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Health Care Provider and Patient Perspectives: Two Views on Making Critical MS Decisions

WHEN:  Friday, May 30, 2014
WHERE:  Product Theater Area
         (between Poster Boards and Exhibitor Lounge)
TIME:  12:00 pm-1:00 pm

TOPICS:  • Why patient preferences are an important consideration in MS
         • Ways to successfully discuss and evaluate efficacy and safety
         • Examples of effective shared decision-making

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We are pleased to present this supplement to the International Journal of MS Care (IJMSC) containing the abstracts from the 2014 Annual Meeting of the Consortium of Multiple Sclerosis Centers (CMSC), held in conjunction with the 2014 Annual Meeting of the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) from May 28 through 31, 2014, in Dallas, Texas. These abstracts include platform, poster, and Whitaker Research Track presentations delivered at the meeting. If you were not able to attend the conference, this is a wonderful opportunity for you to appreciate the diversity and depth of this outstanding group of presentations. The print version of this supplement is being distributed at the CMSC meeting in Dallas to meeting attendees. The electronic version, which is available to all on the IJMSC website at ijmsc.org, can be searched using key words to identify abstracts on topics of individual interest.

We would like to thank Genzyme for their support, which made this publication possible.

We hope that this material will assist you in your care of MS patients and stimulate your interest in furthering research and care in MS.

—Francois Bethoux, MD
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In Vivo Detection of Deep Retinal Neuronal Layer Changes Following Acute Optic Neuritis Utilizing Optical Coherence Tomography–Derived Segmentation

The Role of Vitamin D and Gender in Optic Neuritis

Changes in Step-Down Kinematics Following 16 Weeks of Supervised Progressive Resistance Training for People with Multiple Sclerosis

Magnetization Transfer Imaging in Brain Corticospinal Tract Is Associated with Clinical Walking Performance in Multiple Sclerosis

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(SX12) Self-Reported Bladder and Bowel Symptoms in Multiple Sclerosis Patients

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(SX14) To Pee or Not to Pee? The Utilization of Bladder Scans in Multiple Sclerosis

(SX15) High Fatigue Levels Affect Functional Mobility, Quality of Life, and Depression in People with Multiple Sclerosis

(SX16) Medical Tourism for Chronic Cerebrospinal Venous Insufficiency (CCSVI) Treatment in Multiple Sclerosis

(SX17) Factors Predicting Fatigue Impact in People with Long-Standing Multiple Sclerosis

(SX18) Fatigue and Quality of Life in Multiple Sclerosis Patients

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(SX20) Self-Perceived Reasons for Decreases in Libido in a Cohort of Women with Multiple Sclerosis

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(SX22) Bladder Dysfunction and Disability in People Newly Diagnosed with Multiple Sclerosis

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RESULTS suggest that participants were tested in four conditions: slow vs. fast; coop vs. comp; slow vs. fast; coop vs. slow. Results: Compared with control participants, people with MS were less accurate at discriminating intention, especially comp versus fast and coop versus slow intentions. This effect was more pronounced for high EDSS score. Conclusions: Results suggest that intention-from-movement recognition is deficient in people with MS. Progressing with the MS course, this deficit may help explain the deterioration in interpersonal relationships experienced by people with MS over time.

Disclosure: Nothing to disclose

Keywords: Psychological issues and MS, Social cognition

(CG02) LACK OF PREPAREDNESS FOR TRANSITION OF CARE AMONG ADOLESCENT MULTIPLE SCLEROSIS PATIENTS

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Background: Multiple sclerosis (MS) is a chronic demyelinating disease that requires a skill set to navigate the healthcare system. The American Academy of Pediatrics states, “This process [transition] includes ensuring that high-quality, developmentally appropriate health care services are available in an uninterrupted manner as the person moves from adolescence to adulthood.” Although there are programs in place for other chronic disease states like diabetes and transplant receipt, there is no standard transition of care recommended for MS. The absence of or a delayed transition plan can negatively affect a patient’s care, promoting nonadherence with disease-modifying therapies, reliance on emergency care rather than a focus on preventative care, and the continued dependence on a caregiver for health-care needs.

Objectives: To determine the level of readiness for transition to the adult health-care system in adolescent patients with MS and their caregivers.

Methods: Our multidisciplinary team developed assessments utilizing the recommendations set forth by the American Academy of Pediatrics. We evaluated 11 patients within the Children’s Medical Center Demyelinating Disease Clinic diagnosed with relapsing-remitting MS (RRMS) for at least 6 months, between the ages of 13 and 19 years, and their caregivers. Patients were assessed for readiness to transition to an adult health-care system, basic knowledge about their disease and management, future plans for career, and access to health care. Caregivers independently completed a readiness assessment and subjectively rated their child’s ability to independently explain their knowledge of MS, communicate with the health-care team, acquire medications, and obtain financial coverage. They also rated their anxiety level related to the transition.

Results: Overall, we found discrepancies among patient, caregiver, and nurse assessments of the adolescent’s readiness to transition. On average, the patients scored 65% on the knowledge assessment, which included questions about pathophysiology, medications, health maintenance, and communication.

Conclusions: Patients and caregivers do not reliably assess their readiness for transition. A multidisciplinary transition of care (TOC) program is essential in order to equip adolescent MS patients to navigate the health-care system. It is expected that an effective TOC program will positively affect disease outcomes, likely improving medication adherence, reducing hospitalizations, and improving overall quality of life. Future research will evaluate the impact of TOC annually.

Supported by: None

Disclosure: Audrey Ayres, Teva, Multiple Sclerosis Association of America (consulting fees). Samuel Hughes, Lena Harder, Nothing to disclose. Donna C. Graves, Teva, Biogen, Genzyme, Pfizer (consulting fees). Benjamin Greenberg: Amplimmune, DigiGenix, Accelerated Care Project, Biogen Idec, National Institutes of Health Guthy Jackson Foundation (grant/research support); Biogen Idec (consulting fees); DigiGenix (equity).

Keywords: MS and the caregiver/family, Nursing management in MS, Transition of care
[CG03] PHYSICAL FITNESS, COGNITIVE FUNCTION, AND DISABILITY STATUS IN MULTIPLE SCLEROSIS
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Background: Cognitive impairment is a highly prevalent, poorly managed, and disabling consequence of multiple sclerosis (MS). Exercise training that improves physical fitness (ie, aerobic capacity and muscular strength) represents a promising approach for managing cognitive impairment in people with MS based on the gerontology literature. To date, there is limited evidence that physical fitness is associated with multiple domains of cognitive dysfunction (eg, impaired cognitive processing speed, verbal/visual memory) across the disability spectrum in people with MS. This is a precursory step before designing and testing exercise training interventions for improving cognitive function in MS. Objectives: We examined the associations among aerobic capacity, lower-limb muscle strength, and cognitive functions in people with mild, moderate, and severe disability. Methods: The sample included 63 individuals with mild (n = 21), moderate (n = 21), and severe (n = 21) MS disability based on a neurologic examination for determining Expanded Disability Status Scale (EDSS) scores. The participants underwent neuropsychological assessments of cognitive processing speed (ie, Symbol Digit Modalities Test [SDMT]), verbal memory (ie, California Verbal Learning Test–2 [CVLT-2]), and visual memory (ie, Brief Visuospatial Memory Test–Revised [BVMT-R]). All participants further underwent testing for measuring aerobic capacity (ie, peak oxygen consumption) on a recumbent stepper (NuStep) and muscular strength (ie, peak torque of knee flexors and extensors) on an isokinetic dynamometer (Biodyex). Results: There were significant group differences in cognitive and fitness outcomes among individuals with mild, moderate, and severe disability. SDMT scores, but not CVLT-2 or BVMT-R scores, were associated with aerobic capacity and muscular strength in the overall sample (r′s = 0.41–0.49). SDMT scores were associated with aerobic capacity (r = 0.55) but not muscular strength (r′s = 0.33–0.40) in people with mild disability, and this association was attenuated, but remained statistically significant, after controlling for age as a covariate (pr = 0.41). SDMT scores were not associated with aerobic capacity or muscular strength in people with moderate (r′s = 0.04–0.06) or severe disability (r′s = 0.08–0.14). Conclusions: These results indicate that disability status is a moderator of the association between aerobic capacity and cognitive processing speed, but not a moderator of physical fitness and memory outcomes. This supports aerobic exercise training for improving cognitive processing speed in people with mild MS, and further suggests that aerobic and resistance exercise training might not have as large an effect on cognitive function in people with moderate and severe MS disability.


Keywords: Cognition in MS

[CG04] CLINICAL EFFECTIVENESS OF COGACT TO IMPROVE COGNITIVE AND PSYCHOSOCIAL FUNCTIONING OF PEOPLE WITH MULTIPLE SCLEROSIS
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Background: Despite the urgency of cognitive and psychosocial rehabilitation services as a standard of care, there has been a paucity of efficacy studies designed to investigate these integrated therapeutic approaches in people with multiple sclerosis (MS), with current clinical research highlighting the pressing need for effective rehabilitation techniques within the field of MS. Objectives: To evaluate the clinical effectiveness of a 12-week integrated Cognitive Acceptance and Commitment Therapy (CogACT) program in improving aspects of cognitive and psychosocial functioning including attention, memory, information processing, executive functioning, mood, mindfulness, quality of life, and values-directed living. Methods: Twenty people with MS commenced and completed the 12-week integrated CogACT program, with neuropsychological and psychosocial assessments completed at pre, post, and 3-month follow-up time points. The CogACT program involved 12 weekly therapy sessions that integrated a computerized cognitive retraining program with Acceptance and Commitment Therapy (ACT). The cognitive retraining program was designed to improve attention, information processing, and working memory capacity, while the concurrent ACT program component was designed to enhance psychological flexibility through improvements in self-concept, cognitive defusion, acceptance, mindfulness, values, and committed action. Results: Our results obtained from 20 people with MS indicate that prior to the commencement of the integrated CogACT program, participants reported symptoms of depression, anxiety, stress, and cognitive difficulties in addition to low levels of acceptance, mindfulness, quality of life, and values-directed living. At the completion of the integrated 12-week CogACT program, we observed clinically and statistically significant improvements in all neuropsychological and psychosocial variables assessed. In addition, at 3-month follow-up, these clinically and statistically significant neuropsychological and psychosocial improvements were maintained. Conclusions: To date, cognitive and psychosocial rehabilitation services for people with MS have been relatively neglected, and as a consequence, cognitive and psychosocial strategies and therapeutic treatments are underdeveloped. This research presentation will provide an overview of the novel integrated CogACT program in addition to the presentation of results that support the feasibility and effectiveness of our CogACT program for people with MS.

Supported by: Multiple Sclerosis Society of WA Disclosure: Michelle Byrnes: Multiple Sclerosis Society of WA (grant/research support). Susan Shapland, Jeorge Chambers, Leonie Wellington, Cate Lijens, Simon Ralph: Nothing to disclose.

Keywords: Cognitive rehabilitation, Psychological issues and MS
(CG05) COGNITIVE IMPAIRMENT AND MAGNETIC RESONANCE DISEASE ACTIVITY IN MULTIPLE SCLEROSIS
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Background: Multiple sclerosis (MS) can intermittently lead to the presence of active inflammatory lesions, which acutely interrupt white matter tracts between different parts of the brain, resulting in impaired cognition and memory.

Objectives: MS patients will be more cognitively impaired when assessed during a time point at which they have acute contrast-enhancing lesions on magnetic resonance imaging (MRI), as compared to when they have no contrast-enhancing lesions.

Methods: 75 MS patients underwent a comprehensive cognitive battery at month 0, 6, 12, and 24. Brain MRI with contrast was performed monthly. Cognitive domains assessed included attention/information processing speed, visual-spatial/ executive function, and verbal memory/attention span. MRI scans at the time of cognitive testing were characterized as active versus inactive based on presence or absence of gadolinium-enhancing lesions.

Results: 162 MRI scans were associated with patients with abnormal cognitive tests, and 89 MRI scans were associated with those who had normal cognitive function. 83 MRI scans with gadolinium-enhancing lesions, or “active” scans, were associated with abnormal cognitive function, and 79 “inactive” MRI scans were associated with cognitively intact individuals. Thus, MRI scans with active lesions were not more likely to be associated with cognitive dysfunction (P = .8). Even when comparing only those with severe cognitive impairment within a single domain versus normal cognitive function, no association of brain MRI activity with cognitive dysfunction was observed (P = .6).

Conclusions: Patients with MS were not more likely to have cognitive dysfunction when assessed around the time of active MS lesions as detected on MRI. Additional analyses will be performed in the future to better assess and compare cognitive performance with the volume of acute lesion activity and changes over time.

Supported by: Foundation of the CMSC, National Multiple Sclerosis Society

Disclosure: Victoria A. Levasseur, Gautam Adusumilli, Samantha Lancia: Nothing to disclose. Robert T. Naismith: Acorda Therapeutics, Bayer Healthcare, Biogen Idec, EMD Serono, Genentech, Genzyme, Questcor (consulting fees); Acorda, National Multiple Sclerosis Society (grant/research support).

Keywords: Imaging and MS, Psychological issues and MS

(YVONNE C. LEARMOUTH, ELIZABETH A. HUBBARD, EDWARD MCAULEY, ROBERT W. MOTT)

6 Platforms

(1537-2073) 16.S3.1.1

(CG06) PSYCHOMETRIC PROPERTIES OF QUALITY OF LIFE AND HEALTH-RELATED QUALITY OF LIFE ASSESSMENTS IN PEOPLE WITH MULTIPLE SCLEROSIS
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Background: There is substantial interest in testing interventions for improving quality of life (QOL) and health-related quality of life (HRQOL) in people with multiple sclerosis (MS). Yet there is limited research on the psychometric properties of QOL (eg, Satisfaction With Life Scale [SWLS], Leeds MS Quality of Life Scale [LMSQOL]) and HRQOL (eg, 12-item Short Form Health Status Survey [SF-12], Multiple Sclerosis Impact Scale–29 [MSIS-29]) measures in this population. Such research is important for designing and interpreting interventions.

Objectives: We examined the test-retest reliability, measurement error, and interpretability of QOL (ie, SWLS and LMSQOL) and HRQOL (ie, SF-12 and MSIS-29) measures over 6 months in people with MS.

Methods: Individuals with MS (N = 274) completed the SWLS, LMSQOL, SF-12, and MSIS-29 on two occasions, 6 months apart. We estimated test-retest reliability (intraclass correlation coefficient [ICC]), measurement error (standard error of measurement [SEM] and coefficient of variation [CV]) and interpretability (smallest detectable change [SDC]).

Results: ICC values ranged between moderate and good (ICC range, 0.669–0.883); the LMSQOL had the best reliability and the SF-12 the worst reliability. Measurement error varied among measures (eg, SEM % range, 10.9–30.7); the LMSQOL had the best measurement error and the MSIS-29 the worst measurement error. Interpretability varied among measures (SDC % range, 30.1–89.0); interpretability was best for the LMSQOL and worst for the MSIS-29.

Conclusions: We provide novel data for helping researchers and clinicians select and interpret QOL and HRQOL measures and scores for interventions among people with MS. Such information will better inform our understanding of intervention effectiveness.

Supported by: National Institute of Neurological Disorders and Stroke (grant NS054050)


Keywords: Comprehensive care and MS, Management of activities of daily living in MS, Multiple sclerosis, Quality of life, Health-related quality of life, Reliability, Measurement error, Change scores, Validity, Correlation, Outcome measures, Symptoms

(YVONNE C. LEARMOUTH, ELIZABETH A. HUBBARD, EDWARD MCAULEY, ROBERT W. MOTT)

6 Platforms

(1537-2073) 16.S3.1.1

(DX01) DISABILITY PROGRESSION IN MULTIPLE SCLEROSIS PATIENTS IN THE TYSABRI® (NATALIZUMAB) OBSERVATIONAL PROGRAM (TOP)
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Background: The Tysabri® (Natalizumab) Observational Program (TOP) is an ongoing, open-label, 10-year prospective study of relapsing-remitting multiple sclerosis (RRMS) patients in clinical settings in Europe, Australia, Argentina, and Canada.

Objectives: To assess rates of disease progression in patients with RRMS treated with natalizumab for at least 2 years.

Methods: Patients with at least 2 years of
data were evaluated for disability progression as assessed by ≥ 1.0-point and ≥ 2.0-point increases in Expanded Disability Status Scale (EDSS) score sustained for 6 months. Subgroup analyses investigated the percentage of patients with 6-month confirmed disability progression from baseline to EDSS scores of ≥3.0, ≥4.0, and ≥6.0. Results: As of May 1, 2013, a total of 4821 patients were enrolled; 1080 of 3679 potential 2-year completers (29%) had discontinued treatment. Analyses included 2588 patients with available baseline EDSS scores who had completed at least 2 years in TOP. Patients received a median (range) of 35.5 (4–82) natalizumab infusions. Mean (SD) baseline EDSS score in these patients was 3.4 (1.61). Overall, 303 patients (11.7%) had a ≥1.0-point increase in EDSS score and 88 patients (3.4%) had a ≥2.0-point increase sustained for 6 months. In subgroup analyses, 6-month confirmed EDSS progression to a score of ≥3.0 was seen in 54 of 698 patients [7.7%] with baseline scores of 0.0 to 2.0. Rates of confirmed EDSS progression to scores of ≥4.0 were 7.9% (98 of 1244) in patients with baseline scores of 0.0 to 3.0 and 12.3% (67 of 546) in patients with baseline scores of 2.0 to 3.0. Rates of confirmed EDSS progression to scores ≥6.0 were 2.7% (59 of 2167) in patients with baseline scores of 0.0 to 5.0 and 5.7% (53 of 923) in patients with baseline scores of 3.0 to 5.0. Progression rates among patients who discontinued treatment before and after 2 years will be examined, and analyses of 6-month and 12-month confirmed EDSS progression by subgroups determined by baseline EDSS scores and on-treatment relapse status will also be presented. Conclusions: In this open-label observational setting, the low rate of progression to significant disability milestones, even among patients with greater disability at baseline, suggests a beneficial effect of natalizumab treatment on disability progression.

Supported by: Biogen Idec Inc.


Keywords: Disease-modifying treatments in MS

**[DX02]** RELAPSING-REMITTING MULTIPLE SCLEROSIS TREATED WITH INTERFERON BETA-1A: IMMUNOLOGIC AND SHORT-TERM BRAIN VOLUME CHANGES

Michael G. Dwyer, Robert Zivadinov, Yazhong Tao, Xin Zhang, Cheryl Kennedy, Niels Bergslund, Deepa P. Ramasamy, Jacqueline Durfee, David Hajnucki, Bianca Weinstein-Guttman, Brooke Hayward, Fernando Dangond, and Silva Markovic-Plese.

**Background:** Chronic relapsing-remitting multiple sclerosis (RRMS) progression is associated with decreased brain volume (atrophy). Over the short term, brain volume may change via inflammation-related hydrodynamic changes, which subside following anti-inflammatory therapy (pseudoatrophy). Responses to such therapy may be influenced by patients' immunologic status before and during treatment.

**Objectives:** To compare percent brain volume change (PBVC) between patients with RRMS treated over 6 months with thrice-weekly interferon beta-1a subcutaneously (IFNβ-1a SC) and healthy controls (HCs), and to analyze correlations between immunologic markers and short-term volume changes among treated patients. **Methods:** This 24-week, two-arm (23 RRMS patients receiving IFNβ-1a SC, 15 HCs) pilot study (NCT01085318) evaluated magnetic resonance imaging (MRI) at baseline and 3 and 6 months, and immunologic measures at baseline and 6 months. PBVC using SIENA over 0 to 3, 3 to 6, and 0 to 6 months was assessed within groups using the Wilcoxon signed rank test; differences between RRMS patients and HCs were assessed by Wilcoxon rank sum test. Spearman correlation coefficients were calculated between PBVC and changes in immunologic markers in RRMS patients. **Results:** PBVC between baseline and 3 months was −0.95% (SD 1.712%) among RRMS patients (P = .03) and 0.24% (SD 1.068%) in HCs (P = .36); the difference was significant between groups (P = .02). No significant PBVC was seen with either group over months 3 to 6 or 0 to 6. Decreased percentage of CD4+ T cells producing interferon-γ (IL-17F) over months 0 to 6 was significantly correlated with reduced brain volume over months 0 to 6 (r = .51, P = .02) in RRMS patients. **Conclusions:** IFNβ-1a SC is associated with reduced brain volume over the first 3 months of treatment, but not over 3 to 6 months, an effect consistent with treatment-induced pseudoatrophy. The correlation between decreased percentage of CD4+ T cells producing inflammatory IL-17F and volume reduction is supportive of an early anti-inflammatory therapeutic effect of IFNβ-1a SC.

**Supported by:** EMD Serono, Inc., Rockland, MA (a subsidiary of Merck KGaA, Darmstadt, Germany); Pfizer Inc, New York, NY.

**Disclosure:** Michael G. Dwyer: EMD Serono, Inc., Claret Medical (consulting fees). Robert Zivadinov: Teva Pharmaceuticals, Biogen Idec, EMD Serono, Inc., Novartis, Claret, Sanofi-Genzyme (speaker fees, fees for non-CME services from commercial interests or their agents); Biogen Idec, EMD Serono, Inc., Novartis, Sanofi-Genzyme, Teva Pharmaceuticals (consulting fees, grant/research support); Claret (consulting fees). Yazhong Tao, Xin Zhang: EMD Serono, Inc. (consulting fees). Cheryl Kennedy, Niels Bergslund, Deepa P. Ramasamy, Jacqueline Durfee: Nothing to disclose. David Hajnucki: Biogen Idec, EMD Serono, Inc., Pfizer Inc, Teva Pharmaceuticals (consulting fees, speaker fees, fees for non-CME services from commercial interests or their agents); Bianca Weinstein-Guttman: Biogen Idec, Teva Pharmaceuticals, EMD Serono, Inc., Pfizer, Novartis, Acorda (consulting fees, speaker fees, fees for non-CME services from commercial interests or their agents); Biogen Idec, Teva Pharmaceuticals, EMD Serono, Inc., Pfizer, Novartis, Acorda (grant/research support); Brooke Hayward, Fernando Dangond, and Silva Markovic-Plese: Biogen Idec. (grant/research support); EMD Serono, Inc., Genzyme Inc (consulting fees, grant/research support).

