

2020 CONSORTIUM OF MS CENTERS PLATFORM ABSTRACTS

Disease Assessment and Management

(DAM01)

International Registry Tracking Pregnancy Outcomes in Women Treated with Dimethyl Fumarate

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Background: To date, delayed-release dimethyl fumarate (DMF) exposure during pregnancy has not shown any safety signals in clinical trial and post-marketing data, however the DMF label recommends use during pregnancy only if potential benefit justifies the potential risk to the fetus. In the general population, 62% of pregnancies end in live birth, 22% end in induced abortion, and 16% end in fetal loss. Similar rates have been observed in MS patients.

Objectives: An international registry (NCT01911767) was started to prospectively evaluate pregnancy outcomes in women with MS exposed to DMF since 1 day before the 1st day of their last menstrual period before conception or during pregnancy; results are reported for the US as well as the overall population.

Methods: In this ongoing registry, data were collected at enrolment, 6–7 months of gestation, 4 weeks after estimated delivery date, and at 4, 12, and 52 weeks after birth. Infant and maternal outcomes included: ectopic and molar pregnancies, birth defects, congenital anomalies or infant death occurring at ≤ 52 weeks of age, and maternal death at ≤ 12 weeks post-delivery. Potential birth defects were adjudicated by an external expert. Gestational size was classified as small ($< 10^{\text{th}}$ percentile), appropriate ($10^{\text{th}}-90^{\text{th}}$), or large ($> 90^{\text{th}}$) based on standardized growth charts.

Results: As of April 2019, 263 patients were enrolled; 57 in the US. Median gestational week at 1st DMF exposure was 1 (range: 1-13); median fetal DMF exposure duration was 5 (range: 0.1-40) weeks. Of the 214 pregnancy outcomes reported to date, 197 (92%) were live births and 17 (8%) fetal losses. In the US, 38 pregnancy outcomes have been reported to date, 34 (89%) live births and 4 (11%) fetal losses. Of infants with known gestational age (n=194), 176 (89%) births were full-term and 18 (9%) premature (< 37 weeks). In the US, 30 (97%) births were full-term



and 1 (3%) premature. There were 16 spontaneous abortions (4 in the US; 1 ectopic pregnancy outside of the US), and 1 fetal death at ≥ 28 weeks of gestation. No perinatal, infant, or maternal deaths were reported. Infants (163 with gestational size data) were classified as small 18 (11%), appropriate 134 (82%), and large 11 (7%). Seven (4%) infants had confirmed birth defects.

Conclusions: The adverse pregnancy outcome frequencies from the interim analysis did not exceed those observed in the MS and general populations. No safety signal has been observed to date.

Support: Biogen

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Keywords: Disease-modifying treatments in MS, pregnancy

(DAM02)

Menarche and Relapses in Girls with Pediatric Multiple Sclerosis

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Background: Sex steroid hormones have a clinical impact on the immune system. Puberty may trigger MS disease activity, with mean age of pediatric multiple sclerosis (MS) onset occurring near age 13 years.

Objectives: To evaluate the association between menarche and disease course in pediatric MS through comparison of relapse rates across the pre-menarche, peri-menarche, and post-menarche periods.

Methods: This is a retrospective analysis of a prospectively followed cohort of girls meeting MS criteria within the US Network of Pediatric MS Centers database. Only individuals with known menarche dates were included in the analysis. Relapses were collected prospectively. Both negative binomial and repeated Cox regression models were used to assess the association of pubertal development stage with relapse rate, adjusted for tier of disease-modifying therapy (DMT) and body mass index (BMI).

Results: Of the 503 girls included, onset was during pre-menarche in 53, peri-menarche in 84 (within +/- 1 year of menarche), and post-menarche in 366. The median time of MS onset was 2.5 years after menarche. In adjusted negative binomial analysis, annual relapse rate during the pre-menarche period was 0.43, peri-menarche period was 0.50, and post-menarche period was 0.36 (p=0.16). In adjusted repeated events Cox regression analysis, there was increased hazard to relapse with stage of development from pre-menarche through menarche (pre-menarche HR 0.60 (95% CI 0.45 to 0.79) and peri-menarche HR 0.79 (95% CI 0.62 to 1.02) compared to the reference of post-menarche, p=0.0006).

Conclusions: Before menarche girls have lower relapse rates. Onset of puberty may be a time of increase in disease activity and may require consideration of a change in therapeutic approach.

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Keywords: Epidemiology of MS, Hormonal factors in MS, Natural history of MS

(DAM03)

Complexity of Aging with MS: Graceful Concessions or Kicking and Screaming?

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Background: Over the past 3 decades there has been significant advances in the development of pharmaceutical and rehabilitative treatments for persons with multiple sclerosis (MS), such that life expectancy is continuing to increase. As a result of these advancements, there is a ‘graying’ phenomenon within the global MS population and a demographic shift of the aging landscape. Whilst these advancements are exciting, there also concerns and unknowns regarding what it is like to age with MS.

Objectives: The objectives of this research were to explore the experiences of aging in conjunction with having MS, and the different ways persons over 60 with MS interpreted this phenomena.

Methods: Semi-structured interviews with 40 persons with MS over 60 years were conducted. Thereafter data were subject to a pluralistic analysis approach utilizing phenomenological and narrative traditions.

Results: This research highlighted the complexity of aging with MS and the various ways persons over 60 with MS experience and interpret this phenomena. Most participants experienced a continued progression of physical and cognitive deficits, however aging narratives and what is culturally expected as a person over 60 allowed for positive interpretations of this stage of life. For example, participants diagnosed in early adulthood stated having health problems was ‘normal’ over 60, resulting in a sense of belonging that they had not experienced since being diagnosed. Some participants also perceived they were aging more successfully than peers without MS as they had engaged in health enhancing behaviors from an earlier age, whilst others believed they had ‘aged out’ of MS and were experiencing a peak of health and wellness. Participants who were diagnosed in middle age, however noted a sharp progression of age related and MS symptoms, but stated ‘everyone has something’ and perceived the diagnosis of MS was less impactful in older age with regards to what is expected at this life stage. Concerns remained, however, regarding whether a new physical or cognitive experience was aging or MS, what the future holds regarding losing independence, losing spouses and caregivers, and growing ‘too old’ such that quality of life is completely diminished.

Conclusions: This qualitative research has highlighted the complexity of aging with MS. All participants noted a continued progression of health, physical function and cognitive ability but stated that they felt a sense of normality and were living a life that culturally aligned with aging narratives. Fears about the future do remain as participants were concerned about living too long for being able to thrive. More research must be done that focuses on maintain quality of life among older person with MS as quantity of life continues to increase.

