p.m. *Hotel Regina Palace Lobby*

Welcome Reception  
*Front Terrace*

## DAY 1

## FRIDAY, SEPTEMBER 30

7:00 - Check-In  
8:00 a.m. *Hotel Regina Palace Lobby*

Buffet Breakfast  
for Hotel Regina Palace Guests  
*Liberty*

Welcome and State of the  
Neuromuscular Study Group  
8:00 -  
8:20 a.m. **Dr. Richard Barohn and  
Prof Michael Hanna**  
*Lalique*

### SESSION I: BIG THERAPEUTIC WAVES

**Moderator: James Lilleker, MBChB, Ph.D.**  
*Lalique*

8:20 - Near term prospects for disease targeted  
8:40 a.m. therapies in FSHD  
**Jeffrey Statland, M.D.**  
*University of Kansas Medical Center*

8:45 - Duchenne Muscular Dystrophy: Learning  
9:05 a.m. From Our Failures — a Clinical Trialists View  
**Prof Laurent Servais, M.D., Ph.D.**  
*University of Oxford,  
MDUK Oxford Neuromuscular Centre*

9:10 - The Evolving Therapeutic Options  
9:30 a.m. for Pompe Disease  
**Mazen Dimachkie, M.D.**  
*University of Kansas Medical Center*

9:35 - Update on treatment in CIDP and MMN  
9:55 a.m. **Prof Edwardo Nobile-Orazio, M.D., Ph.D.**  
*Milan University,  
IRCCS Humanitas Research Institute*

10:00 - Refreshment / Exhibitor Break  
10:15 a.m. *Azalea*

10:15 - Therapeutic Promise in Myotonic  
10:35 a.m. Dystrophy Type 1  
**Nick Johnson M.D., Msci, FAAN**  
*Virginia Commonwealth University*

10:40 - Muscle Dysfunction in Myotonia Congenita  
11:00 a.m. **Mark Rich, M.D., Ph.D.**  
*Wright State University*

### SESSION II: N&M IMAGING

**Moderator: James Lilleker, MBChB, Ph.D.**  
*Lalique*

11:05 - Muscle MRI as a tool for the diagnosis  
11:25 a.m. and follow-up of myopathies  
**Giorgio Tasca, M.D., Ph.D.**  
*Fondazione Policlinico  
Universitario A. Gemelli IRCCS*

11:30 - Contribution of nerve and muscle  
11:50 a.m. ultrasound in diagnosis and management  
of peripheral nerve diseases  
**Luca Padua, M.D., Ph.D.**  
*Fondazione Policlinico  
Universitario A. Gemelli IRCCS*



12:00 - 1:30 p.m.	Lunch <i>Liberty Lago</i>
12:00 - 1:30 p.m.	Neuromuscular Study Group Executive Committee Meeting <i>Rhododendro</i>
1:30 - 3:00 p.m.	Coordinators/Evaluators Session Breakout <b>Moderators: Melissa McIntyre, DPT, Marie Wencel, CCRP, Tina Duong, PT, Ph.D., Gita Ramdharry, Ph.D.</b> <i>Margherita</i>
1:30 - 3:00 p.m.	Young Investigator Session Breakout <b>Moderators: Prof Valeria Sansone &amp; Dr. Emma Ciafaloni</b> <i>Lalique</i>
3:00 - 3:15 p.m.	Refreshment / Exhibitor Break <i>Azalea</i>
<b>SHARK TANK SESSION</b>	
<b>Moderator: Aziz Shaibani, M.D., FACP, FAAN, FANA</b> <b>Sharks: Tony Amato, M.D., Tahseen Mozaffar, M.D., Emma Ciafaloni, M.D.</b> <i>Lalique</i>	
3:15 - 5:00 p.m.	Improving the Study of Falls in Muscle Disease <b>Kristina M. Kelly, PT, DPT, MS, EdM, NCS</b> <i>The Ohio State University</i>
	Quantifying Idiopathic Inflammatory Myopathy Associated Cancer Risk via Comprehensive Phenotyping of a Large UK-Wide Cohort <b>Alexander Oldroyd, MBChB, Ph.D., MRCP, MSc</b> <i>University of Manchester</i>