**Keywords:** Disease-modifying treatments in MS, Imaging and MS, Immunology and MS.
(DX03) NO EVIDENT DISEASE ACTIVITY (NEDA): ASSOCIATIONS WITH BRAIN ATROPHY AND FUNCTIONAL OUTCOMES IN PATIENTS FROM THE AFFIRM STUDY
Richard R. Rudick,1 Elizabeth Fisher,2 Andrew Goodman,3 Fred D. Lublin,1 J. Theodore Phillips,4 Amy Pace,5 Shibeshih Belachewa6
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Background: Data from the AFFIRM study showed that patients with relapsing-remitting multiple sclerosis (RRMS) with no evident clinical and radiologic disease activity over 2 years had significantly better quality of life compared with patients who had any clinical or magnetic resonance imaging (MRI) signs of disease activity. Objectives: To investigate the relationship between “no evident disease activity” (NEDA) and measures of brain atrophy and functional outcomes in patients with RRMS over 2 years in the AFFIRM study. Methods: Natalizumab and placebo groups were combined. NEDA was defined as no relapse, no 12-week sustained Expanded Disability Status Scale (EDSS) progression, no gadolinium-enhancing lesions, and no new or enlarged T2 lesions. Percent changes in brain parenchymal fraction (BPF), changes in Paced Auditory Serial Addition Test–3 (PASAT), Timed 25-Foot Walk (T25FW), and Nine-Hole Peg Test (NHPT) as well as rates of confirmed EDSS improvement (12-week sustained decrease of ≥1.0 point) were compared in patients with and without NEDA.

Results: Overall, 27% of patients had NEDA over 2 years: 220 of 600 natalizumab-treated patients (37%) and 22 of 304 placebo-treated patients (7%). In the second year of the study, significantly smaller median percent reductions in BPF were seen in patients with NEDA (−0.15% vs. −0.28%; P = .0055) compared with patients who had any clinical or radiologic disease activity. From baseline to 2 years, patients with NEDA had significantly better outcomes in PASAT (median change, 2.00 with NEDA vs. 1.00 without NEDA; P = .0005), T25FW (median change, 0.00 second with NEDA vs. 0.20 second without NEDA; P < .0001), and NHPT (median change, −0.73 second with NEDA vs. −0.24 second without NEDA; P < .0001). The cumulative probability of EDSS improvement was 36.9% in patients with NEDA and 22.6% in patients with any disease activity (hazard ratio, 1.918 [95% confidence interval, 1.374–2.678]; P = .0001).

Conclusions: Patients with NEDA showed smaller reductions in BPF, more improvement in disability, and better outcomes in cognitive function, walking speed, and upper-extremity function compared with patients with any evident disease activity.

Supported by: Biogen Idec

Disclosure: Richard R. Rudick: Biogen Idec, Novartis, Genzyme (consulting fees); Novartis, Genzyme (grant/research support); Elizabeth Fisher: Biogen Idec, Genzyme/Sanofi, Novartis (consulting fees); National Institutes of Health, Biogen Idec, Genzyme/Sanofi (grant/research support); Andrew Goodman: Acorda, Biogen Idec, EMD Serono, Genzyme/Sanofi, Novartis, Ono, Roche, Sun Pharma, Takeda, Teva (grant/research support); Acorda, Biogen Idec, Genzyme/Sanofi, GW Pharma, Mylan, Novartis, Teva, Vaccinex (consulting fees). Fred D. Lublin: Acorda, Biogen Idec, Novartis, Teva Neuroscience, Genzyme, Sanofi, Celgene, National Institutes of Health, National Multiple Sclerosis Society (grant/research support); Bayer HealthCare Pharmaceuticals, Biogen Idec, EMD Serono, Novartis, Teva Neuroscience, Actelion, Sanofi-Aventis, Acorda, Questcor, Roche, Genentech, Celgene, Johnson & Johnson, Revalesio, Coronado Bioscience, Genzyme, MedImmune, Bristol-Myers Squibb, Xenoport, Receptor, Forward Pharma (consulting fees); Cognition Pharmaceuticals (current financial interest/stock ownership); Multiple Sclerosis and Related Diseases (co-chief editor); J. Theodore Phillips: Acorda, Biogen Idec, Genzyme, Novartis, Teva, Xenoport (consulting fees); Roche (grant/research support). Amy Pace: Biogen Idec (employee, ownership interest).

Keywords: Disease-modifying treatments in MS

(DX04) IMMUNOGENICITY WITH PEGIFERON BETA-1A: 2-YEAR DATA FROM THE ADVANCE STUDY IN RELAPSING-REMITTING MULTIPLE SCLEROSIS
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Background: Development of persistent neutralizing antibodies (NAbs) against interferon beta (IFNβ) has been associated with reduced levels of efficacy on clinical and magnetic resonance imaging variables; thus there is an unmet need for therapies with low levels of treatment-emergent NAbs. Drug modification by attachment of poly(ethylene glycol) (PEG) molecules (pegylation) has been used to increase drug half-life and efficacy, and may also reduce immunogenicity. Subcutaneous (SC) peginterferon beta-1a (PEG-IFNβ-1a), a pegylated IFNβ-1a, is under investigation in the randomized, phase 3 ADVANCE study. During the placebo-controlled first year of this study, the development of antibodies that bind to IFNβ-1a (BAbs) as well as NAbs and anti-PEG antibodies was low and similar for PEG-IFN 125 μg administered every 2 (Q2W) or 4 (Q4W) weeks. Objectives: We assessed the immunogenicity of PEG-IFN in patients with relapsing-remitting multiple sclerosis (RRMS) during year 2 and over 2 years of ADVANCE. Methods: At the end of the first year, patients on placebo were rerandomized to PEG-IFN Q2W or Q4W (during year 2 all patients received dose-frequency-blinded PEG-IFN). Serum samples were collected pre-dose on weeks 60, 72, and 96, and a tiered testing scheme was used to measure anti-IFNβ-1a BAbs (using a validated enzyme-linked immunosorbent assay [ELISA]), the titer of anti-IFNβ-1a NAbs (using a validated cell-based assay), and the titer of antibodies to PEG (using a validated ELISA). We present results for patients with 2 years of data at cutoff.

Results: During year 2, persistent treatment-emergent antibodies were low in those switched to PEG-IFN from placebo and in patients on PEG-IFN Q2W and Q4W over 2 years: BAbs incidence, 1% across groups; NAbs incidence, <1% across groups; anti-PEG antibodies incidence, 3%, <1%, and 2%, respectively; NAbs and anti-PEG antibody titers were low. Incidences over the 2-year observation period for Q2W and Q4W were reported as: BAb, 4% and 2%; NAb, <1% and <1%; anti-PEG, 2% and 6%, respectively. No discernible impact on clinical efficacy or safety was observed in this study.

Conclusions: The overall incidence and titer levels of
treatment-emergent antibodies were low and similar for PEG-IFN Q2W and Q4W over 2 years of treatment, with no discernible clinical impact. Low rates of immunogenicity support the potential benefits of SC PEG-IFN as a treatment for RRMS.

Supported by: Biogen Idec Inc.


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

(DX05) IMMUNOLOGIC MARKERS AND CONVENTIONAL AND ADVANCED MRI AFTER INTERFERON BETA-1A FOR RELAPSING-REMITTING MULTIPLE SCLEROSIS

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Background: Voxel-wise magnetization transfer ratio (VW-MTR) imaging is sensitive to myelin content changes in normal-appearing brain tissue (NABT) and in lesions of patients with relapsing-remitting multiple sclerosis (RRMS), where decreasing and increasing volumes of VW-MTR are suggestive of demyelination and remyelination, respectively.

Objectives: To investigate correlations between immunologic biomarkers and magnetic resonance imaging (MRI) findings following treatment with interferon beta-1a (IFN-β1a) given subcutaneously (SC) in patients with RRMS who had ≥1 relapse in the 12 months prior to participation in a 6-month pilot study (NCT01085318).

Methods: Changes in percentage of CD4+ and CD8+ T cells expressing pro- and anti-inflammatory cytokines were analyzed for correlations with volume changes in NABT and MS lesions (by conventional MRI and VW-MTR imaging) at baseline and 6 months after treatment with three-weekly IFN-β1a SC 44 μg by Spearman rank correlation. Results: 15 of 23 patients had ≥1 relapse in the 12 months prior to study participation. Increases in percentage of interleukin (IL)-4–expressing CD4+ T cells correlated with decreasing T2 lesion volume (r = −0.58, P = .030). Increases in percentage of IL-10–expressing CD8+ T cells correlated with decreasing T1 lesion volume (r = −0.55, P = .043). Increases in the percentage of IL-10–expressing CD4+ and CD8+ T cells correlated with higher volume of increasing VW-MTR in NABT (r = 0.62 and r = 0.56; P = .018 and P = .037, respectively). Decreases in percentage of IL-17F–expressing CD4+ T cells correlated with lower volume of decreasing VW-MTR in NABT (r = 0.69, P = .006). Conclusions: Elevated percentage of anti-inflammatory IL-10–expressing T cells correlated with increasing VW-MTR volume in NABT, suggestive of remyelination, and increasing IL-4 and IL-10 correlated with decreasing lesion volume. Decreasing percentage of pro-inflammatory IL-17F cytokine-expressing CD4+ cells correlated with a smaller volume of decreasing VW-MTR signal in NABT, suggestive of decreased demyelination in patients with RRMS treated with IFN-β1a SC.

Supported by: EMD Serono, Inc., Rockland, MA (a subsidiary of Merck KGaA, Darmstadt, Germany), Pfizer Inc, New York, NY

Disclosure: Silva Markovic-Plese: Biogen Idec (grant/research support); EMD Serono, Inc., Genzyme Inc. (consulting fees, grant/research support). Yachong Tao, Xin Zhang, Michael G. Dwyer: EMD Serono, Inc. (consulting fees). Cheryl Kennedy, Niels Bergsland, Deepa P. Ramasamy, Jacqueline Durfee: Nothing to disclose. David Hajnadi: Biogen Idec, EMD Serono, Inc., Pfizer Inc, Teva Pharmaceuticals (consulting fees, fees for non-CME services from commercial interests or their agents). Bianca Weinstock-Guttman: Acorda, Biogen Idec, EMD Serono, Inc., Novartis, Pfizer, Teva Pharmaceuticals (consulting fees, fees for non-CME services from commercial interests or their agents, grant/research support); Cybergenetics (grant/research support). Brooke Hayward, Fernando Dangond: EMD Serono, Inc., a subsidiary of Merck KGaA, Darmstadt, Germany (employee). Robert Zivadinov: Biogen Idec, EMD Serono, Inc., Novartis, Sanofi-Genzyme, Teva Pharmaceuticals (consulting fees, fees for non-CME services from commercial interests or their agents, grant/research support); Claret (consulting fees, fees for non-CME services from commercial interests or their agents).

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

(DX06) DISABILITY PROGRESSION AFTER SWITCHING FROM NATALIZUMAB TO FINGOLIMOD OR INJECTABLE THERAPIES: A NARCOMS ANALYSIS

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Background: Natalizumab (NAT) is a highly effective treatment for multiple sclerosis (MS). The clinical outcomes of NAT-treated patients who switch to other treatments are not well understood. Objectives: Compare changes in patient-reported disability progression measured by the Patient-Determined Disease Steps (PDDS) between NAT-treated patients who remained on NAT and those who switched treatment after a minimum of 2 years of NAT use. Methods: A total of 547 NARCOMS participants had ≥2 years of continuous NAT treatment and ≥1 follow-up survey that included a PDDS assessment. Changes in PDDS scores from the first survey indicating NAT treatment until final survey were compared between participants whose only disease-modifying treatment during follow-up was NAT (N = 406) and those who switched treatment to fingolimod (FIN) (N = 50; follow-up post-switch, mean [SD] = 15.0 [10.4] months) or to injectable therapies (INJ [interferon beta or glatiramer acetate]) (N = 71; follow-up post-switch = 20.4 [13.9] months). Participants were excluded who switched to other treatments (N = 10) or who lacked PDDS assessment in the first survey during NAT treatment (N = 10). Median group characteristics were similar in all groups (all P > .05); median months of total follow-up were significantly different.
[NAT = 48, FIN = 54, INJ = 60; P < .0001]. Age, gender, and starting PDDS were associated with change in PDDS [all P < .03]; total follow-up time was not (P = .69). Adjusted mean PDDS was not different between groups after 2 years of NAT therapy (P = .11), but at the end of follow-up the mean PDDS increase was 0.31 points for NAT, 0.58 for FIN, and 0.71 for INJ; the difference between NAT and INJ groups was significant (P = .007). In addition, there was a difference between groups in the proportion of participants with ≥1-point increase in PDDS [NAT = 30.8%, FIN = 46.0%, INJ = 42.3%; P = .03] with an odds ratio of 1.9 for FIN versus NAT (P = .03) and 1.6 for INJ versus NAT (P = .06). Conclusions: On average, those who switched to FIN reported larger disability increases than those remaining on NAT. Switching from NAT to FIN or INJ was associated with an increased likelihood of reported disability progression. While disability was similar during 2 years of natalizumab and differed over time including treatment switch, causality cannot be concluded.

Supported by: Biogen Idec

Disclosure: Stacy S. Cefalo; American Academy for Orthopedic Surgery, Department of Defense, GlaxoSmithKline, OrthoBiotech Biontech, Teva Neuroscience (consulting fees); Robert J. Fox; Alleynne, Avanir, Biogen Idec, Novartis, Questcor, Teva, Xenopart (consulting fees); Novartis (grant/research support). Taula Try; Nothing to disclose. Amber R. Salter; GlaxoSmithKline (consulting fees). Denise Campagnolo; Mary Jean Fanelli, Terrie Livingstone; Biogen Idec (employee, stock ownership).

Keywords: Disease-modifying treatments in MS, Natalizumab

REHABILITATION

(RH01) DEVELOPMENT AND VALIDATION OF A MYOMETRIC TEST OF STRENGTH IN LOWER EXTREMITIES FOR MULTIPLE SCLEROSIS PATIENTS USING HANDHELD DYNAMOMETER

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Background: Reliable, quantitative measures of strength are needed for clinical purposes and research in multiple sclerosis (MS). Objectives: We developed a myometric test of strength in lower extremities using a commercially available handheld dynamometer (HHD) and measured reliability characteristics across a range of disability levels in a cross-sectional MS study. Methods: Twenty-one participants with MS were recruited; 7 participants in each of 3 disability levels as indicated by Expanded Disability Status Scale (EDSS) score: EDSS 0 to 3.5 (group 1), EDSS 4.0 to 5.5 (group 2), and EDSS 6.0 to 7.5 (group 3). Participants were strength tested by two physical therapists on two occasions (total of four examinations). The assessment used a standardized protocol for muscle testing with HHD (three trials recording maximum voluntary force [kg]) and included ten muscle groups: bilateral hip abductors (HA), hip flexors (HF), knee extensors (KE), knee flexors (KF), and ankle dorsiflexors (DF). The Lower Extremities Strength (LES) sum score was calculated by summing the peak HHD recording from ten muscle groups. An intraclass correlation coefficient (ICC) of ≥0.85 was used as a reliability benchmark. Manual muscle testing (MMT) was also done for comparison. Results: Strength testing with HHD took 10 minutes on average and was well tolerated. Group 1 had the highest strength recordings for all muscle groups (HHD and MMT) and the highest LES sum score. Within each EDSS category, HHD strength records were highest for KE and lowest for KF. For interrater reliability, only HF and KE had consistent ICCs >0.85 across both visits and all EDSS subgroups. For interrater reliability, most muscle groups and LES sum scores had ICCs >0.85 across both examiners and all EDSS groups. There was no difference in reliability statistics across EDSS subgroups, except for LES sum score, for which reliability was lower at the highest disability level. Conclusions: This was a study of a myometric test of strength in lower extremities for MS patients using an HHD. The test yielded a combined quantitative measure of lower-limb strength (LES sum score) as a global measure. Single-rater reliability was high across a range of disability levels, but interrater reliability was lower. Work is in progress to revise the test and perform a multicenter validation study. Similar research is recommended in upper-extremity strength testing.

Supported by: Biogen Idec

Disclosure: Theodore R. Brown; Acorda, Biogen Idec, Genzyme, Pfizer, Teva Neuroscience (consulting fees); Biogen Idec, Acorda Therapeutics, Nexo Research, Galen Pharmaceuticals, Teva Neuroscience (grant/research support). Virginia I. Simnad; Actelion, Biogen Idec, Novartis, Teva (grant/research support).

Keywords: Comprehensive care and MS

(RH02) ASSESSING MOBILITY IN MULTIPLE SCLEROSIS AND OTHER NEUROLOGIC DISEASES WITH THE iPHONE APP SaGAS 10

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Background: SaGAS 10 is an iPhone app developed as an alternative to the Multiple Sclerosis Functional Composite (MSFC) and as a complement to the Expanded Disability Status Scale (EDSS) for moderately disabled MS patients between EDSS 3.0 and 7.0. Objectives: Assuming that this tool could also be used for other neurologic diseases in which walking and hand function is impaired, we set out to examine the validity and responsiveness of SaGAS 10 in neurologic patients attending a rehabilitation facility. Furthermore, we evaluated whether the Timed 25-Foot Walk (T25FW) has a high correlation with the 2-minute walking distance (2MWD) in patients with slow walking speed. Methods: 646 consecutive patients with different neurologic diseases (MS 296, stroke 152, Parkinson 21, neuromuscular disorders 42, trauma 42, others 93) were assessed at the beginning and at the end of their rehabilitation stay using the Functional Independence Measure (FIM), the Rivermead Mobility Index (RMI), the 2MWD at maximum speed, and the three measures composing SaGAS 10 (the T25FW at fast speed with a flying start and the Nine-Hole Peg Test [NHPT] for each hand separately). Construct validity was assessed with correlations between FIM, RMI, and SaGAS 10, where correlations above 0.7 were hypothesized. Responsiveness was assessed by a receiver operating characteristic (ROC) curve analysis comparing changes in SaGAS 10 with minimal clinically important changes in RMI. An area under the curve (AUC) value of at least 0.7 was considered appropriate. Analyses were performed for each patient group separately. Results:
The correlation of the SaGAS 10 with the RMI was above 0.7 in all of the neurologic diagnostic groups; the highest correlation coefficient was found in patients with stroke: 0.76 (95% confidence interval [CI], 0.65-0.84). The correlation of SaGAS 10 with the FIM was over 0.7 for stroke and MS. The responsiveness was acceptable with AUCs of 0.72 (95% CI, 0.63-0.81) for stroke and values over 0.7 for all groups, with the exception of MS (AUC, 0.58; 95% CI, 0.47-0.69). The effect sizes (ESs) were moderate to high, especially for stroke, with Cohen’s d values of 0.48 for the whole group and higher values for those walking slower (ES 0.61) for speed under 1.04 m/s and ES 0.72 for speed under 0.96 m/s. The correlation between the T2SFW and the 2MWD was 0.63 (95% CI, 0.56-0.69) for those walking slower than 0.96 m/s and 0.64 (95% CI, 0.540-0.73) for those walking faster than 0.96 m/s. Conclusions: These results indicate that SaGAS 10 is valid and sensitive to changes over time and that it could be a useful measure not only for patients with MS, but also for patients with other neurologic diseases. Our results indicate that particularly for slow walkers the T2SFW might be a good alternative to the 2MWD.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Management of activities of daily living in MS, Measurement

(RH03) BALANCE-BASED TORSO-WEIGHTING RESULTS IN FALL REDUCTION DURING SENSORY ORGANIZATION TEST FOR PEOPLE WITH MULTIPLE SCLEROSIS

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Background: People with multiple sclerosis (MS) fall frequently. Balance-based torso-weighting (BBTW) can improve gait speed and increase time spent in single-limb support while walking. However, the association between BBTW and falls has not yet been examined in people with MS. Objectives: Investigate the effects of BBTW on balance and fall frequency recorded by the sensory organization test (SOT) in people with MS. Methods: 51 people with MS with self-identified gait and balance difficulties (Disease Steps 1–4) completed the SOT on the SMART EquiTest® BalanceMaster twice in a single session, once without weights and a second time following placement of weights using the BBTW method. Data were collected as part of an extensive testing protocol, generally lasting 3 to 5 hours, in which participants completed additional impairment and mobility testing with and without weights. A mandatory rest break followed BBTW assessment and weighting with additional breaks given as needed. Participant fatigue in two cases resulted in abbreviated testing. The SOT composite score (CS) recorded participants’ quiet standing for three trials in each of six conditions: eyes open (EO), eyes closed (EC), surround moving (EO), platform moving (EO), platform moving (EC), and platform and surround moving together (EO). The number of falls occurring in all trials of both no weight (NW) and weighted (WT) conditions were tallied. A fall was defined as touching the surround, taking a step, or being caught by an overhead harness. Paired t tests compared participants’ CS and fall occurrence between conditions with alpha set at .05. Results: A statistically significant change (P = .0001) occurred in mean (SD) CS from NW to WT trials, 50.9 (15.07) to 60.1 (14.88), respectively. A change of 8 points in the CS is considered a significant difference. Twenty-eight (55%) participants increased their CS by at least 8 points (range, 8–38), 16 (31.4%) increased by 1 to 7 points, 1 had no change (2%), and 6 (11.8%) decreased their score (range, –2 to –6). Fall occurrence differed between weighting conditions (P = .02). There were 212 (60.7%) falls in the NW and 137 (39.3%) in the WT conditions. No correlation (r = 0.014) was found between number of SOT falls and participant age. Conclusions: A significant decline in fall number and an increase in CS occurred with BBTW during a single testing session despite potential for fatigue. BBTW is a promising intervention that may lead to decreased falls when worn by people with MS.