Disclosure: *Nothing to disclose.*

Keywords: Aging and MS, Management of activities of daily living in MS

(DAM04)

Serum Glial Fibrillary Acidic Protein Is Elevated in a Subset of Neuromyelitis Optica Patients and Associated with Increased Risk of Attacks

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Background: In patients with neuromyelitis optica spectrum disorder (NMOSD), pathogenic anti-aquaporin-4 antibodies cause astroglial injury resulting in increased levels of cerebrospinal fluid glial fibrillary acidic protein (GFAP). N-Momentum is a randomized, placebo-controlled, double-masked trial of inebilizumab, an anti-CD19 monoclonal B-cell depleting antibody, in patients with NMOSD.

Objectives: To investigate the relationship between prospectively sampled serum GFAP (sGFAP) levels and disease activity in N-Momentum trial participants.

Methods: sGFAP (Quanterix Simoa GFAP assay) was measured in 1260 serial and attack-related samples collected from N-MOmentum participants (n=220) and in healthy controls (HC, n=25); the relationship between sGFAP levels and NMOSD attacks was assessed in N-MOmentum participants.

Results: Median (interquartile range [IQR]) sGFAP levels were elevated in NMOSD patients compared with HC (128.3 [92.5, 182.1] vs 73.3 [52.1, 108.7] pg/mL). Elevated sGFAP, defined as ≥ 3 standard deviations above the HC mean (≥ 171 pg/mL), was observed at baseline in 29% (61/215) of NMOSD study participants. Study participants with elevated baseline sGFAP levels were 2.9 times more likely to experience an adjudicated NMOSD attack than those with lower baseline sGFAP during the 28-week randomized controlled period (RCP: $p=0.002$). During the RCP, sGFAP levels increased significantly within 1 week of an NMOSD attack in placebo-treated participants (median fold change [IQR]: 20.2 [4.4, 98.3]; $n=17$ attacks; $p=0.001$) but did not increase significantly during attacks in inebilizumab-treated patients (1.1 [0.75, 24.6]; $n=20$ attacks; $p>0.05$). Of 143 participants who did not have an adjudicated NMOSD attack during the RCP, there were fewer inebilizumab- than placebo-treated participants with elevated sGFAP levels at the end of the RCP (16% [19/117] vs 35% [9/26]). Of 514 samples drawn from inebilizumab-treated patients during the RCP who did not have adjudicated attacks, 14 samples (2.7%) from 12 patients displayed ≥ 2 -fold increase in sGFAP from baseline versus 9 samples (of 116; 8%) from 6 placebo-treated patients (odds ratio: 3.0, $p=0.023$).

Conclusions: NMOSD study participants had increased sGFAP levels compared with healthy controls. sGFAP may prove to be a useful biomarker of attack risk and disease activity and severity.

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Keywords: Non-imaging biomarkers

(DAM05)

Machine Learning Algorithms Applied to Visual Metrics to Classify Demyelinating Disease Diagnosis in Children

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Background: Predicting disease classification in youth with a first episode of demyelination is feasible in some but not all cases. Machine learning algorithms can provide highly accurate predictions of outcomes directly from images, removing a major bottleneck in the speed with which predictions can be made.

Objectives: To use visual metrics to predict disease class in youth with demyelination.

Methods: Standardized, prospectively collected clinical and visual data at disease onset from 224 pediatric subjects, classified using consensus definitions of demyelinating disorders and serum antibody testing for myelin oligodendrocyte glycoprotein (MOG) and aquaporin 4 (AQP4) (Healthy Control (HC)=72, Multiple Sclerosis (MS)=69, anti-MOG=18, Neuromyelitis optica spectrum disorder (NMOSD)=10, Monophasic acquired demyelinating syndromes (MonoADS)=55) were recruited through the Demyelinating Disorders program at The Hospital for Sick Children (Toronto, Ontario) and University of Calgary (2010-2019). We used 9 supervised machine learning algorithms (random forest classifier, CLS bagging classifier, AdaBoost classifier, XGBoost classifier, CLS logistic regression, MLP classifier, CLS SVM, Decision tree, and KNeighbors classifier). Input variables were optical coherence tomography (OCT) parameters including retinal nerve fiber layer (RNFL) and ganglion cell inner plexiform layer thickness (GCIPL), low contrast visual acuity (LCVA) and color vision (CV) for each eye. Separate sets of analyses were run with balanced (n set arbitrarily at 44, oversampling and under-sampling used appropriately) and unbalanced data.

Results: In the analysis of the balanced data set, the Random Forest Classifier (accuracy (a)= 80%, recall (r)= 50%, and precision (p)= 99%), XGB classifier (a=80%, r=50%, p=80%) and Decision Tree (a=90%, r=99%, p=90%) algorithms yielded the highest accuracy, recall and precision levels for each disease class using the combination of RNFL, GCIPL, LCVA and CV. Analysis of the unbalanced data set showed lower overall levels of predictive accuracy (60-90%) for each class using the same algorithms. Use of the OCT data alone yielded lower predictive accuracy in both balanced and unbalanced analyses.

Conclusions: Machine learning algorithms used on combined structural and functional visual metrics may classify youth with demyelinating disorders. Implementation of artificial neural networks using raw OCT data and images as input are underway.

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Keywords: Machine learning and MS

(DAM06)



Updated Recommendations for a Standardized MRI Protocol for Multiple Sclerosis

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Background:

Standardize MRI protocols are important for the diagnosis and monitoring of MS patients. The Consortium of MS Centers (CMSC) convened an international panel of MRI experts to review and update the current guidelines.

Objectives:

To update the standardized magnetic resonance imaging (MRI) protocol and clinical guidelines for diagnosis and follow-up of multiple sclerosis (MS) and develop strategies for them to be universally accepted as standard of care in MRI for MS.

Methods:

The CMSC convened an expert panel in October 2019 to update the standardized MRI protocol. Conference attendees included neurologists, radiologists, MR technologists and imaging scientists with expertise in MS. Representatives from CMSC, magnetic resonance imaging in MS (MAGNIMS), North American Imaging in Multiple Sclerosis Cooperative, National MS Society,



MS Association of America, MRI manufacturers and commercial image analysis companies were present. Before the meeting, CMSC members were surveyed about standardized MRI protocol, gadolinium, diffusion weighted imaging (DWI), and the central vein sign.

Results:

The use of subcallosal plane for consistent repositioning and requirement for thin ($\leq 3\text{mm}$), contiguous slices were re-emphasized. Updated Standardized Brain MRI Protocol includes core sequences optimized for MS lesion detection, and the judicious use of gadolinium when indicated. A new category of optimum plus sequences allows for brain atrophy monitoring and identifying lesions with a central vein sign. Other updates include progressive multifocal encephalopathy surveillance and spinal cord sequences. The group worked to make CMSC and MAGNIMS MRI protocols similar so the updated protocol could ultimately be accepted by international consensus.