3:15 - 5:00 p.m.	Salivary Melatonin: Can this Detect Patients in Myotonic Dystrophy Type 1 (DM1) with Disrupted Sleep Wake Cycle and EDS? <b>Giovanni Colacicco, M.D.</b> <i>The Nemo Clinical Center in Milan Neurorehabilitation Unit University of Milan</i>
	Exploring the Experience of Pain for People with Facioscapulohumeral Muscular Dystrophy and the effects of Physiotherapy/Vojta Therapy <b>Jose Manuel Sanz Mengibar, Ph.D. Physiotherapy</b> <i>University College London Hospital</i>
	Predictive models in spinal muscular atrophy treated patients using machine learning <b>Giorgia Coratti, Ph.D.</b> <i>Fondazione Policlinico Universitario Agostino Gemelli IRCCS</i>
	Therapeutic Dietary Intervention Attenuates Weight Gain From Corticosteroid Use in Boys with DMD <b>Grace Warner Gough, MS, RDN, CD</b> <i>University of Utah</i>
6:30 - 8:00 p.m.	Reception and poster walk through session <i>Azalea</i>
8:00 - 9:00 p.m.	Dinner & Shark Tank Award Announcement <i>New Liberty</i>
9:00 - 11:30 p.m.	Reception <i>Bar Regina Palace</i>

## DAY 2

### SATURDAY, OCTOBER 1

7:00 - Buffet Breakfast  
8:15 a.m. for Hotel Regina Palace Guests

Opening  
8:15 - **Dr. Richard Barohn and**  
8:30 a.m. **Prof Michael Hanna**  
*Lalique*

#### SESSION III: MOTOR NEURON DISEASE CHALLENGES

**Moderator: Dr. Senda Adjroud-Driss**  
*Lalique*

8:30 - Respiratory management of patients  
8:50 a.m. with neuromuscular disease in ALS  
**Lisa Wolfe, M.D.**  
*Northwestern University*

8:55 - Update on Clinical Trials for ALS  
9:15 a.m. **Angela Genge M.D., FRCP(c)**  
*Montreal Neurological Institute and Hospital*

9:20 - Clinical Trials Landscaping in ALS  
9:40 a.m. **James Berry, M.D., MPH**  
*Massachusetts General Hospital*

9:45 - Spinal muscular atrophy: hope vs hype;  
10:05 a.m. guide to handle patients' expectations  
**Prof Eugenio Mercuri, M.D., Ph.D.**  
*Catholic University*

10:10 - Refreshments/Exhibitor Break  
10:30 a.m. *Hotel Regina Palace Lobby*

#### SESSION IV: STRATIFICATION OF NM DISEASES

**Moderator: Dr. Salman Bhai**  
*Lalique*

10:30- Seronegative Myasthenia Gravis  
10:50 a.m. **Vern Juel, M.D.**  
*Duke University School of Medicine*

10:55 - Early detection of peripheral neuropathy  
11:15 a.m. in hATTR  
**Chafic Karam, M.D.**  
*University of Pennsylvania*

11:20 - Updates in the therapeutic landscape  
11:40 a.m. of myositis  
**Julie Paik, M.D., MHS**  
*Johns Hopkins University School of Medicine*

11:45 a.m. - Deconvoluting phenotypic complexity in  
12:05 p.m. myositis: from syndromes to diseases  
**Iago Pinal Fernandez, M.D., Ph.D., Ph.D.**  
*Muscle Disease Unit, NIAMS/NIH Johns Hopkins Neurology Department*

12:10- Myositis Autoantibodies:  
12:30 p.m. What's new?  
**Lisa Christopher Stine, M.D., MPH**  
*Johns Hopkins University*

12:30 - Lunch  
1:30 p.m. *Liberty Lago*

#### SESSION V: TECHNOLOGY AND DIGITAL OUTCOMES IN NMD

**Moderator: Prof Valeria Sansone**  
*Lalique*

1:30 - Video capture and machine learning  
1:45 p.m. to assess hand myotonia and other functional timed tests  
**Tina Duong, PT, Ph.D.**  
*Stanford University*

1:50 -  
2:05 p.m.

Full day infant movement analysis:  
potential for wearable sensors to  
support early identification and  
assessment of neuromuscular diseases

**Beth Smith PT, DPT, Ph.D.**  
*Children's Hospital Los Angeles and  
University of Southern California*

2:10 -  
2:25 p.m.

First regulatory qualification of  
a digital outcome in DMD:  
How can SV95c change the course of  
clinical developments

**Prof Laurent Servais, M.D., Ph.D.**  
*University of Oxford, MDUK Oxford  
Neuromuscular Centre*

2:30 -  
2:45 p.m.