Supported by: Eunice Kennedy Shriver National Institute of Child Health and Human Development
Keywords: Management of activities of daily living in MS

(RH04) EFFICACY OF A BEHAVIORAL INTERVENTION FOR REDUCING SEDENTARY BEHAVIOR IN PEOPLE WITH MULTIPLE SCLEROSIS

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Background: Sitting time (ST), a measure of sedentary behavior, has been identified as a highly prevalent risk factor for morbidity in the general population and individuals with multiple sclerosis (MS), independent of physical activity (PA). To date, there is limited information on the efficacy of behavior interventions for reducing ST in people with MS. Behavioral interventions involve teaching people the skills, techniques, and strategies for behavior change, and have been effective for increasing PA in MS. Objectives: This pilot, randomized controlled trial (RCT) examined the efficacy of a behavioral intervention for reducing ST in people with MS. Methods: The sample consisted of 56 people with MS who were randomly assigned into behavioral intervention and wait-list control conditions. The behavioral intervention, based on social-cognitive theory, was delivered via the Internet and consisted of a dedicated website and one-on-one Skype video chats that taught participants the skills, techniques, and strategies for reducing sedentary behavior. The control condition involved a wait list, and the behavioral intervention was delivered among participants in this condition after study completion. ST was measured by questions on the abbreviated International Physical Activity Questionnaire (IPAQ) before and after the 6-month RCT. The data were analyzed using mixed-model analysis of variance (ANOVA) in SPSS 21.0. Results: The mixed-model ANOVA indicated a statistically significant condition by time interaction on ST (F1,54 = 6.24, P < .005, ηp2 = .10). The behavioral intervention group had a statistically significant reduction in ST from pre-post intervention (P = .027), and the magnitude of the reduction

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was moderate (Cohen’s $d = -0.46$). The control group had a non–statistically significant increase in ST ($P = .168$) and the effect size was small (Cohen’s $d = 0.26$). Conclusions: We provide the first data on the efficacy of a behavioral intervention for reducing ST in people with MS. This highlights the importance of designing and testing the effect of behavioral interventions that reduce ST on secondary outcomes such as function, symptoms, quality of life, and health status in people with MS.


Robert W. Motl: Biogen Idec, Acorda Therapeutics, National Multiple Sclerosis Society, National Institutes of Health, Consortium of Multiple Sclerosis Centers (multiple sources).

Keywords: Complementary/alternative therapies in MS, Management of activities of daily living in MS, Physical activity in MS

(RH05) DOES THE EFFECT OF A PHYSICAL ACTIVITY BEHAVIOR INTERVENTION VARY BY CLINICAL CHARACTERISTICS OF PEOPLE WITH MULTIPLE SCLEROSIS?

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Background: Behavioral interventions based on social-cognitive theory (SCT) and delivered through the Internet have significantly increased physical activity in people with multiple sclerosis (MS). Nevertheless, there has been inter-individual variability in the pattern and magnitude of change. Objectives: This study examined the efficacy of a behavioral intervention based on SCT and delivered through the Internet for increasing physical activity, and the possibility that change in physical activity varied by the clinical characteristics of people with MS. Methods: The sample included 82 individuals with MS who were randomly assigned to one of two conditions, behavioral intervention ($n = 41$) or wait-list control ($n = 41$). We collected information on MS type, disability status, and current disease-modifying and symptomatic medications before the study. All participants further completed the Godin Leisure Time Exercise Questionnaire (GLTEQ) and abbreviated International Physical Activity Questionnaire (IPAQ), and wore an ActiGraph accelerometer over 1 week for measuring minutes of moderate-to-vigorous physical activity (MVPA) both before and after the 6-month intervention period. Results: Analysis of covariance (ANCOVA) indicated that participants in the behavioral intervention participated in significantly higher levels of physical activity than control participants following the 6-month period ($P < .001$). ANCOVA further indicated that MS type (ie, relapsing vs. progressive MS) ($P < .01$) and disability status (ie, mild vs. moderate disability) ($P < .01$) moderated the effect of the behavioral intervention on physical activity. Conclusions: The behavioral intervention was associated with improvements in physical activity, particularly for those with mild disability and relapsing-remitting MS.

Supported by: National Multiple Sclerosis Society (PP 1695)

Disclosure: Robert W. Motl: Acorda Therapeutics, Biogen Idec, National Multiple Sclerosis Society (grant/research support); EMD Serono (fees for non-CME services from commercial interests or their agents). Deirdre Dlugonski, Larra A. Pilotti, Rachel E. Klaren: Nothing to disclose.

Keywords: Complementary/alternative therapies in MS, Management of activities of daily living in MS, Psychological issues and MS

(RH06) IMPAIRMENT IN MOTOR IMAGERY PROGRESSIVELY INCREASES WITH MULTIPLE SCLEROSIS DISEASE EVOLUTION

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Background: Motor imagery (MI) is defined as mental movement execution without any actual movement. Mental movement time in healthy adults is similar to actual movement time (isochrony), while temporal discrepancies between actual and mental movements (anisochrony) could be an expression of neurologic deficits on action representation. In a previous study we showed that in patients with multiple sclerosis (MS), mental states of action are not as accurate as in healthy subjects (HS), with a dilated anisochrony between actual and mental movements. Objectives: Here we investigated whether accuracy of mental movements could be related to the progression of the disease by evaluating MI in HS, people with clinically isolated syndrome (CIS), and people with MS at an early stage of the disease (RR). Methods: 12 HS, 17 CIS, and 15 RR right-handed (Edinburgh Handedness Inventory) subjects were recruited. The following clinical scales were administered: Modified Fatigue Impact Scale (MFIS), Symbol Digit Modalities Test (SDMT), Nine-Hole Peg Test (NHTP), Kinesthetic and Visual Imagery Questionnaire (KVIQ).

Two conditions were utilized: 1) actual task (subjects squeezed a foam ball with a diameter of 7 cm with the dominant/nondominant hand), 2) mental task (subjects imagined squeezing the ball with the dominant/nondominant hand while holding it). Each trial lasted 4 minutes and consisted of four consecutive periods of actual (or mental) task (30 seconds) and rest (30 seconds). Subjects were instructed to actually and mentally squeeze the ball at a self-selected speed, and the numbers of executed and imagined ball squeezes were recorded as reported by the subject. To examine eventual anisochrony between mental and actual movements, we computed the actual/mental ratio (R) of the number of ball squeezes. Results: As expected, HS showed very slight anisochrony ($R = 1.19$ for the right hand; $R = 1.21$ for the left). Increasing anisochrony was computed as a function of disease progression: CIS subjects showed $R = 1.31$ for the right hand and $R = 1.37$ for the left; RR subjects showed $R = 1.48$ for the right hand and $R = 1.60$ for the left. Conclusions: Disease evolution seems at the origin of a progressive temporal dissociation between actual and imagined movements, more relevant for the nondominant versus dominant hand. This study helped to better clarify imagined actions in people with MS in order to possibly identify new rehabilitative strategies to achieve a better quality of life.

Disclosure: Nothing to disclose.

Keywords: CNS repair, Comprehensive care and MS, Motor imagery
SYMPTOM MANAGEMENT

(SX01) THE EFFECTS OF DALFAMPRIDINE EXTENDED RELEASE ON AREAS OF MOTOR FUNCTION BEYOND WALKING IN PEOPLE WITH MULTIPLE SCLEROSIS

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Background: Dalfampridine extended release (D-ER), fampridine outside the United States, is used to improve walking speed in patients with multiple sclerosis (MS). D-ER is a potassium channel blocker that putatively improves neuronal conduction along demyelinated axons. The clinical response to dalfampridine has been variable, classifying individuals as responders or nonresponders based on walking speed. D-ER may have effects on motor areas other than walking.

Objectives: To assess the effect of D-ER treatment in people with MS in treating other clinical aspects beyond walking in a clinical setting. Methods: People with MS who were newly prescribed D-ER (N = 39; 8 males, 31 females; mean age, 54.13 ± 9.9 years; mean disease duration, 12.92 ± 8.8 years; mean Expanded Disability Status Scale (EDSS) score, 5.1 ± 1.6) were included in this observational study. The following outcomes were assessed prior to first dose and 3.5, 7, 10.5, and 14 weeks after drug administration: Timed 25-Foot Walk (T25FW), Six Spot Step Test (SSST), 6-Minute Walk (6MW), Nine-Hole Peg Test (NHPT), Box and Block Test (BBT), and 12-item Multiple Sclerosis Walking Scale (MSWS-12). We analyzed outcomes for all subjects combined (All), and by timed walk responder (TWR) and nonresponder (TWNR) status, as defined by Goodman et al. (2009). Changes from baseline to 14-week follow-up were assessed using paired t tests or Wilcoxon signed rank test. Data were also analyzed using all time points with linear mixed models or Friedman test; the P value was set at <.05.

Results: The All subjects group and TWRs (n = 21; 54%) significantly improved (P < .05) on all outcomes above in pre-post analyses and in linear mixed models over time, with the exception of the TWRs mixed-model analysis for NHPT (nondominant side). TWNRs (n = 8; 21%) significantly improved (P < .05) on the MSWS-12, SSST (nondominant side), and BBT (nondominant side) in the pre-post analyses and improved on the MSWS-12, SSST (both sides), and BBT (both sides) in the mixed-model analyses over time. Conclusions: People with MS newly prescribed D-ER had significant improvements on functional tasks of the upper and lower extremities and self-reported outcomes, even among traditionally timed walk nonresponders.

Supported by: Acorda Therapeutics Inc

Disclosure: Albert C. Lo: National Multiple Sclerosis Society, Veterans Affairs, Acorda Therapeutics Inc, Paralyzed Veterans of America (grant research support, travel reimbursement); Jennifer A. Ruiz, Kayla M. Olson: National Multiple Sclerosis Society, Acorda Therapeutics Inc (grant research support). Claire M. Koenig: Acorda Therapeutics Inc (grant research support). Beth M. Anderson: Nothing to disclose. Elizabeth W. Triche: Mount Sinai Rehabilitation Hospital (consulting fees); National Multiple Sclerosis Society, Acorda Therapeutics Inc (travel reimbursement); National Multiple Sclerosis Society, Acorda Therapeutics Inc, National Institutes of Health (grant research support).

Key words: Comprehensive care and MS, Management of activities of daily living in MS, Symptom management

(SX02) A PILOT STUDY OF THE EFFECTS OF AN 8-WEEK INTEGRATIVE YOGA PROGRAM ON FUNCTION AND QUALITY OF LIFE IN PEOPLE WITH MODERATE MULTIPLE SCLEROSIS–RELATED DISABILITY

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Background: Although there is little formal research evidence for its benefit in people with multiple sclerosis (MS), many participate in yoga programs. A standardized, integrative yoga program was created through a modified Delphi process. This resulted in a comprehensive program specifically designed to be feasible for, and to address the needs of, a group of individuals with moderate disability related to MS. The program was designed with scalable difficulty to meet the heterogeneous capabilities of a sample of people with moderate MS-related disability while maximizing program standardization. Objectives: The first objective was to examine the feasibility of the integrative yoga program for a group of individuals with MS. The second objective was to examine the effects of the program on function, activity, and participation. Methods: Fourteen women (ages 34–64 years, mean 53.5 years) with a confirmed diagnosis of MS and a score of 3 to 6 (mean 4.67) on the Self-Report of MS Disease Severity completed the study. Data collection occurred at three time points: the week prior to beginning the program (week 0), the week following the program (week 9), and a follow-up session (week 16). The 8-week-long program consisted of two 1.5-hour classes each week that included yoga philosophy, breathing, postures, relaxation, and meditation. The battery of tests included measures of physical and cognitive function and quality of life. A series of repeated-measures analyses of variance (ANOVAs) were conducted to examine within-subjects differences between weeks 0, 9, and 16, with planned pairwise comparisons between time points. Results: The integrative yoga program was feasible for use in this sample. Attendance was high, and classes were well tolerated. Significant improvements (P < .05) were found between weeks 0 and 9 in the following tests: Timed 25-Foot Walk (T25FW), Nine-Hole Peg Test–Dominant Hand (NHPT-D), 12-item Multiple Sclerosis Walking Scale (MSWS-12), Modified Fatigue Impact Scale, Multi-Directional Reach Test–Backward (MDRT-B), 12-item Multiple Sclerosis Walking Scale, Modified Fatigue Impact Scale, Mental Health Inventory (MHI), and several subscales of the 36-item Short Form Health Status Survey (SF-36): Mental Component Summary, Social Functioning, Vitality, Role Emotional, and Mental Health. Significant improvements from baseline (P < .05) persisted at week 16 in the T25FW, NHPT-D, SSST, MDRT-B, and MHI. Conclusions: This pilot trial found that the integrative yoga program specifically developed for people with moderate MS-related disability was feasible and well tolerated by the participants. The results of this pilot study
must be interpreted with caution, as there was no comparison group; however, improvements were found in a number of activity- and participation-level outcomes. These improvements were, in general, more persistent at the week 16 follow-up for outcomes that measured performance than for those that were self-reported.

Supported by: None

Disclosure: Nothing to disclose

Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS, Management of activities of daily living in MS

(SX03) CHARACTERISTICS ASSOCIATED WITH SUSTAINED DISEASE PROGRESSION IN PREVIOUSLY RELAPSING MULTIPLE SCLEROSIS PATIENTS

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Background: The emerging definition of secondary progressive multiple sclerosis (SPMS) is based on the concept that MS is a continuously destructive disease in which progressive disability ensues once a threshold is reached. Long-term disease management requires a better understanding of the timing of the gradual transition from the relapsing-remitting to the predominantly progressive phase. Objectives: Describe characteristics of people with relapsing MS who reach a Patient-Determined Disease Steps (PDDS) score of 4 (early cane use) or higher over a 5-year follow-up period.

Methods: We included North American Research Committee on Multiple Sclerosis (NARCOMS) Registry participants who had completed at least one semiannual update survey in each of the 5 years from 2006 to 2010 and were US residents with a diagnosis of MS and a history of relapse[s]. Participants were classified into low disability (LD; PDDS < 3) or high disability (HD; PDDS > 4) groups based on their last PDDS score in 2010. Sociodemographics, MS history, and disability levels are reported using proportions and median values. Statistical comparisons were made with chi-square or Wilcoxon tests, as applicable; P values < .05 were considered meaningful.

Results: Of 5452 eligible participants, 55.6% reported HD in 2010 and 44.4% reported LD. Those with HD were more likely to be male (27.3% HD vs. 16.9% LD, P < .0001), older at diagnosis (39 years HD vs. 38 years LD, P = .004) and at enrollment in NARCOMS (55 years HD vs. 49 years LD, P < .0001), with a longer duration of MS at the start of follow-up (15 years HD vs. 9 years LD, P < .0001). A lower proportion with HD reported relapse in the 6 months before enrollment (14.1% HD vs. 27.9% LD, P < .0001). Retrospectively, those with HD in 2010 had a higher median PDDS score at enrollment in NARCOMS (4 HD vs. 1 LD, P < .0001), at start of follow-up (5 HD vs. 1 LD, P < .0001), and by definition at end of follow-up (6 HD vs. 1 HD, P < .0001), and a greater PDDS worsening between 2006 and 2010 (mean worsening 0.6 points for HD vs. no change for LD, P < .0001). Those with HD also reported greater worsening in the mobility, hand, vision, and bladder/bowel Performance Scales (P < .0001). Conclusions: While participants with HD in 2010 began follow-up in 2006 with a higher level of disability, they also experienced more worsening over the follow-up period compared with those with lower disability. This conclusion assumes a linear increase of the PDDS scale over the follow-up period; therefore, a more detailed longitudinal analysis will also be presented.

Supported by: Novartis Pharmaceuticals; NARCOMS is supported in part by the CMSC and its Foundation.

Disclosure: Stacey S. Cofield: American Shoulder and Elbow Society, Teva Neuroscience (consulting fees); Medimmune, Orphotech Biotech (DSMB), Yuliang Liu, Tuula Tyrö, Nothing to disclose, Jessica Marvel: Novartis Pharmaceuticals Corporation (employee); Ruth Ann Marrie: Bayer, Inc; CIHR; PHAC; MHRC; HSC Foundation, Consortium of Multiple Sclerosis Centers Foundation, Rx & D Health Research Foundation, EMD Serono, MS Society of Canada, MS Scientific Foundation, Sanofi-Aventis (grant/research support), Robert J. Fox: Allozyme, Avanir, Biogen Idec, Novartis, Questcor, Teva, Xenonport (consulting fees); Novartis (grant/research support). Gary Cutter: Alecion, Allozyme, Consortium of Multiple Sclerosis Centers (grant), Diogenix, Klein-Buendel Incorporated, Genzyme, Medimmune, Novartis, Nuron Biotech, Receptos, Spiniflex Pharmaceuticals, Somahultion, Teva Pharmaceuticals, Xenonport (consulting fees); Apteka, Biogen Idec, Cleveland Clinic, Glaxo-SmithKline Pharmaceuticals, Gilead Pharmaceuticals, Medigenetech/ Prolor, Merck/Ono Pharmaceuticals, Merck, Neurken, PCT Bio, Revoleio, Sanofi-Aventis, Teva, Viroq, National Heart, Lung, and Blood Institute (protocol review committee), National Institute of Neurological Disorders and Stroke, NMS (data and safety monitoring committees); Pythagoras, Inc (president of a private consulting company).

Keywords: Disease progression, Disease-modifying treatments in MS, Epidemiology of MS

(SX04) CROSS-PLATFORM COMPARISON OF RETINAL LAYERS IN MULTIPLE SCLEROSIS UTILIZING A NOVEL OPEN-SOURCE OPTICAL COHERENCE TOMOGRAPHY AUTOMATED SEGMENTATION ALGORITHM

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Background: Retinal pathology in multiple sclerosis (MS) is well described. Changes within different layers of the retina in MS may correlate with different aspects of the disease. However, widespread use of discrete retinal layer measures is hampered by a paucity of available automated segmentation algorithms operative across different optical coherence tomography (OCT) platforms. Objectives: To determine cross-sectional and longitudinal agreement of retinal layer thickness measures derived from an open-source, fully automated OCT segmentation algorithm, across two spectral-domain devices (Spectralis and Cirrus HD-OCT), and to compare these measures between MS patients and healthy controls. Methods: Fully automated segmentation of 172 concomitantly acquired Cirrus and Spectralis macular scans, from 68 MS patients and 22 healthy controls, was performed. A longitudinal cohort with 275 scans from 51 subjects with a mean follow up of 1.4 (±0.9) years also underwent segmentation. This recently described and validated segmentation algorithm utilizes a random forest classifier to produce probability maps of boundaries between layers. Results: In the cross-sectional cohort, Bland-Altman analyses revealed low mean differences and narrow limits of agreement (LOA), across both devices, for ganglion cell layer + inner plexiform layer (GCIP) 0.26 µm (LOA: −2.65, 3.17),
inner nuclear layer + outer plexiform layer (INL + OPL) −1.09 µm (LOA: −2.1, 0.02), and outer nuclear layer + photoreceptor segments (ONL + PR) 0.20 µm (LOA: −3.2, 3.6) thickness measures. Larger mean differences with narrow LOA were found for macular-retinal nerve fiber layer (mRNFL) 5.11 µm (LOA: 1.86, 8.34) thickness measures. The mean differences and LOA for all layers were similar between MS patients and healthy controls. Compared to controls, MS patients had reduced mRNFL, GCIP, and ONL thicknesses across both platforms, adjusting for age and gender (P < .05 for all). Using similar analyses in the longitudinal cohort, we compared the changes in layer thicknesses between scanners and found small mean differences for changes in all layers, with moderate LOA, mRNFL −0.19 µm (LOA: −3.9, 3.5), GCIP 0.06 µm (LOA: −2.3, 2.45), INL + OPL 0.015 µm (LOA: −3.5, 3.5), and ONL + PR 0.21 µm (LOA: −3.0, 3.42).

Conclusions: Cross-sectional GCIP, INL + OPL, and ONL + PR thickness measures agree well at the cohort and individual levels, as evidenced by low mean differences and narrow LOA, respectively. In longitudinal comparisons good agreement at the cohort level for changes in all retinal layers with greater variability at the individual level was noted. Utilizing this open-source segmentation algorithm, it would be possible to compare data acquired using different OCT platforms, thereby facilitating broader utilization of OCT as an outcome measure in multicenter clinical trials of neuroprotective and remyelinating therapies.

Supported by: National Multiple Sclerosis Society grants FP-1787-A-1 (PB), R0-1 N5082347 (PAC)

Disclosure: Pawan Bhargava, Andrew Lang, Omar Al-Louzi, Aaron Caras, Shoh Saidit: Nothing to disclose. Jerry Prince, Diagnosoft, Inc. (ownership interest, royalty). Peter A. Calabrese: Biogen Idec, Novartis (grant/research support); MedImmune, Prothena, Vaccinex, Vertex (consulting fees).

Keywords: Imaging and MS, Optical coherence tomography

(SX05) MUSCULOSKELETAL PAIN AND ARTHRITIS IN MULTIPLE SCLEROSIS AND OTHER SUBJECTS WITH PAIN: CASE-CONTROL STUDY

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Background: Subjects who seek treatment for acute or chronic musculoskeletal pain often have arthritis and related conditions. 300 subjects were reviewed: 36 with multiple sclerosis (MS) and 228 controls. Objectives: To measure the relative frequency of arthritis in MS versus other patients with pain: case-control design matched for age and gender.

Methods: All data were retrospectively retrieved from medical records: vital, problem list, medications, progress notes, and imaging and laboratory data. Other covariates were pain location, type, and level; the Pain Disability Questionnaire (PDQ) and laboratory data; and summed score of abnormal joints + spine (C/T/L). The main outcome measure was number of subjects with arthritis (from radiologic report) in cases compared with controls. Secondary measures were pulse pressure; total, functional, and psychosocial subscales of the PDQ; and pain type. Data analysis was performed with IBM SPSS v21, odds ratio (OR) from CEBM calculator. Standard deviations and confidence intervals were reported.