Conclusions:

The international expert group developed revised clinical MRI protocols with the vision and action plans for them to be universally useful, useable and become the standard of care for patients with MS

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Keywords: Disease-modifying treatments in MS, Imaging and MS

Disease Modifying Therapy

(DMT01)

Comparative Effectiveness of Switching from Natalizumab to a Moderate Versus High Efficacy Disease Modifying Therapy in Clinical Practice

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Background: Natalizumab (NTZ) is a highly effective disease modifying therapy (DMT) for relapsing multiple sclerosis (MS). Long-term use of NTZ is limited by potential safety risks that can be reduced by switching to an alternative therapy. However, NTZ discontinuation may trigger rebound disease, resulting in disability. Our previous study showed patients switching to moderate (Mod) DMT vs. high efficacy therapy (HET) were at higher risk of early MRI disease activity by 6 months.

Objectives: To assess the comparative effectiveness of switching from NTZ to a Mod DMT vs. HET in MS patients over 24 months.

Methods: Patients discontinuing NTZ at two MS centers (n=556) who switched to Mod DMT (n=270) vs. HET (n=130) were assessed using propensity score (PS) weighting. PS model covariates included demographics and baseline clinical and radiographic disease characteristics. Outcomes included annualized relapse rate (ARR) and proportions with new T2 and/or gadolinium enhancing (GdE) lesions, absence of disease activity (a composite measure of no relapses and/or MRI activity), time-to-first relapse and GdE lesion, and 20% worsening of the timed twenty-five foot walk (T25FW) and 9-hole peg test (9-HPT). All outcomes were reported as Mod DMT vs. HET.

Results: In our cohort, 48.6% switched to Mod DMT (dimethyl fumarate, n=130; fingolimod, n=140) vs. 23.4% who switched to HET (ocrelizumab, n=106; rituximab, n=17; alemtuzumab, n=7). Reasons for NTZ discontinuation included PML risk (54.9%), breakthrough disease (15.3%), and adverse effects (17.3%). PS weighting demonstrated excellent covariate balance. After PS-adjustment, there were no differences in ARR [rate ratio=1.44, 95% CI (0.69-1.59), p=0.334] or time-to-first relapse [HR=2.12, 95% CI (0.87-5.17), p=0.090] by 24-month follow-up. However, patients switching to Mod DMT had higher proportions with new T2 lesions [OR=2.15, 95% CI (1.18-3.01), p=0.011], new GdE lesions [OR=1.99, 95% CI (1.12-2.73), p=0.022], and 20% worsening of the T25FW [OR=1.83, 95% CI (1.06-3.02), p=0.043] and 9-HPT [OR=1.81, 95% CI (1.05-3.56), p=0.044]; and lower proportion with absence of disease activity [OR=0.41, 95% CI (0.21-0.71), p=0.004]. Switchers to Mod DMT were also at higher risk of earlier time-to-first GdE lesion [HR=6.67, 95% CI (2.06-9.16), p=0.002].

Conclusions: By 24 months, NTZ switchers to Mod DMT vs. HET had lower cumulative probability of no disease activity by 24 months and were at higher risk of disability accumulation.

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Keywords: Comparative Effectiveness, Disease-modifying treatments in MS

(DMT02)

Yearly Efficacy and Safety Outcomes Over 4 Years After Last Alemtuzumab Course in Pooled CARE-MS I and II Patients By Number of Additional Courses Received Through Year 9

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Background: In CARE-MS I and II (NCT00530348, NCT00548405), alemtuzumab treatment (12 mg/day; baseline: 5 days; 12 months later: 3 days) improved clinical and MRI outcomes versus SC IFNB-1a over 2 years in RRMS patients. In 2 consecutive extensions (NCT00930553, NCT02255656 [TOPAZ]), patients could receive additional alemtuzumab (12 mg/day; 3 days; ≥ 12 months apart).

Objectives: Evaluate yearly efficacy and safety of alemtuzumab in pooled CARE-MS patients who did or did not receive additional alemtuzumab through Year 9.

Methods: Pooled CARE-MS patients were stratified by the total number of courses received (exactly 2 courses, exactly 3 courses, ≥ 4 courses). Inclusion criteria: additional alemtuzumab (ie, Courses 3 or 4) received by Month 97 to allow ≥ 12 months of follow-up; no other DMT through Year 9. Data were censored at Course 5 (if received) in the ≥ 4 courses group. Outcomes data were rebaselined after the last alemtuzumab course.

Results: 742/811 (91%) alemtuzumab-treated patients entered the extension and could receive additional courses; Courses 3 and 4 were given most frequently in Years 3 (19%) and 4 (6%), respectively. Of 742 extension patients, 359 (48%), 148 (20%), and 121 (16%) were included in the 2-, 3-, and ≥ 4 -courses groups, with 303, 76, and 15 remaining on study in Year 4 after last course, respectively. Over 4 years after last course, annualized relapse rate was 0.07, 0.08, and 0.23 in the 2-, 3-, and ≥ 4 -courses groups, respectively, and change in mean Expanded Disability Status Scale score at Year 4 versus after last course was -0.06, +0.08, and +0.56, respectively. Over 4 years, 83%, 85%, and 94% were free of 6-month confirmed disability worsening, and 23%, 11%, and 15% had 6-month confirmed disability improvement in the 2-, 3-, and ≥ 4 -courses groups, respectively. In Year 4, 78%, 73%, and 69% were free of MRI disease activity. Serious AEs were generally similar between cohorts during Years 1–3 after last treatment (5.1%–11.4% per year), but low patient numbers in the ≥ 4 -courses group confounded analysis of serious AEs in Year 4 after last course.

Conclusions: Efficacy of additional alemtuzumab was maintained over 4 years after last course in CARE-MS patients, although the ≥ 4 -courses group had higher disease activity and disability, as expected. Alemtuzumab safety was generally consistent between groups, except for the ≥ 4 -courses cohort in Year 4 after last course wherein interpretation was limited by low numbers of available patients.

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Keywords: Disease-modifying treatments in MS

(DMT03)

Efficacy and Safety of Ofatumumab Versus Teriflunomide in Patients with Relapsing Multiple Sclerosis: Phase 3 Asclepios I and II Trials

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Background:

Ofatumumab is the first fully human anti-CD20 monoclonal antibody, administered with a monthly 20 mg subcutaneous (s.c.) dosing regimen.



Objectives:

To investigate the efficacy and safety of ofatumumab versus teriflunomide in relapsing multiple sclerosis (RMS) patients.