Technology and digital outcomes in  
Neuromuscular Disorders: be to tech  
experience at the NeMO Lab

**Dr. Stefano Regondi**  
*NeMO Lab Milan*

2:45 -  
3:00 p.m.

Break  
*Hotel Regina Palace Lobby*

## SESSION VI: ABSTRACT PLATFORM PRESENTATIONS

**Moderator: Eli Naddaf, M.D.**  
*Lalique*

3:00 -  
3:15 p.m.

Effect of different corticosteroid dosing  
regimens on clinical outcomes in boys  
with Duchenne muscular dystrophy: a  
randomized clinical trial

**Robert Griggs, M.D.**  
*University of Rochester*

3:15 -  
3:30 p.m.

Caveolae-Associated Protein (cavin)-4  
autoantibodies in immune mediated  
rippling muscle disease (iRMD)

**Divyanshu Dubey, M.D., M.B.B.S.**  
*Mayo Clinic*

## SPONSOR UPDATES

3:30 -  
3:50 p.m.

DYNE-101 and DYNE-251:  
Moving from bench to clinic to  
deliver potentially transformative  
therapies in DM1 and DMD

**Ashish Dugar, Ph.D. MBA**  
*SVP, Global Medical Affairs,  
Dyne Therapeutics*

3:55 -  
4:15 p.m.

Update on the growing body  
of evidence for Duchenne  
muscular dystrophy therapies

**Dr. Christian Werner**  
*Executive Director, Global Medical  
Affairs - Global DMD Lead,  
PTC Therapeutics*

4:20 -  
4:40 p.m.

Our commitment to NMDs:  
the present and the near future

**Kathryn R. Wagner, M.D., Ph.D.**  
*Global Head Neuromuscular, Roche*

4:45 -  
5:05 p.m.

Following the Science in Rare  
Neurological Diseases

**Cinzia Dorigo, Pharm.D.**  
*Alexion*

## ROBERT C. GRIGGS ANNUAL NMSG KEYNOTE SPEAKER

*Lalique*

7:00 p.m.

Neuromuscular Diseases –  
lessons learnt 1980-2020

**Shree Pandya, PT, DPT**  
*University of Rochester*

7:45 p.m.

Meet for transportation to Isola  
Pescatori for evening activities

8:30 p.m.

Dinner

Evening reception on Borromean Islands  
following dinner

## DAY 3 SUNDAY, OCTOBER 2

7:00 - 8:00 a.m. Buffet Breakfast for Hotel Regina Palace Guests

8:00 - 8:10 a.m. Opening  
**Dr. Richard Barohn and Prof Michael Hanna**  
*Lalique*

### SESSION VII: NMSG YOUNG INVESTIGATORS PROJECTS

**Moderator: Karissa Gable, M.D.**  
*Lalique*

8:10 - 8:25 a.m. Post-translational Modifications of DUX4  
**Renatta Knox, M.D., Ph.D., NMSG Fellow**  
*Washington University School of Medicine*

8:30 - 8:45 a.m. Neuromuscular ultrasound as a biomarker to improve clinical trial readiness in Charcot-Marie-Tooth Neuropathies  
**Tyler Rehbein, M.D., NMSG Fellow**  
*University of Rochester*

8:50 - 9:05 a.m. 2021 Shark Tank Award Update: Circulating Myeloid Profile in Myasthenia Gravis  
**Katy Dodd, MBChB MRCP, Ph.D. Candidate**  
*Manchester Centre for Clinical Neuroscience*

9:10 - 9:25 a.m. 2021 Shark Tank Grant Award Update: Therapeutic Play Gym: Feasibility of a caregiver-mediated exercise system for infants and young children with severe neuromuscular weakness  
**Jenna Linn Lammers, MSR/PT, CNT, PCS**  
*University of Florida*

### ABSTRACT PLATFORM PRESENTATIONS

9:30 - 9:40 a.m. A comparison of in silico predictive tools to robust in vivo functional characterisation of CLCN1 genetic variants in skeletal muscle channelopathies  
**Vino Vivekanandam, MBBS**  
*QS University College London*

9:45 - 9:55 a.m. Neuromuscular junction transmission failure is a translationally-relevant mechanism of sarcopenia  
**W. David Arnold, M.D.**  
*University of Missouri*