Results: There were 300 subjects during the 2-year time period, of whom 55% were female. The mean (SD) age was 56.2 (11.8) in females and 58.1 (13.4) in males. The OR was 0.69 (95% confidence interval [CI], 0.58-0.80). This ratio implies that radiographic evidence of arthritis was less common in cases than in controls. For the variable (spine + joints), score correlated with age: r = 0.336 (95% CI, 0.240-0.429), P < .001. The correlation analyzed by the number of joints involved across gender using the chi-square (χ²) test was 4.346, df = 3, P = .226, not significant (NS). For pain type, 24% had somatic pain, 29% neuropathic pain, and 43% mixed. Cross-tabulation (MS × controls) gave χ² of 2.473, df = 3, P = .482 (95% CI, 0.473-0.492), NS. Pulse pressure differed between cases and controls, with a mean (SD) in controls of 51.3 (14.8) (95% CI, 49.4-53.3) and in cases of 44.3 (11.3) (95% CI, 40.8-48.1). The Mann-Whitney U test was significant for group difference (P < .008). Regression (age = independent variable) showed a significant F test result of 19.072 (P < .001). The R value was 0.381, and the adjusted R² was 0.138. The regression equation was PP = 68.302 − 1.106X + 0.103X² (X = age). 86% of subjects completed the PDQ. In controls, the mean Functional subscale was 43.08 (19.7) (95% CI, 40.67-45.63), Psychosocial subscale was 25.28 (14.4) (95% CI, 23.46-27.21), and total PDQ was 68.03 (31.9) (95% CI, 64.02-72.09). In cases, the means were Functional subscale 48.1 (17.5) (95% CI, 41.2-54.5), Psychosocial subscale 27.1 (12.3) (95% CI, 22.03-32.36), and total 75.1 (28.2) (95% CI, 64.5-87.1). The between-groups analysis of variance (ANOVA) was NS. Conclusions: Despite similar levels of pain, MS subjects had less frequent arthritis than controls with pain. Group differences in pain disability measures including psychosocial and functional were not significant. Pulse pressure was lower in MS subjects than in controls, which differs from recent literature that has reported use of brachial PP as a reliable measure of deconditioning. Our group of cases may be better conditioned than in previous reports of deconditioning in MS.

Supported by: None

Disclosure: Nothing to disclose

Keywords: Epidemiology of MS, Natural history of MS, Psychological issues and MS

(SX06) A COMPREHENSIVE ANALYSIS OF THE DIRECT AND INDIRECT COSTS OF MULTIPLE SCLEROSIS

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Background: There have been many important studies of the costs of multiple sclerosis (MS), but we lack the comprehensive, detailed, and accurate picture we need to improve the lives of people with MS and their families. This study, funded by the National Multiple Sclerosis Society, was designed to provide these data by creating a multidisciplinary team of health economists, health-services researchers, and clinicians; conducting secondary analyses of data sets with representative community and institutional samples of the MS population in the United States; providing detailed data on use and cost of all domains of health and home care services and health-related purchases; providing detailed data on lost employment and education opportunities for
Platforms

Platforms for patients and family caregivers and estimates of indirect costs; and using standardized measures and definitions for comparability with other populations. **Objectives:** The study objectives are to describe health services and health-related expenditures of people with MS living in the community and in nursing homes and estimated direct costs to patients/families and society; employment and educational losses for patients and families and estimated indirect costs; total costs of MS by combining direct and indirect costs; types/extent of paid and family caregiving and estimated costs; and nursing homes with MS residents (size, services, quality). **Methods:** For community residents, we are analyzing data from the 2009 wave of the Sonya Slifka Longitudinal Multiple Sclerosis Study for 2361 individuals with MS who provided, during computer-assisted telephone interviews, the information they had recorded in daily logbooks over 18 to 25 months on health and home care service use and out-of-pocket spending (overnight stays and visits to ERs, day hospitals, doctors/nurses, mental health/rehabilitation specialists, complementary/alternative therapists); work loss days for themselves and their families; and health-related purchases (disease-modifying therapies/prescription medication, home/vehicle modifications, equipment/supplies, transportation). For nursing home residents, we are analyzing data from the Minimum Data Set and Medicare and Medicaid claims for service use in and outside the facility, and data from the Online Survey, Certification, and Reporting to characterize facilities with MS residents. We will use the Medical Expenditure Panel Survey to compare these data with the general population and the Partners Research Patient Data Registry and pricing databases to estimate costs of family home care and direct costs of services and purchases. **Results:** The study team is actively analyzing and producing the data described above. The poster will describe the samples and present the latest findings in the domains of service utilization and health-related purchases for both community and nursing home samples. **Conclusions:** These data will advance understanding of service use, unmet needs, and financial burden.

**Supported by:** National Multiple Sclerosis Society

**Disclosure:** Pfizer, Merck-Serono, Genentech, Novartis, Avanir (meeting honoraria, consulting fees); National Multiple Sclerosis Society (grant/research support); Merck, Schering-Plough, SmithKline (ownership interest).

**Keywords:** Comprehensive care and MS, Economic issues and MS
Background: Multiple sclerosis (MS) is a chronic lifelong disease that causes a wide array of symptoms and disabilities. Most patients and clinicians focus their attention on assessing the motor and sensory deficits of MS and providing appropriate disease-modifying treatments (DMTs). However, the commonly seen symptoms that significantly affect the patient’s quality of life are often dealt with on a secondary basis or overlooked altogether. Physicians specialized in physical medicine and rehabilitation (physiatrists) are trained in providing comprehensive care to patients with neurologic conditions such as MS in order to maximize their function, independence, and quality of life. Physiatrists are qualified in managing genitourinary, bowel, bladder, sensory, fatigue, neuropathic pain, cognitive deficits, wound prevention/management, and evaluation for appropriate assistive devices for mobility and activities of daily living (ADLs). Objectives: To assess the role of a physiatrist in providing comprehensive care to veterans with MS. Methods: The MS Center of Excellence (MSCOE) at the VA New Jersey Healthcare System has incorporated physiatrists into the comprehensive care they provide to veterans with MS in both the inpatient and outpatient setting. Results: Our interdisciplinary team includes a physiatrist with board certification in spinal cord injury medicine, an MS certified social worker, MS certified nurses, and an MS virtual care RN coordinator. The team uses a comprehensive checklist to assess each initial MS patient in order to help identify and address each of the usual symptoms and issues associated with MS. After the assessment, appropriate treatment recommendations are made and most often include initiation of a regular bowel program, evaluation and provision of appropriate rehabilitation and equipment needs, and medication management for fatigue, neuropathic pain, spasticity, and prevention of wounds. If indicated, the appropriate referrals are made to other team members within our MSCOE including neurology (for initiation or maintenance of appropriate DMTs), neuro-urology (for neurogenic bladder management), mental health, physical/occupational therapy, nutrition, and the fitness/exercise program. Caregivers’ needs are assessed and home visits are made by members of the team for those veterans enrolled in our home services program. The MS patients have reported a very high satisfaction rate with the services they have received, often indicating that the issues being evaluated in the clinic have never been addressed before by any other health-care provider. Conclusions: Veterans with MS must deal with secondary complications of their disease that significantly affect their independence and health-related quality of life, and a physiatrist-led interdisciplinary team is a valuable means of optimizing the comprehensive care of these patients.
[CCO3] UNDERSTANDING DRIVERS OF EMPLOYMENT CHANGE IN A MULTIPLE SCLEROSIS POPULATION

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Background: Multiple sclerosis (MS) commonly affects people between the ages of 20 and 40 years, which is an important time for adults’ career progression and earning. Although factors affecting MS patient employment status have been described, a paucity of qualitative decision data exists. Objectives: To understand the key symptoms and factors that lead MS patients to leave the workforce or reduce their working hours. Methods: Adult MS patients who reported leaving the workforce, reducing their work hours, or changing jobs due to MS within the past 6 months were recruited from four US clinical sites. Patients participated in one-on-one semi-structured interviews regarding their MS symptoms and reasons for changing their employment status. All interviews were transcribed and coded for descriptive analyses. Results: 27 adults with a mean age of 46.3 years participated. Most participants were white (81.5%) and female (70.4%); nearly half reported being married (48.2%) and having a college degree (44.4%). Participants reported having MS for a mean duration of 10.9 years, with 51.9% reporting normal, mild, or moderate disability on the Patient-Determined Disease Steps scale; 14.8% reporting gait disability; and 33.3% reporting the need to use a cane or wheelchair. Many participants (n = 11, 40.7%) reported being on disability or having applied for disability in the past 6 months. Participants represented a diverse sample with a wide range of occupations, and reasons for either leaving the workforce or reducing work were often interconnected. Physical symptoms (e.g., fatigue, muscle weakness, visual deficits, weakness) were the most common reasons (77.8%) cited for employment change; 11 (40.7%) participants reported at least one cognitive symptom (e.g., memory loss, lack of mental agility) as a reason for change. Fatigue emerged as the most pervasive symptom and affected both physical and mental aspects of patients’ jobs. Most participants (85.2%) reported ≥2 symptoms as being key drivers for change. Symptoms were not related to a specific type of employment or occupation. Loss of employment had a significant negative impact on patients’ mental status, family life, and financial stability. Conclusions: Fatigue is the most commonly related symptom associated with an MS patient’s decision to leave work or reduce employment, and nearly half of the patients cited at least one cognitive symptom factoring into their decision as well. The negative impact of employment loss should not be underestimated.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Comprehensive care and MS, Education in MS

(CC04) PROVIDING A STRUCTURED MULTIPLE SCLEROSIS EDUCATION PROGRAM WITHIN A MULTIPLE SCLEROSIS COMPREHENSIVE CENTER OF EXCELLENCE IN A PRIVATE PRACTICE

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Background: Texas Neurology has long been known as a comprehensive practice, as we employ numerous subspecialists in many areas of neurology. To enhance our care of multiple sclerosis (MS) patients, we embarked on establishment of a Comprehensive Center of Excellence for MS. It is essential for the Center of Excellence to provide in-depth disease process education, as a literature search revealed that increased knowledge decreases unrealistic expectations of patients related to their disease processes (Cutler A et al. BMJ. 1999;318–322). In addition, patient education may provide patients the confidence to participate in treatment choices (Kapser J et al. Patient Educ Counsel. 2006;62:56–63), which may ultimately have an impact on symptom management, the course of the disease, as well as quality of life (Heesen C et al. J Neurol Sci. 2007;259:109–117).

Objectives: Establishment of a formal, structured, reproducible education curriculum within the Multiple Sclerosis Center of Excellence, which will include pathophysiology, symptoms expectations, treatment options, cognitive-behavioral coping skills/strategies, and prognosis. Methods: Educational classes will be offered through the Center of Excellence at established meeting times for groups or on a 1:1 basis during follow-up visits. The curriculum will be established using the AANN, ARN, and IOMSN Clinical Practice Guideline Series for Nursing Management of the Patient with Multiple Sclerosis. A pre-curriculum and post-curriculum testing instrument will be designed to measure knowledge, adherence, and self-care. Results: Analysis of data will be presented. Conclusions: Multiple sclerosis patients who are knowledgeable regarding their disease process have more realistic expectations, are more adherent to care regimens, participate more fully in their ongoing care, and are more likely to assume responsibility for self-care.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Comprehensive care and MS, MS disease education, Nursing management in MS

(CC05) EFFECTIVENESS OF SERIES-BASED ONLINE EDUCATION IN MULTIPLE SCLEROSIS: PLANNED AND ACTUAL CHANGES TO IMPROVE MOBILITY MANAGEMENT

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Background: Mobility impairment, one of the most recognized physical characteristics of multiple sclerosis (MS), is ranked as a high priority among patients’ concerns. Yet clinicians remain challenged in adequately assessing and treating mobility impairment and its symptoms, including gait problems, spasticity, muscle weakness, fatigue, pain, and balance impairment. Objectives: A study was conducted to determine whether a series of online educational interven-
The purpose and application of these resources, and generalized information. Overwhelming time period, itions to ask, especially at the time of diagnosis. Resources that provide sclerosis (MS) desire more information than they receive, Chapel Hill, 1 Catherine Jacobs, DIAGNOSIS? PEOPLE WITH MULTIPLE SCLEROSIS SHORTLY AFTER (CC06) WHAT ARE THE EDUCATIONAL NEEDS OF education Disclosure: Supported by: Acorda
Keywords: Comprehensive care and MS, Mobility management and education

(CC06) WHAT ARE THE EDUCATIONAL NEEDS OF PEOPLE WITH MULTIPLE SCLEROSIS SHORTLY AFTER DIAGNOSIS?
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Background: Research reports that individuals with multiple sclerosis (MS) desire more information than they receive, especially at the time of diagnosis. Resources that provide information are available, but there are limitations on utilization and application of these resources, including too many sources of information, uncertainty about what questions to ask, inability to find answers to specific questions, overwhelming time period, unaware of potential resources, and generalized information. Objectives: The purpose of this study is to assess the educational needs of people with MS soon after diagnosis. Methods: An eight-question survey was distributed to individuals with MS. Surveys were distributed through the Greater Carolinas Chapter of the National Multiple Sclerosis Society, physical therapists, and self-help group leaders to people living in North Carolina, South Carolina, and New York. Questions asked about time since diagnosis, information considered valuable received at time of diagnosis, information that would have been helpful at diagnosis, level of physical activity, interest in wellness information, and specific areas of interest regarding health and wellness. Frequency of survey responses were analyzed. Results: Data collection is ongoing. Preliminary results from the first cohort of respondents indicate that time since diagnosis ranged from less than 1 year to greater than 10 years, and over 60% have been diagnosed for at least 10 years. Information considered most valuable at time of diagnosis was disease information and medical management. Respondents indicated that they would have liked to receive more information on physical activity, such as exercise routines and the benefits of physical therapy. More than half of the respondents also indicated that psychosocial concerns such as adjusting, influence on employment, and financial concerns were important. Most respondents reported being less active than before their diagnosis, but were very interested in attending a wellness information seminar. Respondents were especially interested in learning more about fatigue, nutrition, exercises to do at home, and cognitive exercise. Conclusions: Preliminary survey results strongly suggest the need for more information, especially concerning physical activity at the time of diagnosis. These data will be used to develop a half-day educational wellness event for people with MS in the Greater Carolinas Region.
Supported by: None
Disclosure: Nothing to disclose
Keywords: Wellness

(CC07) TRAINING PATIENTS WITH MULTIPLE SCLEROSIS TO USE INTERFERON Daymeet Grass Fernandez
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Background: Nurses are very important members of the multidisciplinary team caring for people with multiple sclerosis (MS). They have many functions, including consulting and educating people to achieve better understanding and knowledge about MS in the social and health fields. Moreover, nurses play a crucial role in the pharmacologic treatment of MS patients. Objectives: Train patients and family members in use of the autoinjector for interferon beta-1a (Rebif) 44 µg. Methods: We trained 51 patients (40 females, 11 males) with relapsing-remitting MS of 1 to 10 years’ duration in the basic autoinjection procedure and the use of documents related to body mass and biotype. Results: All the patients learned the techniques and performed auto-injection without problems at the injection site. The patients had clinical improvement confirmed by magnetic resonance imaging. Conclusions: Injections at various sites can be minimized by using the appropriate technique, and proper drug administration ensures optimal treatment, contributing to clinical improvement of patients.
(CC08) ASSESSING REGISTERED NURSES’ KNOWLEDGE OF MULTIPLE SCLEROSIS AND EXPLORING THE ROLE OF THE MS NURSE SPECIALIST IN MEETING THESE NEEDS

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Background: Multiple sclerosis (MS) is the most common neurologic condition in young adults in the United Kingdom, affecting approximately 100,000 people (Heinon & Dorning, 2011); in Northern Ireland we would estimate a population of over 4500 people affected by MS. It is the most common neurologic condition in young adults. People with MS are admitted to district general hospitals throughout Northern Ireland for a variety of reasons. They are cared for by staff who may not have had training in the neurosciences. If nurses have a lack of knowledge, does this create a barrier to care? (Shaw, 2008). Hunderfund et al. (2010) reported that patients are consistently dissatisfied with the information given to them by health-care providers.

Objectives: To assess registered nurses’ current knowledge about MS. To identify gaps in their knowledge in order to inform/target training needs and explore the role of the MS nurse specialist in meeting these requirements.

Methods: Ward managers from medical and surgical wards in four district general hospitals were provided with questionnaires to distribute to their staff members across all bands of qualified nursing staff.

Results: 240 questionnaires were distributed, with 106 questionnaires completed and returned. Over 60% of the nurses questioned received university-based training, and most nurses with MS on an occasional basis. The study showed that the level of knowledge of MS in general nurses is poor, and as a result very few general nurses (10%) felt confident nursing people with MS. Gross and Friedman (2012) reported how negative perceptions of MS by healthcare professionals can be very distressing for patients.

Conclusions: Part of the specialist nurse’s role is to educate not only their patient group but also other health-care professionals such as nurses, allied health professionals, and medical students (Corfield & Kelly, 2009). There is a need for further education and support for general nurses; the findings support the idea that specialist nurses are best placed to provide this education. This will ensure that practitioners are confident and knowledgeable in caring for people with MS, which will ultimately improve the patient experience.

Supported by: Heidi Thompson

Disclosure: Fiona M. Mullan: Merck Serono, Teva Pharmaceuticals, Biogen Idec (travel grants); Merck Serono, Biogen Idec (consulting fees). Heidi V. Thompson: Merck Serono, Teva Pharmaceuticals, Biogen Idec (travel grants); Merck Serono, Biogen Idec (consulting fees).

Keywords: Education, Nursing management in MS

( CC09) DEVELOPING AN INTEGRATED MULTIDISCIPLINARY CARE PATHWAY FOR MULTIPLE SCLEROSIS IN HULL, UK: PROCESS, APPLICATION, AND TRANSFERABILITY

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Background: Neurological Commissioning Support is a not-for-profit voluntary sector-led organization. In 2013 we developed and piloted, in partnership with the specialist multidisciplinary multiple sclerosis (MS) team in Hull, an integrated care pathway (ICP) for MS that will streamline and improve care outcomes for people with MS in Hull but also have wider application for any other specialist MS service. Work on differing elements of the pathway is ongoing. Development of the initial pathway took place within the acute provider trust but also encompassed the five geographically diverse Clinical Commissioning Groups (CCGs) that use MS specialist services from this Hull provider trust. ICPs are designed to improve the quality of care, efficiency, and service planning by commissioners which the NHS in England is currently promoting. Development of ICPs, however, is frequently viewed by clinicians as complex to achieve.

Objectives: Production of a single integrated multidisciplinary care pathway that would identify care requirements in a person with MS from diagnosis through to end-of-life care.

Methods: Drawing on previous work on creating ICPs, our research included use of population data, hospital admission data, and consultation with groups of multidisciplinary professionals and patients. Process mapping was used to identify current care pathways within the Hull provider area and illustrate where services could be streamlined and improved for greater service efficiency and better patient outcomes. Separate pathways were developed across the main areas of MS care, for example, at diagnosis, the introduction of disease-modifying therapy, and rehabilitation. Common problems patients experienced that had resulted in the need for medical and nursing intervention were also identified. Pathways were also developed for these areas and included relapse and urinary tract infection.

Results: The pathway has been developed to improve services in Hull, but the process is also transferable and has enabled other clinicians to understand the process for development. Researching and creating the ICP has revealed good practice, where patients perceive quality and simple solutions for greater service efficiencies. This pathway clearly demonstrates where service improvements and improved patient outcomes can be made.

Conclusions: ICP development overall is time consuming, and some aspects are more challenging than others to implement. Barriers to implementation that can hinder progress in development are limited clinician time and capacity to undertake the work, resistance to change and involvement in the work, as well as poor communication and coordination between MDT members. Behavioral as well as service change is therefore essential for implementation. To aid transferability, the methodology for this development has been documented into manageable steps accompanied by practical online resources.
**Background:** Telemedicine is described as using advanced technologies as a means to exchange health information and provide health-care services across geographic, time, social, and cultural barriers. Telehealth used to be focused on rural health but is now on the radar of CEOs of health-care systems all over the country, and remote monitoring is reportedly used by over 200,000 patients nationwide. Providing care to veterans with multiple sclerosis (MS) can be challenging due to the complex nature of their disease and the wide-ranging impact it has on the patient, their caregivers, families, etc. It also remains a very costly condition to manage. Cost can be measured in dollars as well as the emotional and other stressors it may have on the patient and the family unit. **Objectives:** 1) Demonstrate how the use of My HealtheVet/Secured Messaging (MHV/SM) increases access to the health-care team. 2) Participants will identify three benefits of MHV/SM for patients and providers. **Methods:** This VA’s SCI/D Center has had success with using telehealth technologies since 2000 as a way to increase access to care and decrease the burden to patients and caregivers. My HealtheVet (MHV) is a web-based application that creates an online environment where veterans, families, and clinicians may come together to optimize veterans’ health care. Using MHV, veterans create and use their personal health record to make informed health-care choices, stay healthy, and obtain services when needed. Secured Messaging (SM) is only for nonurgent communication with the health-care team. Veterans can request appointments and prescription renewals, or ask health or administrative questions. Patients can communicate directly with health-care workers about their condition and/or needs. This saves them from trying to track down their providers by phone and receive responses in a timely manner. **Results:** We present the results of a sample of our 28 patients and 5 provider populations who use MHV/SM. 100% of the veterans reported: 1) They had increased communication with the health-care team. 2) They found the MHV website easy to use and useful. 3) They had an increase in quality of care. 4) Veterans are able to order their medications and review results of laboratory tests, x-rays, and magnetic resonance imaging (MRI) scans from home. 100% of the providers who used the technology reported: 1) They found it more helpful and not burdensome. 2) They found it did not take up much time. 3) They would absolutely continue to use the technology. 4) They would recommend this program to other patients. 5) It helped them address patients’ and caregivers’ needs in a timely fashion. **Conclusions:** Use of MHV/SM at home is an asset to decreasing the health-care burden and improving the care of patients with MS. Providers and patients benefit and report improved satisfaction. We recommend the use of this virtual care environment by those providing care to patients with complex medical conditions.