Methods:

ASCLEPIOS I and II were two identical Phase 3, double-blind, double-dummy, active comparator-controlled, parallel-group, innovative, adaptive-design (with flexible duration), multicentre trials in patients aged 18–55 years with an Expanded Disability Status Scale score of 0–5.5 at screening. Patients were randomized (1:1) to receive s.c. ofatumumab 20 mg (loading dose: Days 1, 7, and 14; maintenance dose: every 4 weeks from Week 4) or oral teriflunomide 14 mg once daily, for up to 30 months. The primary endpoint was annualized relapse rate (ARR). Key secondary endpoints included 3- and 6-month confirmed disability worsening (3mCDW/6mCDW), 6-month confirmed disability improvement (6mCDI), magnetic resonance imaging-related outcomes, and serum neurofilament light chain (NfL) levels. Safety and tolerability was also assessed.

Results:

Of 1882 enrolled patients (ASCLEPIOS I/II: N=927/955), 1578 completed the core study. Ofatumumab reduced ARR (ASCLEPIOS I and II: 50.5% and 58.5%), gadolinium-enhancing T1 lesions (97.5% and 93.8%), and new/enlarging T2 lesions (82.0% and 84.5%) versus teriflunomide (all, $p < 0.001$). In the pre-specified ASCLEPIOS I/II pooled analysis, ofatumumab reduced the risk of 3mCDW by 34.4% ($p = 0.002$) and 6mCDW by 32.5% ($p = 0.012$), and numerically increased the probability to achieve 6mCDI by 35.2% ($p = 0.094$), versus teriflunomide. Ofatumumab reduced serum NfL levels versus teriflunomide in the first measurement at Month 3 (ASCLEPIOS I, $p = 0.011$; ASCLEPIOS II, $p < 0.001$) and in all subsequent assessments (all, $p < 0.001$). No difference in the slope of brain volume change from baseline was observed between treatments ($p = 0.116$ [ASCLEPIOS I] and 0.129 [ASCLEPIOS II] versus teriflunomide). Adverse events occurred in 83.6% and 84.2% of patients receiving ofatumumab and teriflunomide, respectively. Systemic injection-related reactions occurred in 20.6% and 15.3% of ofatumumab and teriflunomide-treated patients, respectively. Rates of serious infections (ofatumumab, 2.5%; teriflunomide, 1.8%) and malignancies (0.5% and 0.3%, respectively) were low.

Conclusions:

Ofatumumab demonstrated superior efficacy versus teriflunomide, with an acceptable safety profile, in patients with RMS.

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Keywords: Disease-modifying treatments in MS, Efficacy and Safety, Immunology and MS

(DMT04)

Treatment-Emergent Adverse Events Occurring Early in the Treatment Course of Cladribine Tablets in Two Phase 3 Trials in Multiple Sclerosis



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Background:

Tolerability and adherence to disease-modifying drugs (DMDs) can be influenced by treatment-emergent adverse events (TEAEs) that start soon after therapy initiation. One potential advantage of cladribine tablets is that patients only receive doses for two 4–5 day periods/treatment year.

Objectives:

To identify TEAEs early in the course of treatment in patients enrolled in the Phase 3 CLARITY and ORACLE-MS clinical trials.

Methods:

This was a post-hoc analysis of safety populations in CLARITY and ORACLE-MS studies. Patients received cladribine tablets 3.5mg/kg (cumulative dose over 2 years; N=636) or placebo (N=641). The incidence of early adverse events, TEAEs, serious TEAEs, drug-related TEAEs, and TEAEs leading to discontinuation were summarized based on incidence within 2, 6, and 12 weeks (W) after commencement of therapy.

Results:

The incidence of TEAEs occurring within the first 2–12W of treatment across both trials in both treatment groups was generally low, and the majority of events were mild (placebo: 68.4–53.8%; cladribine tablets: 68.0–54.4%). The most common TEAEs by time epoch after initiating placebo and cladribine tablets 3.5mg/kg treatment, respectively, were: nausea: 3.3% vs 4.9% (2W), 3.7% vs 6.4% (6W), and 4.5% vs 8.0% (12W); fatigue: 2.0% vs 1.4% (2W), 3.1% vs 2.5% (6W), and 4.4% vs 3.1% (12W); headache: 8.3% vs 9.0% (2W), 11.9% vs 14.8% (6W), and 15.1% vs 18.4% (12W); lymphopenia: 0.0% vs 2.5% (6W) and 0.5% vs 6.8% (12W); leukopenia: 0.0% vs 1.3% (12W). Other endpoints to be shown in the final presentation.

Conclusions:

Incidence of TEAEs experienced during the first 12 weeks of treatment with cladribine tablets in Phase 3 clinical trials was low and mostly mild. Nausea, headache, and lymphopenia were seen more frequently in cladribine tablets-treated patients. These findings suggest that cladribine tablets are generally well tolerated, which may facilitate treatment adherence.

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Keywords: Disease-modifying treatments in MS

Cognition . Psychosocial

(PSY01)

A Mindfulness Group Intervention in Newly Diagnosed Persons with Multiple Sclerosis: A Pilot Study

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Background: Relapsing MS is a lifelong disease without a cure, usually diagnosed between 20-40 years of age. Being newly diagnosed with RMS is a highly stressful event due to the unpredictable disease course after diagnosis. Thus, it is imperative that PwMS have the skills and support to cope with the negative physical and emotional effects of the disease.

Objectives: To assess whether an mindfulness-based intervention (MBI) will lessen the negative consequences of stress due to being newly diagnosed with RMS.

Methods: A single-blind, randomized, prospective study of a 10-week MBI vs. usual standard of care alone in persons newly diagnosed (within 1 year) with RMS. Primary outcomes included the Brief COPE measure and the Hospital Anxiety and Depression Scale (HADS). Secondary outcomes included measures of perceived stress, cognitive function, fatigue, and quality of life. Subjects were assessed at baseline, post intervention and 6 months later. Analysis of Covariance (ANCOVA) was used to compare longitudinal changes, with baseline scores employed as covariates.

Results: 25 subjects were recruited (16 MBI, 9 controls); most were women (21, 84%), with a mean age of 38.4 ± 9.5 years. The groups were well matched on baseline characteristics. All



controls completed the study, while 4 MBI participants did not. The MBI group improved significantly on the COPE measure when compared to the control group ($p=0.024$) as well as on the HADS depression subscale ($p=0.007$) pre and post intervention; there was no significant difference over time on the HADS anxiety subscale ($p=0.179$). On the secondary outcomes, there was a significant improvement on the Perceived Stress Scale ($p=0.015$), and a trend towards improvement on the SF-36 ($p=0.073$; quality of life) and the MSNQ ($p=0.066$; perceived cognitive impairment) comparing pre and post intervention assessments. Six month data will be available at the time of this presentation.

Conclusions: This pilot study demonstrates that an MBI improves coping, depression and perceived stress in newly diagnosed persons with RMS.

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Keywords: Comprehensive care and MS, Psychological issues and MS

(PSY02)

Effects of Weekly Participation in a Wellness Program on Self-Reported Measures for People Living with Multiple Sclerosis: A Three-Year Analysis

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Background: The Multiple Sclerosis Achievement Center (MSAC) conducts day wellness programs to address physical, cognitive and social well-being. Program activities include individualized and group exercise, cognitive stimulation, education, socialization, and community outings. Baseline, one-year and two-year follow-up data was collected and presented at previous Consortium of Multiple Sclerosis Centers annual meetings.