10:00 - 10:10 a.m. Symptom Onset In Maternally versus Paternally Inherited Myotonic Dystrophy type 2  
**Paloma Gonzalez-Perez, M.D., Ph.D.**  
*Massachusetts General Hospital*

10:15 - 10:25 a.m. Clinical trial readiness and validation of onsite and remote evaluation in valosin containing protein-associated multisystem proteinopathy  
**Megan Iammarino, DPT**  
*Nationwide Children's Hospital*

10:30 - 10:45 a.m. Break  
*The Regina Palace Lobby*

10:45 - 10:55 a.m. Bridging the preclinical-clinical gap: reverse translation of muscle velocity recovery cycles allows in vivo assessment of skeletal muscle excitability in mice and humans  
**Karen Suetterlin, MBBS, MRCP, Ph.D.**  
*Newcastle University*

11:00 - 11:10 a.m. Proposal for the functional assessment of acute inflammatory neuropathy (FAAIN) in Guillain-Barré syndrome  
**Dra. Zurina Lestay O'Farrill, Ph.D.**

11:15 -  
11:25 a.m.

Survival Motor Neuron Protein:  
Addressing Therapeutic Concerns of  
Sensorimotor Toxicity

**Maria Balch, Ph.D.**  
*The Ohio State University*

11:30 -  
11:40 a.m.

Episodic weakness in patients with  
mitochondrial DNA MT-ATP6 mutations:  
the Queen Square experience

**Chiara Pizzamiglio, M.D.,  
Ph.D. Candidate**  
*QS University College London*

#### ABSTRACT FLASH PRESENTATIONS

11:45 -  
11:55 a.m.

Risk factors for falls and fracture  
in myositis: A cross-sectional study  
of 470 patients

**Salman Bhai, M.D.**  
*UT Southwestern*

11:57 a.m. -  
12:07 p.m.

Towards digital monitoring of  
Amyotrophic Lateral Sclerosis (ALS)  
patients: a deep learning-based  
application to assess the evolution  
of dysarthria via the analysis of  
multimedia data

**Michela Coccia, M.D.**  
*The Nemo Clinical Center in Ancona*

12:10 -  
12:20 p.m.

Unmasking anti-HMGCR myopathy: the  
hurdles of a prompt recognition

**Andrea Barp, M.D.**  
*The Nemo Clinical Center in Trento*

12:22 -  
12:32 p.m.

Motor Outcomes to Validate Evaluations  
in Facioscapulohumeral muscular  
dystrophy (MOVE FSHD): Protocol for  
an observational study

**Michaela Walker, MPH, CCRP**  
*University of Kansas Medical Center*

Closing

12:35 -  
1:35 p.m.

Lunch  
*Liberty Lago*

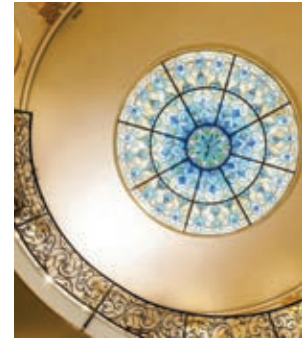
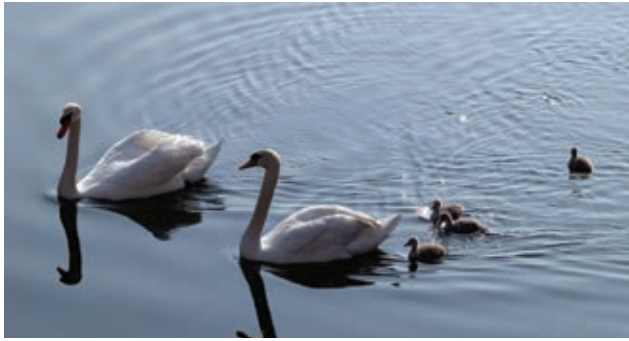


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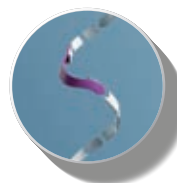


### Our Mission

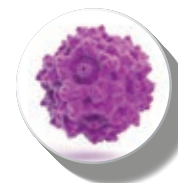
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# Update on the growing body of evidence for Duchenne muscular dystrophy therapies

Please join us on Saturday 1 October, 2022  
16:25–16:45 CEST | Sala Lalique

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supports the Lambert-Eaton myasthenic syndrome (LEMS) Community and



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