**Supported by:** None  
**Disclosure:** Sue Thomas, Jane Fowler; Biogen Idec (grant/research support)  
**Keywords:** Comprehensive care and MS, Economic issues and MS, Integrated care pathway in MS

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**Background:** Telemedicine, in particular the virtual home visit, is a useful application of technology that could be applied to the field of multiple sclerosis (MS). This technology could increase access to neurologic care for the many MS patients who do not currently receive care from a neurologist. Nearly 30% of MS patients do not receive care from a neurologist. The costs of travel to distant neurology clinics can be prohibitive for poor patients. Patients with mobility dysfunction may also have limited access to neurologists due to travel limitations. Telemedicine, specifically the virtual home visit, has the potential to increase access to neurologic care for MS patients who cannot travel to neurology clinics due to the associated costs or mobility limitations. Telemedicine is the provision of health care or health education using audiovisual (AV) connections. Virtual home visits are one particular application of telemedicine. Providers conduct initial consultations or follow-up visits while the patient is at home using an AV connection. Virtual home visits have been successfully utilized in several other neurologic subspecialties. For example, a study by movement disorder specialists at the University of Rochester found virtual home visits for Parkinson’s disease patients to be feasible. Patients and caregivers also reported high levels of satisfaction with the virtual visits, in part due to substantial savings of time and money because travel to the neurology clinic was avoided. A review of the literature did not reveal any examples of MS specialists providing virtual house calls to patients. However, other applications of telemedicine have been successfully used in MS care, including MS specialists providing consultations to distant health-care providers. Given the success of other neurologic subspecialties using virtual home visits, combined with the clear need to increase MS patients’ access to neurologic care, using virtual home visits could address this need. **Objectives:** To determine whether virtual home visits for MS patients are feasible and satisfactory to patients. **Methods:** The MS Clinic at the University of Rochester will conduct a small randomized trial to assess the feasibility and satisfaction of virtual home visits for MS patients. If this is shown to be feasible, later studies will focus on the important question of whether this technology can increase access to neurologic care for the many MS patients who currently lack this access.

**Supported by:** None  
**Disclosure:** Nothing to disclose  
**Keywords:** Virtual care
(CC12) THE EVOLVING KNOWLEDGE OF MULTIPLE SCLEROSIS IN LATIN AMERICAN COUNTRIES IN THE 20TH CENTURY
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Background: Details on the evolution of knowledge of multiple sclerosis (MS) in Latin America in the 20th century are not well known. Objectives: In the present study the evolving knowledge of MS in Latin America in terms of its clinical, diagnostic, anatomo-pathological, epidemiological, genetic, and therapeutic aspects is reviewed. Methods: Authors reviewed papers cited in PubMed and SciELO, and other articles from Latin America. Results: Since the first case reported in Brazil in 1923, cases and case series of MS were reported in most Latin American countries throughout the 20th century. Epidemiological data were available from studies conducted in Mexico, Cuba, Cuban-Americans, and Martinique. Observations point to an apparent increase in its frequency without a north-south gradient. The mechanisms that contributed to increased identification and frequency of MS in Latin America were improvement of medical education and diagnostic techniques, as well as dissemination of genetic susceptibility. Numerous Latin American countries had neurologists dedicated to the specialized care of people with MS, and disease-modifying therapies were extensively introduced. MS was diagnosed among Mestizos, Caucasoïds, and African Americans, but not in nonmixed Indoamerican groups. Clinical manifestations of MS in Latin America were largely similar to those described elsewhere. The first familial association of MS was reported in Brazil. The Latin American Committee for Treatment and Research in MS (LACTRIMS), Latin American associations of people with MS, and the Consortium of Multiple Sclerosis Centers provided increased benefits for people with MS. Conclusions: This study provides more complete knowledge of MS in Latin American countries during the 20th century.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Epidemiology of MS

(CC13) DELIVERING SOCIAL WORK SERVICES TO MULTIPLE SCLEROSIS PATIENTS THROUGH VIDEOCONFERENCING TECHNOLOGY
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Background: Access to social work services for multiple sclerosis (MS) patients may not appear as the “most effective” use of time for disabled patients, primarily because preparation for outpatient clinical visits is time-consuming and may require the assistance of another person, that is, the caregiver. As a result, patients often try to avoid going to a medical center for care and most often neglect seeking social work services because they may not have “social work needs.” Unfortunately, for most disabled veterans, social work services may be life-changing. Social workers within a health-care system address the biopsychosocial needs of patients, which include coordinating, monitoring, evaluating, and advocating on behalf of the patient and/or the family to facilitate appropriate services. The use of videoconferencing technology to address patients’ needs reduces barriers to patients’ receiving benefits and services. Understanding the benefits and use of videoconferencing technology for direct social work practice in veterans’ homes will improve access to care, minimize complications of medical needs, and facilitate ongoing psychosocial rehabilitation. Objectives: 1) Demonstrate how the use of videoconferencing technology is successful in providing direct social work interventions. 2) Participants will identify three social work interventions that can be utilized through videoconferencing technology. 3) Participants will be able to describe methods for identifying appropriate participants. Methods: Veterans with MS who would require outpatient or in-home visits to complete applications, annual evaluations, or other case management services are offered a visit through use of telehealth equipment rather than an in-person clinic visit. Access to a computer with a webcam is essential. Patients are educated about the use of technology and the benefits of having face-to-face contact with a provider in the comfort of their homes. Results: Clinical visits are scheduled through a telehealth coordinator. Veteran and provider are joined through technology. Conclusions: The use of videoconferencing technology to provide social work services to veterans with MS is an innovative method to provide cost-effective, accessible health care. Providing social work services from the home setting is more comprehensive. Family members can also participate with permission of the veteran.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Comprehensive care and MS, Equipment in MS, and the caregiver/family

(CC14) TO WHAT DEGREE ARE PEOPLE WITH MULTIPLE SCLEROSIS IN GREATER MANCHESTER SATISFIED WITH THE SERVICES OFFERED TO THEM?
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Background: Multiple sclerosis (MS) is an inflammatory disorder of the central nervous system characterized by unpredictable relapses and/or accumulation of disability. It requires a multidisciplinary approach, and national guidelines (NICE CGB) recommend which services should be available. A recent MS Society publication and the domains set in the 2013/14 NHS outcome framework highlight the need to improve service provision. The development of the “friends and family test” (FFT) hopes to achieve this. Objectives: To determine the standard of health-care services provided in Greater Manchester to people with MS. Methods: Patients were interviewed in controlled environments at eight locations (four outpatient, two day-case units, and two community) using a structured questionnaire based around the FFT. Results: Seventy-five patients (51 women, 68%) participated, of whom 75% had relapsing-remitting MS, 17% secondary progressive MS, and 8% primary progressive MS. At least two patients from each borough of Greater Manchester were interviewed. The most frequently consulted
providers were MS nurses (n = 75), neurologists (n = 75), and GPs (n = 71). MS nurses and neurologists demonstrated the highest FFT scores (70.7 and 60, respectively) and psychologists the lowest (24.6). The most commonly requested services were from psychologists (19%) and physiotherapists (11%). **Conclusions:** Satisfaction is good for MS nurses and neurologists, measured by the FFT. People with MS seem less likely to consult their GP. This could have implications for the workload of MS nurses. Patients would most likely access to psychology and physiotherapy services. In addition to repeating this audit, this report proposes that service professionals be surveyed to gather their perspectives.

**Supported by:** None

**Disclosure:** Karen Vernon: Merck Serono, Teva, Genzyme, Novartis, Bayer, Biogen Idec (conference sponsorship, consulting fees). David Ross; Paul Talbot: Merck Serono, Teva, Genzyme, Novartis, Bayer, Biogen Idec (conference sponsorship, consulting fees, grant/research support); Mitsubisi (grant/research support); Fran Jackson: Biogen Idec (conference sponsorship), Genzyme (consulting fees). Aeesa Pervez: Nothing to disclose.

**Keywords:** Comprehensive care and MS, Nursing management in MS, Satisfaction with MS services

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**CC15 SHARED DECISION MAKING IN MULTIPLE SCLEROSIS: OPTION GRID POINT OF CARE ENGAGEMENT TOOLS FOR DISEASE-MODIFYING TREATMENT (WORK IN PROGRESS)**

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**Background:** There has been a dramatic increase in FDA-approved disease-modifying treatment (DMT) options for multiple sclerosis (MS) over the past decade. DMTs vary greatly in efficacy, administration, monitoring, tolerability, and adverse effects. No single DMT has yet been identified as the most effective treatment for all MS patients, making DMT decisions highly preference-sensitive for patients and providers. Decision support is indicated in preference-sensitive decisions and can improve decision quality, but no comprehensive, easy-to-use, and current decision aid currently exists for DMTs in MS. One novel type of concise yet comprehensive decision support tool is called an Option Grid (OG). OGs can be used in clinical encounters to improve the quality of DMT decisions using a shared decision-making approach. **Objectives:** To develop two evidence-based, peer-reviewed, and patient-advised OGs for DMTs in relapsing-remitting MS (RRMS), one for injectable and infusible DMTs and one for oral DMTs. **Methods:** We are developing OGs for DMTs in RRMS using a four-part process featuring a balanced, multiple-stakeholder approach. The four-component process includes an evidence synthesis of DMTs, an assessment of the OGs by an expert panel of MS clinicians and scientists, commentary by shared decision-making and decision-science experts, and feedback from MS patients obtained through focus groups. The OG designs will follow standard OG format (see www.optiongrid.co.uk), which consists of one-page tables providing concise information on DMTs categorized by frequently asked questions (FAQs) that are of high interest and relevance to patients facing DMT decisions. Prototype OGs will be subjected to reviews by the Option Grid Collaborative (shared decision-making experts), a panel of MS clinician and research experts, and National Multiple Sclerosis Society patient advisory groups for review. We will incorporate feedback from these groups into the final OG versions. Once the OGs are finalized, they will be published on the Option Grid Collaborative website, where they will be freely available in the public domain (http://www.optiongrid.org/optiongrids.php). **Results:** This is a work in progress initiated in Summer 2012, with anticipated completion by Fall 2014. A progress report, including prototype OGs, and a summary of initial peer reviews will be available for presentation at the 2014 CMSC conference. **Conclusions:** Evidence-based, peer-reviewed, and patient-advised OGs for DMTs in RRMS can be incorporated in the clinical setting in a shared decision-making approach and have the potential to improve DMT decision quality and treatment adherence.

**Supported by:** None

**Disclosure:** Nothing to disclose

**Keywords:** Comprehensive care and MS, Disease-modifying treatments in MS, Shared decision-making

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**CC16 CREATING A COMPREHENSIVE CENTER OF EXCELLENCE FOR PEOPLE WITH MULTIPLE SCLEROSIS IN A PRIVATE PRACTICE**

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**Background:** Multiple sclerosis (MS) is a chronic neurologic disease requiring a lifetime of coordinated care. As a large private neurology practice managing hundreds of patients with MS, we recognized the need to develop a comprehensive, patient-centered program that would coordinate long-term care for the patient with MS. Literature reviews, discussions with key MS opinion leaders, networking with established MS centers, partnering with national MS support and self-help groups, and attending the Linda Morgante MS nurse leadership program along with the CMSC annual meeting were strategies utilized to develop the framework for the Multiple Sclerosis Center of Excellence at Texas Neurology. **Objectives:** To create a comprehensive center of excellence that would coordinate ongoing care for the MS patient. **Methods:** A clinical staff committed to our mission to develop our MS Center of Excellence was assembled. The MS team included physicians, advanced practice providers, an MS-certified nurse, CMAs, social workers, a neuropsychologist, a psychologist, IV clinic RNs, a registered dietitian, and community (inpatient and outpatient) physical therapy/occupational therapy/speech therapy providers. Ongoing MS team meetings were conducted to identify strategies to develop structured, layered patient education modules, provide neuropsychological screening/evaluation/treatment, provide psychosocial case management, facilitate rehabilitation service management, and provide current disease and symptom management. **Results:** Comprehensive, coordinated care will be delivered to the patient with MS utilizing a multidisciplinary health management approach. A high level of satisfaction will be recognized by the patient receiving care at the MS Center of Excellence at Texas Neurology. Additionally, the clinical staff will report satisfaction working as a team meeting the comprehensive, coordinated needs of the patient with MS. **Conclusions:** Patients with
MS require comprehensive, coordinated care throughout their lifetime. The development of an MS Center of Excellence will provide a collaborative team to partner with the MS patient to achieve quality of life goals and overall wellness.

Disclosure: Biogen, Novartis (speakers’ bureau)

Keywords: Comprehensive care and MS, Coordination of MS care

(CC17) ADVANCED PRACTICE CLINICIANS’ PERSPECTIVE: MANAGEMENT OF PATIENTS ON ORAL DISEASE-MODIFYING THERAPY FOR MULTIPLE SCLEROSIS

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Background: Nurse practitioners (NPs) and physician assistants (PAs) are vitally important in the diagnosis and management of patients with multiple sclerosis (MS). Effective treatment requires clinicians to be thoroughly knowledgeable of individual patient profiles and other key considerations when treating patients with MS in the current, rapidly evolving therapeutic landscape. To this end, a unique panel of advanced practice clinicians (APCs; defined as NPs, PAs, and other prescribing advanced practice nurses) was assembled from 30 different clinical practice settings (academia, free-standing MS centers, collaborative private practices, and independent NP practices) in the United States and Canada. The panel addressed issues of importance to patients with MS and their caregivers regarding oral disease-modifying therapies (DMTs). Objectives: To develop comprehensive best practice guidelines for the management of patients receiving oral DMTs, based on recommendations from an expert panel comprising APCs who specialize in treating and managing patients with MS. Methods: The panel discussed oral DMTs available to patients with MS and identified best practice guidelines for the management of patients receiving these treatments. APC experts participated in detailed discussions of current treatments followed by interactive workshops. Using case studies and interactive sessions, APCs identified important treatment considerations, including management strategies, based on patient profiles and current stage of treatment (initiation, maintenance, or long-term treatment). Results: The APC panel developed specific management strategies for multiple treatment approaches, emphasizing the needs of the individual patient. The panel identified the following key factors to consider when evaluating patients for the treatment of MS: disease activity, prior DMT use, child-bearing potential, general health, occupation, insurance, home life and lifestyle choices, and patient concerns. The panel used these key patient factors and characteristics of emergent DMTs to develop a detailed set of guidelines for each specific treatment stage. Conclusions: The heterogeneity of MS requires highly individualized treatment plans. These best practice guidelines provide NPs and PAs with guidance for employing unique and effective treatment options for patients with MS who are receiving oral DMTs.

Supported by: Genzyme, a Sanofi company

Disclosure: Mary Filipi: Biogen Idec (grant/research support); Biogen Idec, Acorda, Teva, Questcor, Genzyme (speakers’ bureau, fees for non-CME services from commercial interests or their agents). John Kramer: Avanir, Biogen, Novartis, Serono, Teva (consulting fees). Mary Margaret Hillstrand: Genzyme, Acorda, Biogen Idec, EMD Serono (consulting fees); Stratis-2 MS (grant/research support). Teresa Frohman: Genzyme, Acorda, Biogen, Novartis (consulting fees). Megan Weigel: Genzyme (consulting fees); Acorda, Bayer, Biogen Idec, Genzyme, Novartis, Serono, Pfizer, Questcor, Teva Neuroscience (speakers’ bureau, fees for non-CME services from commercial interests or their agents). Akanksha Mittal; Colleen Miller: Genzyme, a Sanofi company (employee).

Keywords: Comprehensive care and MS, Disease-modifying treatments in MS, Nursing management in MS

(CC18) CLINICAL CHARACTERISTICS ASSOCIATED WITH HIGH-COST MULTIPLE SCLEROSIS PATIENTS USING CLAIMS AND MEDICAL RECORDS DATA, STRATIFIED BY COST

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Background: Multiple sclerosis (MS) is a chronic debilitating disease that affects the central nervous system. Little clinical information can be obtained from administrative claims data, and medical record review is necessary. Objectives: To assess clinical characteristics of patients via medical record review, stratified by low, medium, and high cost, as determined from administrative claims. Methods: Newly diagnosed MS patients aged ≥18 years in the HealthCore Integrated Research Environment (HIRE™) during an intake period of 1/1/2007 to 4/30/2011 were identified. Annualized MS-related cost was computed and patients were stratified into high, medium, and low cost groups. A total of 400 patients with confirmed MS diagnosis and documentation of brain magnetic resonance imaging (MRI) were selected for medical record review. Bivariate analyses and multivariate logistic regression models were used to identify factors associated with high-cost patients. Patient demographics and clinical characteristics were explored in the bivariate and multivariate analyses. Results: 400 patient medical records were abstracted, with 84, 132, and 184 patients in the low, medium, and high cost groups, respectively. Patients had a mean age of 41 years at MS diagnosis, and 70% were female. 97% of patients had brain MRI results documented in their medical records. Of 389 patients with MRI results, 32% of low, 54% of medium, and 35% of high had active lesions (P < .01). Common symptoms reported were numbness (53%), fatigue (59%), and pain (59%). 14% low, 40% medium, and 33% high-cost patients had relapsing-remitting disease (P < .01). 52% of the patients had gait impairment, ranging from 38% of low, 44% of medium, to 64% of high (P < .01). Additionally, patients with baseline documentation of other brain MRI results not related to T2 imaging, active lesions, demyelination, black holes, or brain atrophy (OR, 2.67; 95% confidence interval [CI], 1.53-4.65) and baseline corticosteroid use (OR, 3.01; 95% CI, 1.66-5.45) were more likely to be high-cost MS patients (P < .01). Conclusions: Baseline use of corticosteroids and documentation of other...
brain MRI results were significantly associated with high-cost MS patients. This study provides insight into factors associated with high-cost MS patients and may help to prospectively identify potential high-cost MS patients who may benefit from cost-effective proactive clinical management.

Supported by: HealthCore, Novartis, Novartis Pharmaceuticals

Disclosure: Debra E. Eisenberg, HealthCore, Inc (employee); Prakash Navaratnam, Novartis Pharmaceutical Corporation, Merck & Company, McNeil Pharmaceuticals, Leo Pharmaceuticals, Gilead Pharmaceuticals (fee for non-CME services from commercial interest or their agents); Xuehua Ke, Nadia Ramsey, HealthCore, Inc (employee).

Howard Friedman, DataMed Solutions LLC, Novartis (consulting fees).

Neetu Agashivala, Rahul Sasang: Novartis Pharmaceuticals Corporation (employee and stockholder).

Timothy Vollmer, Biogen Idec, Teva, Genzyme, Ono, Elan, Novartis, National Institutes of Health, Avanir, Janusen Research (grant/research support); Sanoﬁ, Novartis, Novartis Japan, Teva, Teva Canada Innovations, Roche, Biogen Idec, Xenoport, University of Florida PeerView, Krog & Partners, National Multiple Sclerosis Society, University of St. Louis, Acorda, Mylan, Genzyme, Deloitte Consulting (consulting fees).

Keywords: High-cost MS patients

(CC19) COPING WITH AN UNPREDICTABLE DISEASE TRAJECTORY: FINDINGS FROM A NATIONAL NEEDS ASSESSMENT

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Objectives: This mixed-methods study explores the challenges of living with the uncertainty of multiple sclerosis (MS). While uncertainty may be inherent to many chronic conditions, it may be exacerbated for MS patients given the highly variable and unpredictable nature of the disease. Analysis of quantitative and qualitative data collected through a national MS needs assessment found that coping with the day-to-day and long-term uncertainty of the disease was among respondents’ greatest concerns and identiﬁed ways in which those challenges affect their lives. Methods: The study utilized data from a 2012 national MS needs assessment conducted by the Multiple Sclerosis Association of America in cooperation with the North American Research Committee on Multiple Sclerosis and the Rutgers University School of Social Work. Responses were received from 1051 subjects, for a 42% response rate. The 110-question survey, which was developed in collaboration with MS experts and patients, included open- and closed-ended questions. Data were collected via mail and online surveys. Analysis included frequencies, t tests, and analysis of variance. In addition, qualitative data were explored using a combination of conventional and summative content analysis methods. Results: Of the 36 need areas rated by respondents, coping with the long-term and day-to-day uncertainty of MS were among the most frequently reported. (Fatigue management/energy conservation was the most often reported need.) Almost 50% of subjects reported needing help with day-to-day coping, while almost 56% reported needing assistance with coping with long-term uncertainty. Analysis identiﬁed several statistically signiﬁcant differences. People with unmet needs for assistance, less education, lower incomes, and no health insurance reported higher levels of need related to coping with uncertainty. Qualitative analysis of open-ended questions further elucidated the ways in which respondents attempted to organize their lives despite the unpredictable disease trajectory. Conclusions: Findings from this study highlight the importance of addressing issues related to uncertainty and coping for MS patients. MS patients particularly seek ways to plan for their futures despite uncertainty. Lack of access to psychosocial education and skill development and mental health resources for many people living with MS are barriers to addressing this critical need.