Objectives: To determine, through the use of patient reported outcome (PRO) measures, if members of these wellness programs improve in areas of self-reported disease impact and quality of life over a three year period.

Methods: Initial analysis, comparing data of baseline and one-year participation in these wellness programs, was completed through paper/pencil outcome measures between December 2016 and August 2017 for 95 people with multiple sclerosis (PwMS). Of those 95, two-year data for 70 PwMS was collected in January 2019 and three-year data is anticipated for 66 people. Outcome measures used for these analyses include the Multiple Sclerosis Impact Scale (MSIS-29), Multiple Sclerosis Self-Efficacy Scale-10 item (MSSE), Godin Leisure Time



Exercise Questionnaire (GTLEQ) and Neuro-QoL (questions from the Anxiety, Depression, Emotion & Behavior, Positive Affect, Cognition, Ability to Participate, and Social Roles sections were used). All outcomes were completed onsite at the MSAC as part of the members' weekly participation in the program. Analysis will be completed to compare data from the initial analysis to the three-year results.

Results: As previously reported, a correlation between reports of Self-Efficacy, Anxiety, Ability to Participate, and Positive Affect (per MSSE & Neuro-QoL) were seen with both one and two-year analyses. Analysis of baseline to two-year data demonstrated statistically significant changes in Neuro-QoL sections Ability to Participate ($p=.02$) and Social Roles ($p=.001$). Another notable change in the two-year analysis was an increase in physical activity, as measured by GTLEQ (average change of 2.34 from baseline to 2 years). Data analysis will measure any changes in three-year data compared to baseline, one-year and two-year results.

Conclusions: Complete collection and analysis of three-year comparative data will be finalized in February 2020 for presentation at the meeting.

Disclosure: *Brian Hutchinson: Biogen (speakers bureau). John Schafer: Biogen, EMD Serono, Genentech, Sanofi Genzyme, Teva Neuroscience (speakers bureau). Lacey Sayre, Tiffany Malone: Nothing to disclose.*

Keywords: Comprehensive care and MS, Psychological issues and MS, Wellness

(PSY03)

Examining Multi-Level Environmental Correlates of Physical Activity Among Older Adults with Multiple Sclerosis

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Background: With a growing population of older adults with multiple sclerosis (MS), appropriate strategies are needed to promote physical activity (PA) as a second-line approach for symptom management.

Objectives: This cross-sectional study examined built environment, social environment, and individual social cognitive theory (SCT) variables as hierarchical correlates of PA in older adults with MS using a social ecological model (SEM) framework.

Methods: Three hundred sixty-three participants completed the online survey including: demographics, The Abbreviated Neighborhood Walkability Scale (NEWS-A), Social Provisions Scale (SPS), Exercise Self-Efficacy Scale (EXSE), Multidimensional Outcome Expectations Scale for Exercise Scale (MOEES) and Godin Leisure-Time Exercise Questionnaire (GLTEQ) Total and Health Contribution score (HCS). Spearman's Rank-Order correlation analyses were



used to examine associations among NEWS-A subscales, SPS, EXSE, MOEES, and GLTEQ Total and HCS. We then conducted hierarchical, linear regression analysis whereby we regressed GLTEQ with NEWS-A subscales (built environment) in Step 1, SPS (social environment) in Step 2, then EXES and MOEES (individual determinants) in Step 3.

Results: Land-use mix diversity, land-use mix access, street connectivity, and aesthetics were significantly correlated with GLTEQ Total, whereas land-use mix diversity, land-use mix access, infrastructure and safety for walking, aesthetics, and crime were significantly correlated with GLTEQ HCS. Hierarchical linear regression analyses were then conducted whereby we regressed GLTEQ Total with NEWS-A subscales (Step 1) with significant associations noted for land-use mix diversity and aesthetics ($R^2=.09$), Step 2 included SPS with significant associations noted for SPS, land-use mix diversity, and aesthetics ($R^2=.15$), and finally EXSE and MOEES were included in Step 3 and were the only significant correlates of GLTEQ total ($R^2=.38$). Regarding GLTEQ HCS, land-use mix diversity, aesthetics, and crime were significant correlates in Step 1 ($R^2=.10$), SPS and land-use mix diversity were the only significant correlates in Step 2 ($R^2=.14$), and EXSE was the only significant correlate in Step 3 ($R^2=.36$).

Conclusions: This study provides guidance for researchers and practitioners on relevant targets for tailoring PA interventions for older adults with MS and supports the continued emphasis on self-efficacy as a primary predictor of health behavior change and maintenance.

Disclosure: *Nothing to disclose.*

Keywords: Management of activities of daily living in MS, Older adults with MS, Psychological issues and MS

(PSY04)

Effect of Nabiximols Cannabinoid Oromucosal Spray on Depressive Symptoms, Suicidality, and Cognition in Patients with Multiple Sclerosis (MS)

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Background: Substantial evidence has shown nabiximols, a complex botanical mixture containing delta-9-tetrahydrocannabinol and cannabidiol as the principal cannabinoids, can reduce spasticity associated with MS. This analysis assesses whether nabiximols affects other patient outcomes such as depressive symptoms, suicidality, and cognition.



Objectives: Report the effect of nabiximols on depression, suicidality, and cognition using data from 2 placebo-controlled randomized controlled trials, GWSP0604 (12 weeks) and GWMS1137 (48 weeks), in patients with spasticity due to MS.

Methods: Mood and suicidality were assessed using the Beck Depression Inventory-II (BDI-II) in both trials. In GWMS1137, suicidality was assessed using the Columbia-Suicide Severity Rating Scale (C-SSRS) and working memory/processing speed using the Paced Auditory Serial Addition Test (PASAT). The combined PASAT total score was calculated combining both PASAT-3 and -2 tests scores (total of 120 points). Outcome differences between nabiximols and placebo are summarized.

Results: 241 patients from GWSP0604 and 121 from GWMS1137 were included. The baseline and end-of-treatment mean BDI-II total scores were 8.7 vs 9.5 for nabiximols and 9.7 vs 10.4 for placebo in GWSP0604, and 15.7 vs 12.5 for nabiximols and 13.5 vs 11.1 for placebo in GWMS1137. Differences between nabiximols and placebo of the BDI-II change from baseline adjusted means were -0.06 (-1.62, 1.49) in GWSP0604 (no significant difference) and -0.29 (-2.91, 2.33) in GWMS1137 (statistically non-inferior). Question 9 of BDI-II (suicidal thoughts or wishes) showed no notable treatment differences in either trial, with only 1 patient treated with nabiximols reporting a score ≥ 2 . On the Columbia-Suicide Severity Rating Scale, 3 (5.1%) patients randomized to placebo and 1 (1.6%) to nabiximols had a 'flag' (ie, 'Yes' as a response), but further questioning revealed no emergent suicidal ideations or behavior in any of these patients. For GWMS1137, the baseline and end-of-treatment PASAT total score means were 71.3 vs 78.6 for nabiximols and 74.5 vs 82.7 for placebo; increases may reflect practice effects. Treatment difference of the adjusted mean was -1.47 (-6.41, 3.48), indicating nabiximols does not adversely affect working memory/cognitive processing speed in MS patients over a 48-week period compared with placebo.

Conclusions: Nabiximols had no notable effects on depression, suicidality, or working memory/processing speed in patients with MS.

Disclosure: *John DeLuca:* Biogen IDEC (consulting fee, contracted research, speakers bureau). Celgene, Novartis (consulting fee). EMD Serono (contracted research). Sanofi-Genzyme (speakers bureau). *Professor Dawn Langdon:* Nothing to disclose. *Joris Berwaerts:* GW Pharmaceuticals (salary). *Joanne Wagner:* Greenwich Biosciences/GW Pharmaceuticals (salary). GW Pharmaceuticals (ownership interest).

Keywords: Complementary/alternative therapies in MS, MS symptom management , Psychological issues and MS

(PSY06)



Multiple Sclerosis Management: Predicting Disease Trajectory of Multiple Sclerosis on Multi-Dimensional Data Including Digital Cognitive Assessments and Patient Reported Outcomes Using Machine Learning Techniques

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Background: Multiple Sclerosis (MS) disease impact is traditionally measured by MRI changes, relapse rates and EDSS. Combining multidimensional PRO and objective disease impact information independent of EDSS might enhance clinical decision making. As patient-tracking sources expand beyond what is traditionally captured in an office visit, clinicians need tools to help integrate these varied streams of data. Machine learning has the potential to help clinicians predict meaningful patient outcomes from multi-dimensional and quantified data sources.

Objectives: To demonstrate the feasibility of predicting clinical outcomes in Multiple Sclerosis using standard machine learning methods on multi-dimensional data including digital cognitive assessments and Patient Reported Outcomes (PROs).

Methods: Machine learning models were trained on EHR data, cognitive domain scores and PRO data. A prediction model was created given the patient's record. 80% of the dataset was used in training, 20% in testing with an ensemble learning method (random forest classifiers) used to construct a multitude of training decision trees, which then outputted the mean prediction of the individual trees.

Results: The training set consisted of 258 PwMS (72.5% female, average age = 46.2±10.2) over a three year period. Untuned models calculated F1 scores ($2 * [\text{Precision} * \text{Recall}] / [\text{Precision} + \text{Recall}]$), Precision, Recall and Accuracy for multiple models predicting PROs and DMT choice. The most precise and accurate models were for the Driving (0.913, 0.904, 0.942, 0.912), Modified Falls Efficacy Scale (0.789, 0.796, 0.792, 0.829), Depression (0.711, 0.765, 0.714, 0.718), Fatigue (0.716, 0.782, 0.699, 0.755) and Employment (0.672, 0.753, 0.668, 0.705).

Conclusions: Machine learning combined with objective measures of disease impact and PRO can provide important information to predict economically important and disability relevant outcomes, potentially enhancing treatment decisions. These results show promising predictive accuracy to be used in a variety of advisory applications and potentially reduce disease related disability. The results of the other models demonstrate the feasibility of using machine learning in a broader network of clinical sites that will allow for greater accuracy, precision and recall.



The eventual goal is that these models can be used as an aid in the shared decision making process, and to reduce inappropriate healthcare costs.

Disclosure: *Mark Gudesblatt: Acorda, Amgen, Medtronic, Saol Therapeutics (speakers bureau). Biogen, EMD Serono, Novartis, Sanofi, Teva (contracted research). Jared Srinivasan, Olivia Kaczmarek, Daniel Kantor, Daniel Golan, Marijean Buhse, Lori Fafard, Timothy Fratto: Nothing to disclose. Myassar Zarif: Acorda, Biogen, Genzyme, Teva (speakers bureau). Barbara Bumstead: Biogen, Genzyme (speakers bureau). Jeffrey Wilken: Biogen (contracted research). EMD Serono (speakers bureau). Genzyme (contracted research, speakers bureau). Cynthia Sullivan: Roche (contracted research). Glen Doniger: NeuroTrax (salary).*

Keywords: Comprehensive care and MS, Machine Learning, Natural history of MS

Rehabilitation Presentations

(RHI01)

Significant Structural Neuroplasticity Changes Can Follow Physical Behavioral Change Therapy for MS

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Background: Constraint-Induced Movement Therapy (CIMT) is a form of physical Behavioral Change Therapy (BCT) that can significantly improve paretic limb use in the community in progressive MS for at least 1 year (Mark et al 2018). Although a few forms of BCT can increase real-life physical activity in MS, none thus far has been examined for whether such treatment can change cerebral cortical grey matter structure.

Objectives: To evaluate whether CIMT vs. dose-matched control physical training can change cortical grey matter structure in progressive MS.

Methods: 20 chronic MS adults matched for unilateral arm disability were randomized to 35 hours/2 weeks of either CIMT or a holistic Complementary and Alternative Medicine (CAM) program (yoga, aquatic therapy, massage, relaxation techniques). Paretic limb use was measured with the Motor Activity Log (MAL), which has been validated against real-world upper limb accelerometry. Pre- and post-treatment 3 Tesla structural brain MRI scans were performed. Tensor-Based Morphometry (TBM) and Voxel-Based Morphometry (VBM) were used to evaluate group-level changes in primary motor cortex (M1) structure contralateral to the more-affected arm. Whole-brain statistics were conducted using one-sample *t*-tests within Statistical



Parametric Mapping software with a cluster-extent threshold of 10 voxels and false discovery rate of 0.1.

Results: The two groups were identical in high expectancy to benefit. CIMT produced a much larger Effect Size ($d' = 3.2$) on the MAL than did CAM ($d' = 0.7$). TBM detected an increase in the thickness of M1 after CIMT but not after CAM. VBM detected a change in M1 after CIMT, suggesting an increase in cortical density or volume or both. No change was detected after CAM.

Conclusions: TBM and VBM suggest that CIMT increases M1 thickness and either volume or density in MS, unlike dose-matched CAM. The findings suggest for the first time that physical BCT can significantly stimulate cortical neuroplasticity in a degenerative CNS disorder. The findings accord with our previous findings of post-CIMT significant white matter structural improvement in progressive MS (Barghi et al 2018) and grey matter increases in stroke (Gauthier et al 2008) and cerebral palsy (Sterling et al 2013). Together, these findings suggest that a specific form of physical BCT can not only stimulate physical activity in the community over the long term but also well improve neurological structure for progressive MS.