Supported by: None

Disclosure: Nothing to disclose

Keywords: Comprehensive care and MS, Coping with uncertainty, Psychological issues and MS

(CC20) PATTERNS IN MULTIPLE SCLEROSIS NEEDS OVER TIME

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Objectives: Utilizing data collected through a 2012 national needs assessment, the study documented the ways in which psychosocial support, wellness, multiple sclerosis (MS) treatment, medical advocacy, access to resources, and signiﬁcant care needs among people living with MS change in relation to the length of time one has lived with the disease. Analysis identiﬁed high levels of need among respondents adapting to the diagnosis and those who had been living with the disease for 25 years or more. In addition, psychosocial support and wellness needs were both elevated and most likely to be unmet. Methods: The study utilized data from the 2012 national MS needs assessment conducted by the Multiple Sclerosis Association of America in cooperation with the North American Research Committee on Multiple Sclerosis and the Rutgers University School of Social Work. Responses were received from 1051 subjects, for a 42% response rate. The 110-question survey, which was developed in collaboration with MS experts and patients, included open- and closed-ended questions. Data were collected via mail and online surveys. Analysis included frequencies, t tests, and analysis of variance. In addition, qualitative data were explored using a combination of conventional and summative content analysis methods. Results: The newly diagnosed population reported the highest levels of need related to psychosocial support, wellness, MS treatment, medical advocacy, and access to resources. Needs decreased gradually as respondents gained experience with the disease, reaching a low among respondents who were between 10 and 14 years from diagnosis. An extended period of stability continued until about 25 years post-diagnosis, when a marked increase occurred. While the level of need changed across time living with MS, psychosocial support and wellness-related needs were consistently the most frequently reported needs and the least likely to be met for all groups. Conclusions: Findings from this study identify two critical time periods during which people living with MS may beneﬁt from intensive case management and other services to address high levels of MS-related needs. In particular, efforts should focus on reducing the extended adaptation phase, marked by high but declining levels of need, among newly
diagnosed respondents. Finally, resources are needed to address the consistently high levels of need related to psychosocial support and wellness, areas that may fall outside of the domain of traditional health-care providers.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Comprehensive care and MS, MS patient needs, Psychological issues and MS

(CC21) A FINGOLIMOD SERVICE—A MULTIPLE SCLEROSIS NURSE PERSPECTIVE AND PATIENT OUTCOMES
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Background: As a regional prescribing center in the United Kingdom, the Queen Elizabeth Hospital Birmingham provides the initial screening and initiation of fingolimod to a number of peripheral areas within the West Midlands. Objectives: The poster explores the setting up of the fingolimod service and the screening and initiation process. Patient outcomes were also important to the team and are presented within the poster. Methods: Patient outcomes were also measured via a patient questionnaire to explore their views of the service, including the screening process and initiation of the therapy. Results: The patient outcomes demonstrated very high satisfaction levels with the service provided. Conclusions: The fingolimod discussion groups provide education and screening to a large number of patients in a timely and safe manner, which has ultimately reduced waiting times for initiation of treatment.

Supported by: None
Keywords: Disease-modifying treatments in MS

(CC22) BETACONNECT AUTOINJECTOR: PATIENT/ CAREGIVER SATISFACTION
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Background: Patients with multiple sclerosis (MS) must undergo treatment with disease-modifying therapies (DMTs) over the long term in order to manage this chronic disease. Interferon beta-1b (IFNβ-1b) is an injectable DMT that has demonstrated long-term safety and efficacy. Use of an auto-injector such as BETACONNECT for IFNβ-1b may reduce discomfort and provide more consistent injections, thereby increasing patient satisfaction with treatment. Objectives: To assess patient satisfaction with the BETACONNECT autoinjector. Methods: Patients undergoing treatment with IFNβ-1b and caregivers of such patients were recruited to answer a 13-question survey related to BETACONNECT after participating in a human factors test session that included a simulated injection with the device. Participants provided a number on a rating scale on which 1 was negative and 5 was positive. Half of the participants were trained in how to use the device before the session. All data were qualitative and may not be representative of the population due to sample size. Results: 32 patients and 30 caregivers participated. Most of the features of the BETACONNECT autoinjector were rated very positively by patients and caregivers. Both groups found performing injections to be very easy (patients, mean rating 4.8; caregivers, 4.6) and both were very confident that they could perform an injection (patients, 5.0; caregivers, 4.9). Features intended to reduce the pain/discomfort of injection were given highly positive ratings, such as the adjustable injection speed (patients, 4.4; caregivers, 4.3) and automatic insertion/retraction of the needle (patients, 4.7; caregivers, 4.8). The injection reminder function was also rated positively (patients, 4.3; caregivers, 4.4). Responses were generally similar between the trained and the untrained groups for both patients and caregivers, with two exceptions: untrained caregivers rated the adjustable injection depth setting as more beneficial than trained caregivers (4.6 vs. 3.9), and untrained patients rated not seeing the needle before and after injection as more important than trained patients (4.5 vs. 3.4). Conclusions: Most features of the BETACONNECT device were rated positively by patients and caregivers, with only slight differences between those who were trained and those who were not trained. These findings suggest that the use of BETACONNECT may increase patient satisfaction with treatment and potentially increase adherence of patients on IFNβ-1b therapy.

Supported by: Bayer HealthCare Pharmaceuticals; data were collected by Gfk
Disclosure: Samuel F. Hunter: Acorda, Bayer HealthCare, Biogen Idec, Genzyme-Sanoﬁ, Novartis, Questcor, Teva (speaking fees); Ananir, Abbvie, Biogen Idec, Genzyme-Sanoﬁ, Osmotica, Roche, Teva (grant/ research support); Bayer HealthCare, Biogen Idec, Genzyme-Sanoﬁ, Roche, Osmotica (consulting fees). Hans J. Jensen, Paul E. Fabricius: Bang & Olsøen Medicom (employee). Mark Rametta: Bayer HealthCare (employee).
Keywords: Comprehensive care and MS, Disease-modifying treatments in MS, MS and the caregiver family

(CC23) GETTING THE INTERMITTENT CATHETER THE PATIENT NEEDS: CONSIDERATIONS IN CODING, COVERAGE, AND DOCUMENTATION
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Nurses with knowledge of catheter features, the Healthcare Common Procedural Coding System (HCPCS), reimbursement guidelines, and proper documentation have the essential information needed to ensure that patients performing intermittent self-catheterization receive the best product for their individualized needs. Urologic nurses and associates invest a notable amount of time educating patients who need to self-catheterize. Some of this time is spent helping the patient accept the need and increase their comfort level in performing the procedure. Time is also spent selecting the optimal product(s) for the patient’s needs to effectively manage their condition. Patient comfort, preference, compliance, and clinical outcomes are all critical considerations for clinicians. Product features, such as a hydrophilic coating or a Coudé tip for intermittent catheters (ICs), play a significant part in the selection of the right products for the patient. Additionally, catheter reimbursement guidelines often dictate which products are available and what steps health-care providers can take to ensure that patients get the best product to meet their needs. Wherever the brand or type of catheter selected is not
specified on the prescription, such as “hydrophilic coated,” suppliers can substitute the brand they choose, including lower-quality products that cost the supplier less, with the patient paying the exact same out-of-pocket copay. Understanding reimbursement will enable clinicians to help the patient select the best intermittent catheter for their clinical needs that is also covered by their insurance at home, while avoiding additional documentation needs and/or product supply issues. Clinicians will gain the knowledge to help ensure that patients get the catheter they need, such as proper documentation for reimbursement and how to indicate the specific catheter choice on the prescription. Patient compliance is key to a successful bladder management program, and a catheter that is preferred by the patient and easy to use can increase long-term compliance. For IC users, increased compliance with their prescribed catheter regimen leads to better outcomes and a reduction in urinary tract infections. There is no single catheter that is best for every patient. There are different materials, coatings, design of tips, eyelet shape and quality, size, flexibility, lubrication process, and/or packaging. Catheter choice should be based on the clinical assessment and patient choice. ICs are reimbursed the same, meaning that the more technologically advanced catheters, such as hydrophilic coated ICs, cost the exact same amount to the health system and to the patient as standard ICs, such as uncoated catheters that require additional lubricant cost.

Supported by: None
Keywords: Economic issues and MS, Equipment in MS, Reimbursement

(CC24) AN INTERDISCIPLINARY APPROACH TO TREATING PEOPLE WITH MULTIPLE SCLEROSIS: THE ROLE OF SOCIAL SERVICES
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Background: The role of medical social work has inherently taken place in an inpatient hospital setting. Providing comprehensive care in an outpatient setting now entails a broader approach to treating the individual with chronic illness as a whole person. Quality of life issues, which include an initial diagnosis, work and family issues, financial constraints due to multiple sclerosis (MS) medications and treatment, as well as the impact of symptoms and disability impairment, all play a role in addressing comprehensive MS care. Objectives: The purpose of this work is to address the importance of providing a continuum of care that includes an interdisciplinary team approach. The role of social work in an outpatient setting that treats people with MS entails quality of life issues and addressing the everyday concerns that stem from living with a chronic lifelong illness. Methods: Our MS outpatient clinic provides an interdisciplinary approach that includes a neurologist, neuropsychologist, nurse, nutritionist, and social worker. Physical and occupational therapists are also readily utilized in an outpatient as well as inpatient rehabilitation setting. The role of social services entails providing resource options, coordinating services and referrals, providing counseling, assisting with advanced directives, and addressing work- and family-related concerns. These responsibilities are coordinated and communicated to the MS team for a comprehensive approach to treatment. Results: Coordination of care facilitated by the social worker and the rest of the MS team will be demonstrated by successfully managing the person with MS over their lifetime of care. Conclusions: Integrating a social worker into an MS interdisciplinary team is essential to address the multiple needs that accompany living with a chronic illness. People with MS require a case management approach to enhance quality of life and promote wellness, address disability and work concerns, cope with sustained physical and cognitive impairments, and assist with family, financial, psychological, and spiritual issues. Currently, any MS Center of Excellence will warrant an interdisciplinary team approach to promote quality comprehensive patient care.
Disclosure: Nothing to disclose
Keywords: Comprehensive care and MS, MS and the caregiverfamily

(CC25) EMPLOYMENT OF PEOPLE WITH MULTIPLE SCLEROSIS: A SYSTEMATIC APPROACH AND COMPREHENSIVE QUESTIONNAIRE
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Background: Employment is an essential issue of participation in our society. This is even more so for people with a chronic illness such as multiple sclerosis (MS), and it is applicable on a micro, meso, and macro level. Employment on the micro level, the level of the patient and his immediate environment, is related to self-realization, autonomy, structuring of time, social contacts, and self-esteem. On the higher meso level, different organizations related to employment of people with MS, such as MS societies, MS centers, labor unions, and so on, are developing an increasing awareness of the importance of employment and its relevance for patients with MS. Ensuring the accompaniment and/or the pursuit of employment can be perceived as a measure of quality of care. Employment is an important contemporary issue on the societal level: there is a growing conviction in Europe that everybody will have to work more and longer to maintain the current level of prosperity. Therefore, a number of employment-promoting policies have already been implemented to enhance the degree of employment of vulnerable individuals with chronic illnesses. Objectives: Our goal was to develop a systematic questionnaire to determine the spectrum of employment-related problems encountered by people with MS. Methods: An initial survey was issued to 32 patients with MS involved in a care program in the National Multiple Sclerosis Center in Melsbroek, Belgium. All patients were employed or looking for employment at that time. This survey inquires about the possibilities and obstacles that people with MS experience in the reality of their daily work or search for work. A systematic review of the literature was conducted, and relevant organizations were contacted for their insights on this topic. People with MS were questioned by a collaborator of the social work department using our standardized questionnaire. Results: Due to the growing importance of employment in the multidisciplinary guidance of people with MS, there is a need for a compact, comprehensive questionnaire that permits efficient detection of all relevant employment-related issues. In particular, we found that even with strong divergence in the employment-related situation of each...
patient, this systematic assessment tool is a valuable guideline to reveal individual needs and requirements. **Conclusions:** The ultimate goal is to offer flexible, customized vocational guidance involving professionals and organizations on all levels. Easy accessibility of clear and adequate information about MS and about the possibilities for people with MS in the labor market is crucial, both for the person with MS and for their environment. We elaborate on several recommendations to improve communication on the level of the person with MS, on the level of organizations involved in MS, and on the global societal level.

**Supported by:** None
**Disclosure:** Nothing to disclose
**Keywords:** Comprehensive care and MS, Employment in MS

### (CG26) DEVELOPMENT OF A SURVEY TO UNDERSTAND THE EXPERIENCE OF DISABILITY RETIREMENT IN MEN WITH MULTIPLE SCLEROSIS

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**Background:** Needing to cease paid work prematurely due to multiple sclerosis (MS) symptoms is a reality for many men due to the high MS disease incidence and prevalence in mid-life. Research exists to guide clinicians on strategies to prolong the working lives of men with MS by managing symptoms and introducing workplace accommodations. However, there is little research on how to help men psychosocially when they transition to unpaid work prematurely. Because healthy men struggle with the psychosocial transition to retirement, even when it is planned and at a socially appropriate time in the life trajectory, it is likely that men with MS have even more difficulty with the retirement transition. There is very little information on this topic in the literature; therefore, a survey of the population of interest is needed to verify whether transition to nonpaid work is problematic for men with MS and, if so, why. **Objectives:** The objective of this presentation is to describe the development of the Experiences with Disability Retirement of Men with MS Survey (EDRM). **Methods:** The survey was designed using the tailored method approach to encourage maximal response rates. Content was determined using information from 1) literature on successful retirement transition for people without a disability, factors that influence successful disability transition, and occupational adaptation in people with MS; 2) interviews with two men who ceased work prematurely due to MS symptoms; and 3) the Canadian Occupational Performance Model of Engagement. Once version 1.0 of the survey was developed, it was administered to two men with MS who had ceased work within the previous 10 years to further establish content validity and ease of administration. Qualitative methods were used to verify that the survey captured all relevant information and had ease of use for the target population. A “think-aloud” strategy was used in interviews with the men to understand how participants arrived at their answers to the survey questions. Data were audiotaped and transcribed and analyzed using qualitative description. **Results:** Presentation of the EDRM survey at the CMSC conference will provide health professionals with an opportunity to contribute to the survey content areas. This further validation of content will allow for a robust survey that can provide empirical evidence on how men with MS cope with a transition to nonpaid work. **Conclusions:** Transition to nonpaid work is a new area for research in MS. Development of a methodologically robust survey is important to gather information for healthcare providers to provide optimal care to men dealing with premature cessation of paid work.

**Supported by:** None
**Disclosure:** Nothing to disclose
**Keywords:** Disability retirement, Employment in MS, Psychological issues and MS

### COGNITION, DEPRESSION, AND PSYCHOSOCIAL

**(CG07) INFLUENCE OF PSYCHOTHERAPY ON LONGITUDINAL CHANGE IN EMOTIONAL AND PHYSICAL FUNCTIONING IN PRIMARY PROGRESSIVE MULTIPLE SCLEROSIS**

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**Background:** A recent literature review found strong evidence that stress was linked with the onset of multiple sclerosis (MS) or relapse of symptoms (Artemiadis et al., 2011). Cognitive, emotional, and behavioral reactions to diagnosis and disease progression were also predictive of illness-related functional impairment (Dennison et al., 2010). Furthermore, there is evidence that for patients with MS, emotional distress such as depression or anxiety, fatigue, and quality of life are all reciprocally related to disease progression (Pitton-Vouyovitch et al., 2006). The disease progression of MS was also associated with other physiological changes including autonomic dysfunction (Flachenecker et al., 2001). However, several mind-body interventions such as exercise, cognitive-behavioral therapy, relaxation, and stress management were beneficial for patients with relapsing-remitting MS (RRMS) to improve stress, locus of control, and emotional distress (Artemiadis et al., 2012); quality of life (Sung et al., 2013); fatigue (van Kessel et al., 2008); and the occurrence of new brain lesions (Mohr, 2012). However, the majority of studies focus on patients with RRMS rather than those with primary progressive MS (PPMS). The proposed study is designed to investigate whether or not a group of patients who self-select to receive psychological services have improved courses in their emotional and physical functioning as a result of these services. **Objectives:** This study primarily aims to identify whether or not the receipt of psychological services results in positive emotional and physical changes over time for patients diagnosed with PPMS. **Methods:** Participants are 637 patients with PPMS seen at the Mellen Center for Multiple Sclerosis Treatment and Research at the main campus of the Cleveland Clinic Foundation in Cleveland, Ohio, between 1/1/2010 and 12/15/2013. Data were retrospectively gathered using the Knowledge Program Data Registry (Irene Katsan, MD, Cyrus Registry, IRB #07-591). Data elements obtained from the registry include a variety of psychological and medical measures of emotional and physical functioning such as European Quality of Life, Multiple Sclerosis Performance Scales (MSPS), Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Scale–7 (GAD-7), Pain Disability
To assess personality presence of cognitive and emotional changes. Regarding instability, 5 (10%) showed broad instability, a more stable attitude. Regarding instability in the reception of stimuli, subjects performed the action in ascending order, $P \leq 0.001$ for all). The results of the TPC showed that 38 (76%) people had an orderly implementation and 9 (18%) had a methodical one, indicating rigidity in behavior. 29 (58%) subjects performed the action in ascending order, indicating a more stable attitude. Regarding instability in the reception of stimuli, 15 (30%) people showed moderate instability, 5 (10%) showed broad instability, and 2 (4%) showed limited instability, demonstrating that regardless of the magnitude of the stimulus received, the trend was toward reception instability. In terms of the formal aspect of the construction, most prevalent was the carpet (a checkerboard design) in at least one of the pyramids, with 33 (66%) subjects. 18 (36%) people had the carpet in all three pyramids, indicating the presence of cognitive and emotional changes. Regarding colors: blue, red, green, violet, orange, black, white, and gray showed $P \leq 0.001$ and yellow and brown $P \geq 0.001$, indicating emotional change with a trend toward impulsivity. A weak statistical correlation was found indicating that RRMS is prevalent in women ($P = 0.444$); no correlations were found between any other group. Conclusions: Personality traits present in this sample using the TPC were stiffness, emotional instability in receipt of stimuli, low tolerance for frustration, and certain cognitive and emotional difficulties, with a tendency to develop obsessive-compulsive disorder.

**Supported by:** ABEM–Associação Brasileira de Esclerose Múltipla

**Disclosure:** Nothing to disclose

**Keywords:** Psychological issues and MS

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### (CG08) EVALUATION OF PERSONALITY TRAITS IN PATIENTS WITH MULTIPLE SCLEROSIS

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**Background:** Multiple sclerosis (MS) is a chronic disease involving demyelination of the central nervous system. It causes a variety of symptoms depending on the affected region, including emotional and cognitive changes and psychiatric disorders. **Objectives:** To assess personality traits of patients with MS using the Test Color Pyramid Pfister (TPC). **Methods:** The TPC consists of the construction of three pyramids with colored cards on a mold. The sample was intentional, and the test was administrated to 50 patients in a charitable institution. We evaluated the impairment of patients by the Expanded Disability Status Scale (EDSS) score and the type of MS. **Results:** The sample consisted of 38 (76%) women and 12 (24%) men; 31 (62%) were over 40 years old, 34 (68%) had EDSS scores between 2.5 and 7.5, and 37 (74%) had the relapsing-remitting type of MS (RRMS; $P \leq 0.001$ for all). The results of the TPC showed that 38 (76%) people had an orderly implementation and 9 (18%) had a methodical one, indicating rigidity in behavior. 29 (58%) subjects performed the action in ascending order, indicating a more stable attitude. Regarding instability in the reception of stimuli, 15 (30%) people showed moderate instability, 5 (10%) showed broad instability, and 2 (4%) showed limited instability, demonstrating that regardless of the magnitude of the stimulus received, the trend was toward reception instability. In terms of the formal aspect of the construction, most prevalent was the carpet (a checkerboard design) in at least one of the pyramids, with 33 (66%) subjects. 18 (36%) people had the carpet in all three pyramids, indicating the presence of cognitive and emotional changes. Regarding colors: blue, red, green, violet, orange, black, white, and gray showed $P \leq 0.001$ and yellow and brown $P \geq 0.001$, indicating emotional change with a trend toward impulsivity. A weak statistical correlation was found indicating that RRMS is prevalent in women ($P = 0.444$); no correlations were found between any other group. **Conclusions:** Personality traits present in this sample using the TPC were stiffness, emotional instability in receipt of stimuli, low tolerance for frustration, and certain cognitive and emotional difficulties, with a tendency to develop obsessive-compulsive disorder.

**Supported by:** ABEM–Associação Brasileira de Esclerose Múltipla

**Disclosure:** Nothing to disclose

**Keywords:** Psychological issues and MS

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### (CG09) CASE REPORT: THE PERSON AFFECTED BY MULTIPLE SCLEROSIS AND QUALITY OF LIFE

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**Background:** Multiple sclerosis (MS) is a chronic, demyelinating, progressive, and debilitating disease. The damage to the myelin occurs randomly and impairs the transmission of nerve impulses. Symptoms vary according to the region of the nervous system affected. The disease and resulting need to adapt to a new way of living (personal, social, and professional) are significant factors that compromise psychological status and quality of life. **Methods:** This is a case study of a man, 50 years old, single, university graduate, diagnosed in 1998 with relapsing-remitting MS (RRMS). He had an Expanded Disability Status Scale (EDSS) score of 7.0, and had used a wheelchair for 6 years. Because of his limited mobility, he had lived with his family since 2002. The house had many stairs, making locomotion difficult. He had experienced depression, without treatment, because he depended on others for locomotion, which compromised his quality of life (QOL). This situation continued until September 2012, when he moved to a community for people with disabilities, an environment without stairs, and began using a motorized wheelchair, which gave him mobility and independence. In November 2012, in a neurorehabilitation institution that provides clinical care, he was administered the Multiple Sclerosis Quality of Life–54 (MSQOL-54); the scores were 28.41 for physical health and 38.23 for mental health. In October 2013, the same instrument yielded scores of 55.29 for physical health and 66.30 for mental health. A factorical battery personality test (BFP) was used to assess depressive traits. The patient was found to be within the accepted normal range for the psychological test questions on neuroticism, extroversion, socialization, development, and being open to receiving stimulus. **Results:** The patient attributed his improvement to the change in his physical environment, which improved his QOL. **Conclusions:** These results demonstrate the importance of QOL for people with chronic illness.