Disclosure: *Nothing to disclose.*

Keywords: CNS repair, Imaging and MS, Management of activities of daily living in MS

(RHI02)

A New Look at the Symbol Digit Modalities Test in Multiple Sclerosis and Disabilities

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Background: Reduced information processing speed (IPS) is the most common cognitive impairment in MS, related to reduced employment and physical ability. The Symbol Digit Modalities Test (SDMT) is the gold standard measure of IPS in MS (Benedict et al 2017). Although many investigators have suggested that performance on the SDMT involves multiple cognitive processes, there has been little attempt to tease apart what specific cognitive processes may affect the IPS score on the SDMT. Improved understanding of the cognitive processes that contribute to IPS on the SDMT could support future cognitive rehabilitation trials to treat impaired IPS in MS.

Objectives: Assess specific eye movement measures during the SDMT to suggest what specific cognitive processes may underlie IPS on the SDMT in MS.



Methods: We recruited a convenience sample of 38 adults with MS, without clinical oculomotor impairment, who performed the SDMT while an infrared eye tracker recorded their eye movements. Eye positions were sampled at 10Hz. Data were exported to a database for subsequent specific eye movement measures: (1) Search organization as calculated by the “best r” metric (index of primarily orthogonal search progress; Mark et al 2004); (2) total of upward saccades from the lower area on the page of test symbols to the answer key at the top, inferred as a measure of symbol working memory. Spearman’s rho was performed to assess correlations between the variables and the SDMT IPS score (correct responses in 90 seconds).

Results: The mean SDMT IPS score was 38 (SD = 14). Both best r and total of upward saccades significantly positively correlated with the SDMT IPS score (best r, rho = 0.45, p = 0.004; upward saccades, rho = 0.62, p < 0.0001).

Conclusions: Both search organization and total of upward saccades were positively correlated with the IPS score. The latter result was unexpected: the faster on the SDMT, the more often subjects checked the answer key. The results suggest that lower-scoring MS subjects, who less often checked the answer key during the test, may have become lost during their visual search, as reflected by their poorer search organization. Upward saccades may not so much represent working memory but rather as a strategy to assure successful test completion that is not effectively used by lower-scoring persons with MS. Further research will be needed to assess the criterion validity of specific SDMT eye movement measures relative to standard cognitive test assessments.

Disclosure: *Nothing to disclose.*

Keywords: Information Processing Speed, Management of activities of daily living in MS

(RHI03)

Creating a Yoga Program As Part of a Comprehensive Multiple Sclerosis Care Model

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Background:

Multiple sclerosis (MS) impacts both physical and emotional health. Comprehensive programs addressing health and wellness are essential to improve quality of life.

We offer a multidisciplinary approach to treatment, comprising a dedicated medical team, education, social work, rehabilitation, research, and a health and wellness program. The benefits



of yoga are increasingly recognized and subsequently requested by patients, yet dedicated programs aimed specifically for persons with MS are limited. MS specialty centers are challenged to explore ways to include yoga into a comprehensive care plan.

Objectives:

We present our experience at the Cleveland Clinic Lou Ruvo Center for Brain Health in creating the Yoga for MS program as an integral component to comprehensive care.

Methods:

Our center is contracted with a local yoga company to provide weekly sessions, using philanthropy funding. There are 3 instructors- one who leads and two others who assist, observe and take notes. Because participants regularly engaged in dialogue before and after sessions, a 60-minute support/community sharing session was added prior to the yoga session. Our social worker attends each session and facilitates as needed. Topics include implications for physical and mental health, as well as coping strategies and the importance of treatment adherence. An instructional video and meditation literature are available for use at home.

Results:

The Yoga for MS Program started in November 2017, initially in a private setting with one instructor. In response to our patients' needs, we hired a yoga company with multiple instructors at a yoga studio in October 2018. Our current space can comfortably support 18 participants, including wheelchairs, scooters and walkers. To date, we have 12 participants who have a 75% attendance rate in a 12-week session. Average class size in the first year was 4, and now has doubled to 8, the largest being 14.

Yoga staff observed over time increased flexibility among the participants. The participants also report reduced stress, increased use of coping strategies, and positive effects on strength, balance, self-esteem, and confidence. Participants also share resources and report feeling like they are "really in this together."

Conclusions:

A Yoga for MS Program can address the physical and emotional well-being of patients with MS as part of a comprehensive care model. Future studies addressing the direct benefits of yoga on MS outcomes are being explored.



Disclosure: *Sandra Chapman, Ruth Almen: Nothing to disclose. Carrie M. Hersh: Biogen, Genentech (consulting fee, contracted research). EMD Serono (consulting fee). Genzyme, Novartis (consulting fee, speakers bureau). PCORI (contracted research). Le H. Hua: Biogen, Celgene, EMD Serono, Genentech, Novartis (consulting fee). Genzyme (consulting fee, speakers bureau).*

Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS, Yoga

(RHI04)

Feasibility of "Sit Less, Move More": An Intervention for Reducing Sedentary Behavior Among African-Americans with MS

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Background: Sedentary behavior (SB) is a major concern in multiple sclerosis (MS), as it may accelerate disease progression and exacerbate physical disability. This is especially concerning in African-Americans, a segment of the MS population who present with greater neurological disability than Caucasians and for whom little MS research data are available.

Objectives: The current study examined the feasibility of an intervention focused on reducing SB in African-Americans with MS.

Methods: We recruited 30 ambulatory and physically inactive African-Americans with MS (age=44y) to participate in the "Sit Less, Move More" (SLMM) program. SLMM consisted of a 12-week behavioral intervention that used text-messaging along with Social Cognitive Theory-driven newsletters and behavioral coaching for reducing SB. Feasibility was assessed on four domains: process, resource, management, and scientific outcomes. Participants wore activPAL (AP) and ActiGraph (AG) activity monitors at 3 time points (prior to week 1 (T1), during week 6 (T2), and after week 12 (T3)) to measure changes in time spent sitting (AP data) and time spent in sedentary behavior (AG data). Estimates of effect size (Cohen's *d*) were calculated to describe the treatment effect of SLMM on SB.

Results: *Process:* Of the 64 persons initially contacted, 45 were assessed for eligibility, 31 were sent the informed consent document (ICD), and 30 returned a signed ICD and were included in the study. *Resources:* All participants returned T2 testing materials, and 29 (95%) returned T3 testing materials. Twenty-five (83%) participated in all behavioral coaching sessions. Total study costs were \$7,242.38 USD including costs for materials, postage, equipment, and participant remuneration. *Management:* Total personnel time to complete the study was 130h. Only 13 participants had valid AP data at all 3 time points, whereas 24 participants had valid AG data at



all 3 time points. *Scientific outcomes*: No adverse events were reported. There was a small treatment effect on time spent sitting ($d=-0.13$) and sedentary time ($d=-0.19$).