**Supported by:** ABEM–Associação Brasileira de Esclerose Múltipla

**Disclosure:** Nothing to disclose

**Keywords:** Management of activities of daily living in MS, Psychological issues and MS

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### (CG10) CORRELATION OF MEMORY DISORDERS WITH PREFRONTAL AND LIMBIC SYSTEM LESIONS IN PATIENTS WITH MULTIPLE SCLEROSIS

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**Background:** Multiple sclerosis (MS) is one of the most prevalent demyelinating diseases of the central nervous system. As in other chronic neurologic diseases, impairment in cognitive functioning and memory is common. MS is an inflammatory disease resulting in demyelinating plaques in various regions of the brain. The location of plaques in parts of the prefrontal area and limbic system may lead to memory disorders. This investigation was conducted to study the association between memory disorders and location of plaques.
in the limbic system and prefrontal area in patients with MS. **Objectives:** Recognizing memory disorders due to brain lesions. **Methods:** The sample was selected consecutively from patients with MS who are registered with the Isfahan MS Society. The Brain System Test (BST) and Memory Test (MT) were administered to the participants, and their brain magnetic resonance imaging (MRI) scans were analyzed by a radiologist in order to identify the number of plaques in the limbic system and prefrontal area. The results of the BST and MT and the location of plaques were analyzed for any association. **Results:** The chi-square analysis showed a significant relationship ($P = .005$) between MS plaques and prefrontal dysfunction and memory disorders; however, no significant relationship was found ($P = .106$) between MS plaques and limbic system dysfunction and memory impairment ($P > .05$). The results showed that the most common memory impairment was in the field of short-term memory ($P = 77.8\%$). **Conclusions:** The results of this study suggest that memory impairment is more correlated to injury to the prefrontal region in MS patients.

**Disclosure:** Nothing to disclose

**Keywords:** Psychological issues and MS

(CG11) **COGNITIVE DEFICITS, CEREBROSPINAL FLUID PLEOCYTOSIS, AND WHITE MATTER LESIONS FOLLOWING PARVOVIRUS B19 INFECTION IN AN IMMUNOCOMPETENT ADULT**

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**Background:** Parvovirus B19 (PVB19) is a ubiquitous airborne virus that causes erythema infectiosum ("fifth disease"). Neurologic complications after PVB19 exposure are thought to be transitory and infrequent in the adult population. Cognitive deficits and white matter changes have not been described in immunocompetent adults. **Objectives:** To present a case of a young woman who developed cognitive deficits and subcortical white matter lesions subsequent to parvovirus B19 (PVB19) infection and to review the literature on neurologic complications of parvovirus B19 infection. **Methods:** Case report. **Results:** A previously healthy, 33-year-old woman developed flu-like symptoms 4 days after her daughter was diagnosed with erythema infectiosum. A few days later she noticed memory problems, lack of concentration, word-finding difficulties, dizziness, and generalized joint and body pains. PVB19 IgG and IgM titers were elevated in serum, and viral DNA by PCR in serum showed 9800 copies. Cerebrospinal fluid (CSF) studies revealed mild lymphocytic pleocytosis (12 white blood cells/cc). Magnetic resonance imaging (MRI) of the brain demonstrated numerous small subcortical and juxtacortical white matter lesions, but no periventricular abnormalities. Extensive infectious, inflammatory, and neoplastic causes of encephalopathy were unrevealing. Intravenous immunoglobulin (IVIG) was administered for 6 months due to persistent viremia. At 2-year follow-up, the patient’s symptoms improved significantly, although she continues to have cognitive deficits on neuropsychological testing as well as vestibular and sensory symptoms. Viral PVB19 DNA in serum and CSF were undetectable at the last follow-up. **Conclusions:** Persistent cognitive deficits and subcortical white matter lesions can be seen following PVB19 infection in an immunocompetent adult. Patients with neurologic symptoms following PVB19 infection should have serologic and spinal fluid examination assessments for PVB19 as well as MRI of the brain. IVIG should be considered for symptomatic patients with persistent PVB19 viremia.

**Supported by:** None

**Disclosure:** Nothing to disclose

**Keywords:** Parvovirus B19, Cognitive deficits, CSF pleocytosis

(CG12) **RANDOMIZED CONTROLLED TRIAL OF PHYSICAL ACTIVITY AND COGNITION IN PEOPLE WITH MULTIPLE SCLEROSIS**

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**Background:** Slowed cognitive processing speed is common, debilitating, and difficult to manage in people with multiple sclerosis (MS). Researchers have recently advocated for physical activity as a behavioral approach for managing reduced cognitive processing speed in MS. **Objectives:** The present study adopted a randomized controlled trial (RCT) design and examined the effect of a physical activity behavioral intervention on cognitive processing speed among people with MS who have mild or moderate disability status. **Methods:** 82 MS patients were randomly allocated into intervention or waitlist control conditions. The intervention condition received a theory-based program for increasing physical activity behavior that was delivered via the Internet and one-on-one video chat sessions with a behavior-change coach. Participants completed self-report measures of physical activity and disability status, and underwent the oral Symbol Digit Modality Test (SDMT) before and after the 6-month period. **Results:** Mixed-model analysis of variance indicated a significant time × condition × disability group interaction on SDMT scores ($P = .02$, partial-$\eta^2 = .08$), such that individuals with mild disability in the intervention condition demonstrated a clinically meaningful improvement in SDMT scores (~6-point change). Further, among those who received the intervention, changes in physical activity were positively associated with changes in SDMT scores in individuals with mild ($P = .45$, $P = .04$) but not moderate ($P = .12$, $P = .33$) MS disability, such that greater increases in physical activity were associated with greater improvements in SDMT scores. **Conclusions:** The current study supports physical activity as a promising tool for managing cognitive impairment in people with MS and suggests that physical activity might have specific effects by disability status on cognition in this population.

**Supported by:** National Multiple Sclerosis Society


**Keywords:** Cognition in MS
(CG13) THE RELATIONSHIP BETWEEN BIPOLAR DISORDER AND MULTIPLE SCLEROSIS
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Background: Multiple sclerosis (MS) is a chronic, auto-immune demyelinating disease affecting approximately 400,000 Americans. Emotional disturbances are common and consist of mood and affective instability. Early recognition of mood disorders in MS patients is essential, as appropriate psychiatric symptom management is a major factor in morbidity and MS treatment compliance. Bipolar spectrum disorders (BD), in particular, have been linked to MS disease onset and symptom severity. Objectives: We sought to determine whether BD occurs more frequently among MS patients compared with the general US population and whether this comorbidity is associated with worse quality of life (QOL).

Methods: We conducted a retrospective analysis of 99 consecutively recruited patients with clinically definite MS (2010 McDonald’s criteria), evaluated at a single ambulatory MS center between June and December 2013. MS subtype, medication, and disease duration were abstracted from the medical record. Patients were classified as having suspected BD via a positive score on the self-administered Mood Disorder Questionnaire (MDQ) or previous psychiatric evaluation. Prevalence was measured and compared to the reported rate of positive MDQ screens in American adults. Symptom severity was assessed via the self-recorded Multiple Sclerosis Quality of Life–54 (MSQOL-54) instrument. Respectively physical (MSQOL-P) and mental (MSQOL-M) health composite scores were dichotomized as <50 or ≥50 to indicate poor or good QOL, and compared among MS patients with and without suspected BD.

Results: The sample included 99 individuals with MS: mean age, 48 ± 11 years; 73/99 (74%) female; 83/99 (84%) relapsing-remitting subtype; mean MS disease duration, 8.5 ± 6.4 years. 18/99 (18%) of patients screened positive for or carried a prior diagnosis of BD, relative to a reported prevalence of 3.7% in the community. MS individuals with poor MSQOL-P and MSQOL-M scores were more likely to have suspected BD (P = .02 and P < .001, respectively) and shorter disease duration (P = .04 and P < .001) than patients with good QOL. After adjustment for MS disease duration, suspected BD was independently associated with poor MSQOL-P (P = .03, OR 3.5; 95% confidence interval [CI], 1.1-11.1) and MSQOL-M (P = .001, OR 8.5; 95% CI, 2.5-29.1).

Conclusions: In our MS cohort we noted a higher-than-expected prevalence of suspected BD, which was independently associated with poor physical and mental health-related QOL. If confirmed in future studies, this knowledge may aid in the design of specific interventions targeting affective disturbances, and may help improve MS patients’ QOL.

Supported by: FCMSC Medical Student Research Scholarship Program
Disclosure: Seth Levin, Ankur Butala, Nicole Ross, Nils Henninger, Carolyn Griffin: Nothing to disclose. Peter Riskind: Biogen Idec, Hoffmann-La Roche, Novartis, Diogenes (grant/research support); Sanofi-Aventis, Genzyme Corporation (consulting fee). Carolina Ionete: Acorda Therapeutics, Biogen Idec, Genzyme Corporation, Teva Pharmaceuticals (grant/research support).

Keywords: Comprehensive care and MS, Epidemiology of MS, Psychological issues and MS

(.CG14) MINDFULNESS IN MULTIPLE SCLEROSIS (MIMS)
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Background: Multiple sclerosis (MS) is a chronic, potentially disabling disease of the central nervous system (CNS). MS can present with unpredictable physical, sensory, emotional, and psychological symptomatology. A major area of concern for individuals with MS is stress, a factor that is highly related to quality of life (QOL) (Kargiotis, 2010). MS can undermine a person’s QOL both directly and indirectly, exacerbating stress and affecting coping ability (Zweibel, 2009; Moore, 2013). Mitigating the associated stress caused by MS through healthy coping skills and stress reduction techniques can potentially enhance QOL for those living with MS. Studies have suggested that stress reduction may help a broad range of individuals to cope with clinical and non-clinical problems. One such intervention that has been shown to effectively reduce stress is mindfulness-based intervention (MBI). It is based on concepts of mental training that propose that non-judgmental awareness of moment-to-moment experience (ie, mindfulness) may positively affect accuracy of perception, acceptance of intractable health-related changes, realistic sense of control, and appreciation of available life experiences (Kabat-Zinn, 2009; Grossman, 2004).

Objectives: To enhance the QOL of people with MS through mindfulness-based techniques. Methods: The Mindfulness in MS (MiMS) program is a weekly patient program designed to enhance the QOL of people with MS through mindfulness-based techniques. The MiMS program consists of 6 weekly, 1-hour group meetings. The group consists of a maximum of 10 participants. The format includes lectures, discussions, and mindfulness exercises—such as body awareness, breathing, progressive relaxation, meditation, visualization, and hypnosis. The participants are given educational material reflecting the group activities and are encouraged to practice during the week. Auditory and visual aids are utilized. Results: Anecdotally, patients have reported improved ability to cope with stressful life situations and enhanced relaxation. Many participants remark that techniques for stress reduction carry over into their daily lives. Specific mindfulness stress reduction strategies will be presented. Over the next 6 months, the efficacy of the program will continue to be assessed via QOL measures. Conclusions: Mindfulness-based techniques can enhance the QOL of individuals with MS by providing healthy coping skills to manage stress. MiMS can augment the comprehensive care provided to patients with MS.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS, Quality of life management

(CG15) NONPHARMACOLOGIC APPROACH TO DISRUPTIVE BEHAVIORS DUE TO COGNITIVE IMPAIRMENTS
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Background: The Centers for Medicare and Medicaid Services (CMS) has challenged long-term-care facilities to...
increase the use of antipsychotics to manage dementia in the geriatric population. In Massachusetts, an approach called OASIS was instituted in ten pilot facilities. The Boston Home successfully applied to be the 11th facility in this pilot and to try the OASIS approach with a younger population of individuals with cognitive impairments secondary to multiple sclerosis (MS) who exhibited disruptive behaviors and/or behaviors that were difficult for caregivers to manage. **Objectives:** 1) To reduce the number of patients without psychiatric diagnoses who are receiving antipsychotics for disruptive or difficult behaviors. 2) To incorporate behavior-management techniques into the role of all caregivers as a core competency. 3) To reduce the number of patient and/or caregiver concerns expressed to management about difficult interactions between patients and caregivers. **Methods:** 1) Train all staff in OASIS principles and STAR responses modified to address the needs of this population. 2) Establish an OASIS interdisciplinary team to review individual cases, guide care plan changes, and mentor staff. 3) Develop performance standards that reflect core competency in OASIS principles. 4) Create opportunities to celebrate positive OASIS experiences. **Results:** 1) 28% decrease in use of antipsychotics overall and 100% decrease in use of antipsychotics for individuals without psychiatric diagnoses. 2) 85% of all staff (including nonclinical staff) completed 8 hours of training in OASIS principles and STAR responses. 3) An increase in the use of medication with patients and caregivers and staff education and a decrease in disciplinary action as solutions to patient complaints about interactions with staff. 4) Modified OASIS standards are now a standard component of the employee orientation, continuing education, and performance evaluation process. **Conclusions:** Adults with cognitive impairments due to MS respond positively to the OASIS model of behavior management and require less antipsychotic medication when these techniques are used by caregivers. Mediation and education successfully resolve the majority of concerns that arise out of patient and caregiver interactions.

**Supported by:** Mass Senior Care Foundation

**Disclosure:** Nothing to disclose

**Keywords:** MS and the caregiver/family, Nursing management in MS, Psychological issues and MS

(CG16) WHAT DOES THIS SCORE MEAN? A CLINICAL STANDARD-SETTING METHOD APPLIED TO NEURO-QOL OUTCOMES IN A SAMPLE OF INDIVIDUALS WITH MULTIPLE SCLEROSIS

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**Background:** There are few established methods that include qualitative methods to interpret meaningful classifications between standardized patient-reported outcomes.

**Objectives:** To establish clinically relevant classifications for four Neuro-QOL measures (mobility, upper-body function, fatigue, and sleep). **Methods:** We adapted an educational standard-setting methodology, bookmarking, to identify cut-scores for symptom severity based on Neuro-QOL scores. Following this method, clinical “vignettes” were developed at multiple points along the continuum of symptom severity. Each vignette included five Neuro-QOL items selected from the item bank and the corresponding IRT-predicted responses for each item at the specified severity level. Two groups of expert panels were identified: a clinician group, and a group of individuals with multiple sclerosis (MS). Panelists individually rated the vignettes for a given domain by symptom severity. In separate, 1-day, in-person workshops the panel of individuals with MS and the panel of clinicians identified adjacent vignettes they judged to represent the threshold between two levels of severity for a given domain. After an iterative process of discussion, judgment, review of validity evidence, and reconsideration of thresholds, the panel of people with MS and the clinician panel reached consensus on thresholds for each of the four targeted measures. Cut-scores were defined as the mean location for each pair of threshold vignettes. **Results:** People with MS and clinician panels derived identical thresholds for severity levels of mobility and sleep. For the domains of upper extremity and fatigue, there was 75% and 88% concordance, respectively. In every case of divergence, people with MS set higher thresholds for more severe classifications of symptoms (by 0.5 SDs) than did clinicians. **Conclusions:** We adapted a standard-setting exercise commonly used in educational testing to establish interpretation thresholds for four Neuro-QOL measures and achieved strong congruence between panels of people with MS and clinicians about where those thresholds rest for each of the measures.

**Supported by:** National Multiple Sclerosis Society

**Disclosure:** Nothing to disclose

**Keywords:** Neuro-QOL, Psychological issues and MS

(CG17) QUALITY OF LIFE RISK STRATIFICATION IN MULTIPLE SCLEROSIS—AN APPROACH TO MEETING THE NEED

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**Background:** Quality of life (QOL) risk factors in multiple sclerosis (MS) vary among individuals coping with the disease. Just as it became necessary at one time to stratify patients into the category of relapsing-remitting MS, secondary progressive MS, or primary progressive MS, perhaps the time has come at which stratification from a QOL perspective has potential for delivering more focused, comprehensive care. The Total Life Care Clinic (TLC) was established in 2011 at University of Texas Southwestern Medical Center Clinical Center for Multiple Sclerosis in Dallas, Texas. The mission is to comprehensively assess and provide resources for ongoing care to prevent life-threatening events (eg, infection, falls, impaired mobility, psychosocial decompensation) that can lead to hospitalization, increased economic burden, and ultimately decreased QOL for the person with MS. Effective case management promotes individual responsibility, increases patient empowerment, and improves QOL.

**Objectives:** During the implementation of this multidisciplinary program, a risk stratification system was developed in order to more effectively utilize limited health-care resources to offer maximum assistance to as many patients as possible. **Methods:** The TLC team (consisting of nurse practitioner, nurses, social worker, physical therapist, and dietitian) carefully evaluated the needs of each individual participating in the...
Cognitive dysfunction (CD) has been included screens for attention problems, for example, the computerized symbol-digit coding task. Impairments observed in individuals with MS, such as processing speed and attention, are the most common findings among our MS clients during their office visit to identify individuals at risk for cognitive impairment. It is our practice to utilize computer screening in the office to stratify QOL risk factors, a more focused delivery of care can be achieved. We believe that QOL risk stratification has the potential to affect clinical practice as providers attempt to maximize resources needed for complicated coordination of care.

Supported by: None


Keywords: Comprehensive care and MS

**(CG18)** USING COMPUTERIZED SCREENING EFFICIENTLY DURING AN OFFICE VISIT TO IDENTIFY NEUROPSYCHOLOGICAL ISSUES IN PATIENTS WITH MULTIPLE SCLEROSIS AT TEXAS NEUROLOGY

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**Background:** Texas Neurology is in the process of becoming a Center of Excellence for multiple sclerosis (MS), and currently serves approximately 1200 individuals with MS. About 50% of all MS patients experience cognitive dysfunction. In addition, many studies have reported high rates of emotional problems, including depression and anxiety. Our practice decided to utilize computer screening in our MS clients during their office visit to identify individuals with potential cognitive impairment, depression, or anxiety. As processing speed and attention are the most common impairments observed in individuals with MS, we elected to screen patients with the computerized symbol-digit coding task in CNS Vital Signs’ neurocognitive battery. We also included screens for attention problems, depression, and anxiety. **Objectives:** To identify MS clients at risk for cognitive impairment, depression, or anxiety in order to refer them for appropriate treatment. As the physical symptoms of MS are more apparent, emotional and cognitive symptoms may be underreported and undertreated. To provide comprehensive treatment to our patients, we wanted to assess their cognitive and emotional functioning efficiently at an office visit. **Methods:** MS clients will be consented to undergo brief (<10 minutes) computerized screening at their regularly scheduled office visit. They will complete Symbol Digit Coding and Finger Tapping from the CNS Vital Signs neurocognitive battery, as well as the Zung Self-Rating Depression Scale, Zung Self-Rating Anxiety Scale, and Adult ADHD Self-Report Scale Symptom Checklist. If the screen is positive for cognitive impairment, patients will be referred for more comprehensive neuropsychological screening or a full neuropsychological evaluation. If clinically significant levels of anxiety and depression are observed, patients will be referred for medication management and/or cognitive behavioral therapy.

**Results:** Analysis of MS screening data will be presented. **Conclusions:** A brief computerized office screen can be beneficial to identify MS clients at risk for cognitive impairment or emotional dysfunction and assist with comprehensive symptom management. The screen can be an efficient tool to tailor treatment in a Comprehensive MS Center of Excellence and ensure that patients will be referred appropriately to specialists who will discuss risks and benefits of treatment options, identify resources for patients to learn psychosocial coping skills and neurocognitive compensatory strategies, and assist in promoting overall health and wellness.

Supported by: None

Disclosure: Nothing to disclose

**Keywords:** Comprehensive care and MS, Neuropsychology and computer screening in MS, Psychological issues and MS

**(CG19)** COGNITIVE DYSFUNCTION: COMPARISON IN MULTIPLE SCLEROSIS WITH HUMAN CONTROLS

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**Background:** Cognitive dysfunction (CD) has been reported in approximately 60% of patients with multiple sclerosis (MS). CD is a cause of significant disability and affects modalities such as memory and information processing speed (IPS). Establishing CD in MS patients compared to human controls could enable earlier intervention and management of distressing symptoms. **Objectives:** To compare the IPS domain of CD in MS patients with human controls. A secondary objective was to compare the results of IPS from the computerized cognitive testing program (NeuroTrax) to those obtained from the Brief International Cognitive Assessment System (BICAMS). **Methods:** To address the question of the IPS domain of CD between the groups, we utilized two tests: computerized cognitive testing (NeuroTrax) and the BICAMS test battery. Results from other cognitive modalities were measured and IPS was selected for comparison between MS and controls. The NeuroTrax test comprises three levels of timed arithmetic problem sets to measure IPS. The Symbol Digit Modalities Test (SDMT) from the BICAMS test was used to evaluate IPS. There were 28 MS patients age-matched to 28 controls in the study. **Results:** The cohort (n = 28 MS patients) included 86% females. The cohort age ranged from 25 to 56 years, with a mean age of 41.5 (SE = 9) years. The duration since MS diagnosis ranged from 1 to 26 years. Data were analyzed by paired t test to measure the difference in IPS of MS patients compared to controls. We found significant differences in IPS between MS patients and controls that are detectable by both the BICAMS and NeuroTrax tests (P < .0001). We observed a strong correlation (r = 0.57) between the BICAMS and NeuroTrax tests when measuring the IPS modality. **Conclusions:** The study

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reveals significant differences in the IPS domain between MS patients and controls as demonstrated by the BICAMS and NeuroTrax tests. Our study is unique due to utilization of both the BICAMS and NeuroTrax tests and the comparison of MS patients to human controls. It reinforces the existing literature regarding CD in MS. The findings can be applied clinically to anticipate deficits and intervene early in the course of MS.

Support: None
Disclosure: Nothing to disclose
Keywords: Comprehensive care and MS, Human controls, Psychological issues and MS

(CG20) COGNITIVE EVOLUTION IN TYSABRI (NATALIZUMAB)-TREATED MULTIPLE SCLEROSIS PATIENTS

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Background: Cognitive dysfunction affects 40% to 60% of multiple sclerosis (MS) patients and progresses over time. Natalizumab has been shown to be superior to placebo in preserving cognitive function for the first 2 years of therapy.

Objectives: The objectives are to understand the impact of natalizumab on cognition beyond 2 years of therapy and investigate whether baseline characteristics are predictive of clinical response. Methods: This is a single-center, 24-month, observational study. 63 patients treated with natalizumab were assessed prior to monthly infusions using the Cogstate battery and Symbol Digit Modalities Test (SDMT). The Beck depression questionnaire was also administered at baseline and every fourth month prior to infusion. Patient demographics, MS treatment history, Expanded Disability Status Scale (EDSS), Multiple Sclerosis Severity Scale (MSSS), and natalizumab treatment duration were collected at baseline. Patients with cognitive impairment from other causes were excluded. A linear mixed model was conducted with time on natalizumab (4 years, n = 12) as a between-subjects factor, time point as a within-subjects factor, and age, EDSS, type of MS, and number of prior drug treatments as covariates. The current data are from the 12-month interim analysis.