Conclusions: The SLMM intervention is safe and feasible for African-Americans with MS, and yielded a small reduction in SB. The intervention was low-cost and well-received as an approach for reducing sedentary behavior, and overall, our results suggest that the SLMM program progress towards a phase II trial to determine its efficacy for reducing sedentary behavior in African Americans with MS.

Disclosure: *Jessica F. Baird, Jeffer E. Sasaki, Brian M. Sandroff, Rob Motl: Nothing to disclose. Gary Cutter: Avexis Pharmaceuticals, Biogen, Biolinerx, Brainstorm Cell Therapeutics, Click Therapeutics, CSL Behring, Galmed Pharmaceuticals, Genentech, Genzyme, Gilgamesh Pharmaceuticals, GW Pharmaceuticals, Hisun Pharmaceuticals, Horizon Pharmaceuticals, Klein-Buendel Incorporated, Medday, Medimmune, Merck, Merck/Pfizer, Neurim, NHLBI (Protocol Review Committee), NICHD (OPRU oversight committee), Novartis, Ophazyme, Opko Biologics, Osmotica Pharmaceuticals, Perception Neurosciences, Reata Pharmaceuticals, Receptos/Celgene, Recursion Pharmaceuticals, Roche, Sanofi-Aventis, Somahlution, Teva pharmaceuticals, TG Therapeutics, Vivus (fees for non-cme/ce services received directly from commercial interest or its agent). MGFA MG Registry, NARCOMS (contracted research). Pythagoras Inc (ownership interest).*

Keywords: Sedentary behavior

(RHI05)

The Effect of Aerobic Fitness on Physical and Cognitive Function and Brain Volume in Older Adults with MS

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Background: There is evidence for the beneficial effects of aerobic exercise training on physical and cognitive function in persons with multiple sclerosis (MS). Improvements in function may be associated with the effects of aerobic fitness on deep gray matter (DGM) structures within the brain such as the hippocampus, thalamus, and basal ganglia. To date, we are unaware of research that has examined the effects of aerobic fitness in older adults with MS. Given the aging of the MS population, such an investigation is warranted.

Objectives: The current study examined the effect of aerobic fitness on physical and cognitive function and DGM brain structures relevant to these outcomes in older adults with MS.

Methods: We recruited ambulatory adults (55+ years of age) with MS (n=20, age=63y). All participants underwent an assessment of aerobic fitness using a maximal, incremental exercise test on a recumbent stepper, assessments of walking speed (Timed 25-foot Walk) and walking



endurance (Six-Minute Walk), assessments of cognitive function (Symbol Digit Modalities Test [SDMT]; Brief Visuospatial Memory Test [BMVT]; California Verbal Learning Test, [CVLT]), and a 3T MRI of the brain. We dichotomized participants into a “low fit” group (n=10) and “high fit” group (n=10) based on the results of the exercise test and calculated effect sizes (Cohen’s *d*) between the groups for all outcome measures.

Results: Aerobic fitness had a large effect on both walking speed ($d=-0.99$) and walking endurance ($d=1.51$). There was a moderate effect of aerobic fitness on cognitive function (SDMT $d=0.57$; CVLT $d=0.48$; BVMT $d=0.67$). The effect of aerobic fitness on DGM brain structures varied by structure. There was little to no effect on the thalamus ($d=0.19$) and hippocampus ($d=-0.01$), whereas there was a moderate effect on the basal ganglia ($d=0.53$).

Conclusions: Our results provide novel evidence demonstrating a positive effect of aerobic fitness on physical and cognitive function in older adults with MS. As aerobic fitness is modifiable by aerobic exercise training, our results suggest that participation in regular physical activity may be an approach to ameliorate the consequences of aging with MS. Our results further suggest that improvements in function may be mediated by an effect of aerobic fitness on DGM brain structures; however, additional research is warranted to comprehensively investigate the neural adaptations associated with aerobic fitness in this population.

Disclosure: *Jessica F. Baird, Marcas Bamman, Cynthia Brown, Rob Motl: Nothing to disclose. John R. Rinker: Biogen-Idec, EMD Serono (contracted research).*

Keywords: Exercise, Imaging and MS

(RHI06)

Functional Electrical Stimulation Cycling Exercise Reduces Lower Limb Strength Asymmetry in Persons with Multiple Sclerosis

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Background: Lower limb strength asymmetries (i.e., difference $\geq 10\%$ between contralateral muscle groups) have been associated with mobility impairment in persons with multiple sclerosis (PwMS), and may be a target for exercise training interventions aiming to improve mobility. Functional electrical stimulation (FES) cycling is an adapted exercise modality that has demonstrated preliminary benefits for mobility and fitness outcomes in PwMS with mobility impairment, but its potential effects on lower limb strength asymmetry remains unknown.



Objectives: To assess the effect of FES cycling exercise on lower limb strength asymmetry in PwMS who have mobility impairment (i.e., Expanded Disability Status Scale (EDSS) 5.5-6.5), and to explore associations between change in lower limb strength asymmetry and change in mobility outcomes.

Methods: Peak torque was recorded bilaterally for knee extensors (KE) and flexors (KF) using an isokinetic dynamometer, and was then used to generate lower limb strength asymmetry scores ($1 - (\text{torque}_{\text{weak}} / \text{torque}_{\text{strong}}) \times 100$). Mobility outcomes included the Timed 25-Foot Walk (T25FW) and the 2-Minute Walk (2MW). Participants received 24 weeks (3x/week) of either FES cycling or passive leg cycling (PLC). The FES condition actively cycled while receiving mild electrical stimulation to the quadriceps, hamstrings, and gluteal muscle groups. Exercise intensity was set at 40 to 60% of heart rate reserve, with exercise duration gradually increasing from 10 to 40 minutes per session over the course of the intervention. The PLC condition was identical to the FES condition, but did not receive electrical stimulation and did not actively cycle.

Results: Eight PwMS (mean age (SD)= 52.9 (7.9); median (IQR) EDSS= 6.3 (0.5)) completed the intervention. The FES cycling condition demonstrated a small decrease in KE ($d = -0.33$) and KF ($d = -0.23$) asymmetry compared to the PLC condition. Small-to-moderate associations were observed between change in KE asymmetry and change in T25FW ($\rho = -0.43$) and 2MW ($\rho = -0.24$). A moderate association was observed between change in KF asymmetry and change in T25FW ($\rho = -0.31$), while no association was observed with change in 2MW ($\rho = -0.07$).

Conclusions: FES cycling may be efficacious for reducing lower limb strength asymmetry and improving mobility in PwMS who have mobility impairment. These preliminary results will inform future FES cycling investigations with larger sample sizes.

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS, Functional Electrical Stimulation