Results: Irrespective of time on natalizumab, significant improvements were observed in executive function (P < .0001), verbal memory (P < .0001), and working memory (P < .0001), whereas processing speed (P = .19) and attention (P = .15) remained unchanged. Only one patient had clinically meaningful decline, defined as a decline of 1 or more standard deviations over 3 consecutive months on two or more Cogstate tests. Conclusions: Interim analysis suggests that natalizumab can preserve cognitive function and the ability to learn beyond 2 years of continuous therapy.

Supported by: Biogen Idec

Keywords: Cognitive function in MS, Disease-modifying treatments in MS, Psychological issues and MS

(CG21) MRI AND CSF ANALYSIS OF COGNITIVE IMPAIRMENT IN MULTIPLE SCLEROSIS

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Background: Forty percent to 60% of multiple sclerosis (MS) patients experience cognitive decline, particularly in the areas of complex attention, information processing speed, episodic memory, and executive function. Studies utilizing magnetic resonance imaging (MRI) suggest that the severity of cognitive decline may be related to the degree of brain atrophy, although the correlation is not strong, suggesting complex factors in the pathogenesis of cognitive dysfunction in MS. Cerebrospinal fluid (CSF) biomarkers of neurodegeneration have been analyzed for different types of dementia, such as Alzheimer’s dementia. These markers, such as A-beta-42 protein and Tau, have not been evaluated in MS patients. Additionally, inflammatory CSF markers, such as interferon-alpha (IFN-alpha), have been associated with cognitive dysfunction in, for example, HIV-associated neurocognitive disorders (HAND). It is possible that these biomarkers, in conjunction with certain brain MRI findings, may predict the severity of cognitive decline in relapsing-remitting MS patients.

Objectives: The purpose of this ongoing study is to identify brain MRI patterns and CSF biomarkers in cognitively impaired relapsing-remitting MS patients.

Methods: NeuroQuant® software will be used to measure various aspects of brain atrophy, for example, hippocampal volume. Double inversion recovery (D) SPACE will be used to evaluate gray matter lesion load, and diffusion kurtosis imaging (DKI) will be used to evaluate white matter integrity at 3.0 Tesla. CSF analysis will include measurement of A-beta-42 protein, Tau, IFN-alpha, and other neurodegenerative and inflammatory markers.

Results: Data are currently being collected for this study. We hypothesize that cognitively impaired relapsing-remitting MS patients will have a greater degree of hippocampal atrophy, greater gray matter lesion volume, and greater reductions in white matter fractional anisotropy on MRI. Also, these patients will have greater levels of CSF inflammatory and neurodegenerative biomarkers compared to MS patients who are not cognitively impaired.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Imaging and MS, Immunology and MS, Psychological issues and MS

(CG22) THERAPEUTIC DOCUMENTARIES OF PEOPLE WITH MULTIPLE SCLEROSIS AND THE EFFECTS ON THEIR FAMILIES IN ZIMBABWE

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Background: This research project focuses on people with multiple sclerosis (MS), relating their success stories and challenges faced in living with MS in Zimbabwe, where there is no access to disease-modifying therapies (DMTs). It profiles the lived experiences of people with MS and the impact on their families, such as how the nonaffected family members can at times suffer from even more stress, anxiety, or depres-
It is unknown, however, how intellectual enrichment affords this benefit. Herein we investigate whether working memory capacity (WMC) is the mechanism through which higher intellectual enrichment helps to preserve memory. Working memory is the system involved in the control, regulation, and maintenance of only a limited amount of information, and WMC is a useful individual difference metric that is highly correlated with intelligence. **Objectives:** The aim of the present study was to investigate whether WMC can explain the relationship between intellectual enrichment and long-term memory, thereby helping to explain mechanisms of cognitive reserve. **Methods:** The sample consisted of 75 (65 female) patients diagnosed with MS. The average age was 49.45 (±9.76) years, with an average of 15.33 years of education. Intellectual enrichment, long-term memory, and WMC were estimated using the standardized scores of the WTAR, delayed recall of the HVLT-R, and Digit Span Total from the WAIS-IV, respectively. We investigated this hypothesis using a mediation analysis by conducting a series of simple and multiple hierarchical linear regressions and testing for mediation with a Sobel test. **Results:** Intellectual enrichment significantly predicted long-term memory ($b = .300$, $P = .009$) and the mediator, WMC ($b = .148$, $P < .001$). WMC significantly predicted long-term memory ($b = 1.57$, $P < .001$). In the final step, WMC fully mediated the relationship between intellectual enrichment ($b = .122$, $P = .37$) and long-term memory ($b = .127$, $P = .03$); the Sobel test of mediation was significant ($Z = 2.99$, $P = .003$). **Conclusions:** Through an exploratory mediation analysis, the present findings suggest that WMC fully mediates the relationship between intellectual enrichment and long-term memory in MS. Future research will be necessary to explicate any type of causal relationship between these variables. The present findings are an initial step in understanding the relationship between intellectual enrichment, working memory, and long-term memory.

**Supported by:** National Institutes of Health grant R00 HD060765 (JFS), National Multiple Sclerosis Society Postdoctoral Fellowship Grant MB0024 (IS)

**Disclosure:** Nothing to disclose

**Keywords:** Cognition, Psychological issues and MS

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**CG23** Working Memory Mediates the Relationship Between Intellectual Enrichment and Long-Term Memory in Multiple Sclerosis: An Exploratory Analysis of Cognitive Reserve

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**Background:** Roughly half of individuals with multiple sclerosis (MS) show signs of memory impairment, including decline in long-term memory. The cognitive reserve hypothesis states that people with greater lifetime intellectual enrichment (frequently estimated using indices of premorbid verbal intelligence) are protected against disease-related memory decline.

**Methods:** It is unknown, however, how intellectual enrichment affords this benefit. Herein we investigate whether working memory capacity (WMC) is the mechanism through which higher intellectual enrichment helps to preserve memory. Working memory is the system involved in the control, regulation, and maintenance of only a limited amount of information, and WMC is a useful individual difference metric that is highly correlated with intelligence. **Objectives:** The aim of the present study was to investigate whether WMC can explain the relationship between intellectual enrichment and long-term memory, thereby helping to explain mechanisms of cognitive reserve. **Methods:** The sample consisted of 75 (65 female) patients diagnosed with MS. The average age was 49.45 (±9.76) years, with an average of 15.33 years of education. Intellectual enrichment, long-term memory, and WMC were estimated using the standardized scores of the WTAR, delayed recall of the HVLT-R, and Digit Span Total from the WAIS-IV, respectively. We investigated this hypothesis using a mediation analysis by conducting a series of simple and multiple hierarchical linear regressions and testing for mediation with a Sobel test. **Results:** Intellectual enrichment significantly predicted long-term memory ($b = .300$, $P = .009$) and the mediator, WMC ($b = .148$, $P < .001$). WMC significantly predicted long-term memory ($b = 1.57$, $P < .001$). In the final step, WMC fully mediated the relationship between intellectual enrichment ($b = .122$, $P = .37$) and long-term memory ($b = .127$, $P = .03$); the Sobel test of mediation was significant ($Z = 2.99$, $P = .003$). **Conclusions:** Through an exploratory mediation analysis, the present findings suggest that WMC fully mediates the relationship between intellectual enrichment and long-term memory in MS. Future research will be necessary to explicate any type of causal relationship between these variables. The present findings are an initial step in understanding the relationship between intellectual enrichment, working memory, and long-term memory.

**Supported by:** National Institutes of Health grant R00 HD060765 (JFS), National Multiple Sclerosis Society Postdoctoral Fellowship Grant MB0024 (IS)

**Disclosure:** Nothing to disclose

**Keywords:** Cognition, Psychological issues and MS

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**CG24** Patient Anxiety About Contracting Progressive Multifocal Leukoencephalopathy While Treated with Natalizumab

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**Background:** Multiple sclerosis (MS) patients treated with natalizumab experience varying levels of anxiety about contracting progressive multifocal leukoencephalopathy (PML). **Objectives:** To determine whether patients’ anxiety levels about contracting PML while treated with natalizumab are related to their objective risk for PML and/or their level of psychosocial support from the infusion group and nursing staff. A possible correlation with demographic and other clinical characteristics was also evaluated. **Methods:** 75 MS patients treated with natalizumab at the Winthrop Comprehensive MS Care Center in Mineola, New York, were surveyed in June 2013. Infusions were given in a...
Case reviews illustrate progressive aphasia, MS and Huntington's disease, in presentation to MS. We present a case of a patient with a diagnosis of a second neurodegenerative disease similar to MS. We describe three cases, and psychiatric problems, in an attempt to highlight the overlap in psychiatric symptoms in the relative rarity of comorbidity of the diagnoses and emphasize the benefit of integrated behavioral medicine throughout diagnosis and treatment. Objectives: To describe three cases of patients with rare comorbid MS and second neurodegenerative disease; to highlight the overlap in psychiatric symptoms in the relative rarity of comorbidity of an MS diagnosis and a second neurodegenerative disease; to emphasize the benefit of integrated behavioral medicine throughout diagnosis and treatment. Methods: Case review of patient with MS and Huntington’s disease, a patient with MS and primary progressive aphasia, and a patient with MS and parkinsonism. Results: Case reviews illustrate enhanced benefit of integrated behavioral medicine in caring for patients with complex neurologic conditions presenting with concomitant cognitive, behavioral, and emotional disturbances. Conclusions: Behavioral medicine played a significant role in each of these cases. However, behavioral medicine integrated into the care team was present only in the case of the patient with Huntington’s disease. The other two cases had contact with psychology and neuropsychology services through independent outside providers and had records forwarded for treatment by neurology teams, often limiting the availability of direct consultation between providers. Behavioral medicine as part of a care team can be especially helpful with assessing the emotional and cognitive symptoms in relationship with neurologic symptoms, and developing a treatment strategy that is informative to the other disciplines while considering the needs of the patient. This can lead to a faster and more accurate diagnostic picture and provides a framework for treatment as symptoms change in a timely manner.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Comprehensive care and MS, Psychological issues and MS

(CG26) EFFECTS OF COGNITIVE-BEHAVIORAL TREATMENT FOR INSOMNIA ON INSOMNIA, DEPRESSION, AND FATIGUE IN PATIENTS WITH MULTIPLE SCLEROSIS
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Background: The prevalence of sleep disorders among patients with multiple sclerosis (MS) is high. According to a recent survey of approximately 7700 individuals with MS, over half (56%) reported sleep disturbances, including insomnia (Tyrer et al., 2013). Insomnia, or difficulties with initiating or maintaining sleep, is linked with deleterious effects on both physical and mental health. Several studies have demonstrated significant relationships among insomnia, fatigue, and depression for people with MS (Bamer et al., 2010; Fleming & Pollak, 2005; Merlino et al., 2009; Najafi et al., 2013; Stanton et al., 2006). To date, however, no research has examined the effects of psychotherapeutic treatment that targets sleep disorders within this population. Objectives: The purpose of this research is to evaluate the effectiveness of cognitive-behavioral therapy for insomnia (CBT-I) for patients with MS. In accordance with the literature that links insomnia with higher rates of depression and fatigue within

Disclosures: Nothing to disclose.
this population, this study will examine the effects of CBT-I on individuals’ experiences of insomnia, depression, and fatigue. **Methods:** A retrospective outcome data analysis will be conducted for patients with MS who have participated in individual or group CBT-I at the Neurological Institute’s Sleep Disorders Center at the Cleveland Clinic Foundation (CCF). The proposed sample will include all patients with a diagnosis of both MS and insomnia who participated in individual or group CBT-I sessions at CCF’s Sleep Disorders Center between 2008 and 2013. Scores from several self-report measures—Patient Health Questionnaire (PHQ-9), Fatigue Severity Scale (FSS), and Insomnia Severity Index (ISI)—will be used to assess depression, fatigue, and insomnia, respectively, at pre- and post-treatment intervals. **Results:** The data analysis is in progress. Results will be provided at the 2014 CMSC conference. **Conclusions:** Conclusions will be provided at the 2014 CMSC conference.

**Supported by:** None

**Disclosure:** Nothing to disclose

**Keywords:** Psychological issues and MS, Sleep

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**(CG27) BRIEF INTERNATIONAL COGNITIVE ASSESSMENT FOR MULTIPLE SCLEROSIS TABLET APPLICATION**

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**Background:** Approximately 50% of individuals with multiple sclerosis (MS) develop cognitive impairment. Early detection of cognitive difficulties may lead to improved outcomes. Self-report is often used to screen for cognitive dysfunction, but metacognition is often impaired. Thus, objective tests are the best way to diagnose and track cognitive change over time. However, neuropsychological evaluations are expensive and time-consuming and require neuropsychologists for interpretation. Therefore, the BICAMS, a truncated battery with strong psychometrics (sensitivity 94%, specificity 86%), was developed as a way for MS medical personnel without training in neuropsychology to track cognition over time. Despite the BICAMS strengths, there are barriers preventing providers from adopting this recommended assessment. Although the original intent of the BICAMS was to create an intuitive assessment for non-neuropsychologists, the scoring and interpretation require precious clinic time and necessitate an understanding of psychometric information such as z scores and percentiles. The increasing emphasis on paperless systems may also render paper administration of the BICAMS obsolete. Given that tablet computers [eg, iPad] are common in many medical facilities, this technology has the potential to make the BICAMS accessible to providers. **Objectives:** To test the reliability of a BICAMS “app” that will reduce administration time, allow for quick and easy scoring, and provide interpretation of test scores. **Methods:** This CMSC-funded pilot study will enroll 100 participants with MS (two groups, N = 50). **Interrater and parallel forms reliability** is assessed using two test administrators scoring participant responses simultaneously—one on the paper BICAMS and the other on the BICAMS app. Half of the testing sessions are led by the paper administrator (Group A) and half by the app administrator (Group B). **Concurrent validity** is assessed using an analogous design. Although participants are only exposed to the material once, participant responses are recorded on both administration methods. Intraclass correlations will be used to examine the agreement between scores from Groups A and B. A Bland-Altman plot will be used to examine difference across the continuum of cognitive function (ie, whether the agreement is consistent across cognitive function). **Results:** This study is a work in progress; data collection is underway. **Conclusions:** Preliminary results will be presented at the 2014 CMSC annual meeting.

**Supported by:** CMSC

**Disclosure:** Meghan Beier, Kevin Alschuler, Dawn Ehde: Nothing to disclose. Dagmar Amtmann: Acorda (consulting fees).

**Keywords:** Neuropsychological assessment

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**(CG28) A PROSPECTIVE MULTICENTER STUDY FOR ASSESSING THE VALIDITY OF THE MUSIQOL INSTRUMENT AMONG ARABIC-SPEAKING PATIENTS WITH MULTIPLE SCLEROSIS**

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**Background:** The Multiple Sclerosis International Quality of Life (MusiQOL) questionnaire has previously been validated in other languages, but so far no tool for assessing quality of life (QOL) in patients with multiple sclerosis (MS) has yet been validated in the Arabic language. **Objectives:** To prospectively assess correlations between MusiQOL scores and disease activity (Expanded Disability Status Scale; EDSS) and progression (annualized relapse rate; ARR) over 12 months in Arabic-speaking patients with MS treated with the serum-free formulation of subcutaneous (SC) interferon beta-1a (IFNβ-1a). **Methods:** This prospective, international, multicenter cohort study recruited Arabic-speaking patients with MS who had been treated with serum-free SC IFNβ-1a for ≥6 months prior to entering the study. Patients’ disease characteristics were assessed at baseline, month 6, and month 12. The MusiQOL questionnaire was administered at baseline and month 12. Changes from baseline in MusiQOL total and subdomain scores were compared using the paired t test. Correlations between changes in these scores from baseline and important clinical parameters were analyzed using the Pearson correlation coefficient and the point-biserial correlation coefficient. **Results:** A total of 152 patients were included: 65.13% were female; mean (SD) age was 33.52 (0.85) years; mean MS duration, 4.4 (0.33) years; and mean baseline EDSS score, 2.04 (0.11). Mean (SD) MusiQOL total score was 65.55 (1.31) at baseline and 66.79 (1.32) at month 12 (P = .28). There was no correlation between MusiQOL total score and ARR (r = –0.11, P = .17), but ARR was negatively correlated with change from baseline in the MusiQOL symptom domain (r = –0.28, P < .01). There was no correlation between change from baseline in MusiQOL total score and EDSS score at month 12 (r = –0.11, 0.1733). **Conclusions:** These findings suggest that QOL, as assessed by the Arabic-language version of MusiQOL, cap-
CG29 Predictors of Institutionalization for People with Multiple Sclerosis

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Background: Multiple sclerosis (MS) is a chronic, progressive disease of the central nervous system. While the disease course is highly variable, a significant portion of people with MS may spend more than 10 years living with severe disability, and many of those will eventually require full-time institutional care. Despite the high personal and economic costs of this care, little is known about predictors of institutionalization.

Objectives: Identify predictors of institutionalization among people with MS.

Methods: Longitudinal data from a university MS clinic database were extracted to explore nursing home placement of an urban subgroup. Cox regression analysis was performed with potential predictors including age at MS onset and sex, as well as measures obtained at the first MS clinic assessment: MS course, Expanded Disability Status Scale (EDSS) score, and disability in specific functional systems.

Results: Older age at onset and higher baseline scores in specific functional systems (cerebellar, bowel/bladder, brainstem, and cerebral/mental) were significant predictors of nursing home placement.

Conclusions: Patients with older age at MS onset and those with impairment in specific functional systems (cerebellar, bowel/bladder, brainstem, and cerebral/mental) during their disease course may be at higher risk for future institutionalization. Further research is needed to confirm these findings and to improve efforts to monitor and minimize the institutionalization of people with MS.

Supported by: University of Saskatchewan Dean’s Summer Student Award

Keywords: MS and the caregiver/family, Nursing management in MS

CG30 Clinical Practice Guideline on Assessment and Management of Psychiatric Disorders in Individuals with Multiple Sclerosis

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Background: Individuals with multiple sclerosis (MS) are at increased risk of emotional disorders. If these disorders are not detected and treated, they can worsen functioning and quality of life, interfere with adherence to treatments for MS, and increase the risk of suicide. Since most MS patients are in regular contact with neurologists and/or primary-care physicians, providing guidance on improving detection, diagnosis, and treatment practices should help prevent or reduce these negative outcomes.

Objective: To disseminate evidence-based recommendations for screening, diagnosing, and treating psychiatric disorders in individuals with MS.

Methods: We reviewed the literature from 1950 to August 2011 and evaluated the evidence according to AAN guideline standards.

Results: Weak evidence shows that certain screening tools may help identify emotional disorders in individuals with MS: the CNS Emotional Lability Scale for pseudobulbar affect (PBA), the Beck Depression Inventory and a two-question tool for depressive disorders, and the General Health Questionnaire for broadly defined emotional disturbances. The evidence is not sufficient to support or refute the usefulness of other screening tools, diagnostic instruments, or clinical procedures or the impact of somatic/vegetative symptoms on the accuracy of screening tools and diagnostic instruments. Weak evidence shows that certain treatments may be effective for emotional disorders in individuals with MS: a 16-week program of individual telephone-administered cognitive-behavioral therapy (T-CBT) for treating depressive symptoms; dextromethorphan/quinidine for PBA. Clinicians may consider a telephone-administered CBT program for treating depressive symptoms (Level C). Although pharmacologic and nonpharmacologic therapies are widely used to treat depressive and anxiety disorders in individuals with MS, evidence is insufficient to support or refute the use of the antidepressants and individual and group therapies reviewed here (Level U). For PBA, a combination of dextromethorphan and quinidine may be considered (Level C). Evidence is insufficient to determine the psychiatric effects in individuals with MS of disease-modifying and symptomatic therapies and corticosteroids; risk factors for suicide; and treatment of psychotic disorders (Level U). Research is needed on the effectiveness in individuals with MS of pharmacologic and nonpharmacologic treatments commonly used in the non-MS population. There is evidence supporting the effectiveness of some pharmacologic therapies for depressed mood and anxiety in people without MS. Many of these therapies have not yet been studied exclusively in the MS population. Despite

Supported by: University of Toronto, University of California, San Diego, National Institute of Mental Health, National Multiple Sclerosis Society

Disclosure: Nothing to disclose

Keywords: CG29 Predictors of Institutionalization for People with Multiple Sclerosis, CG30 Clinical Practice Guideline on Assessment and Management of Psychiatric Disorders in Individuals with Multiple Sclerosis
lack of evidence in individuals with MS, these therapies are commonly used to treat emotional disorders in this population. The guideline is limited to the studies that meet AAN levels of quality for analysis. Much more research is needed in this area. Examples of studies that could provide evidence to improve detection, diagnosis, and treatment practices include the following: For screening and diagnosis, head-to-head comparisons of screening tools and diagnostic instruments to determine which best identify particular emotional symptoms (eg, depressed mood, anxiety) and emotional disorders (eg, major depressive disorder, adjustment disorder); evaluations of methods to train MS clinicians to identify emotional disorders, educate individuals with MS and family members to recognize emotional symptoms, and encourage open discussion of these problems; comprehensive evaluations of screening initiatives including feasibility, cost, use of results, and outcomes; comparisons of methods to distinguish, in an individual, sources of somatic and neurovegetative symptoms that could be attributed to both an emotional disorder and MS; assessments of instruments to screen for and diagnose euphoria, apathy, and emotional dysregulation; appraisals of standard screening and diagnostic instruments to identify and determine the prevalence of other psychiatric disorders among individuals with MS. For treatment, large, methodologically rigorous, randomized, placebo-controlled studies to evaluate nonpharmacologic and pharmacologic therapies with strong evidence of efficacy and widespread use for treating emotional disorders in individuals without MS. Examples include double-blind, comparative-effectiveness trials of commonly used antidepressants with attention to their impact on outcomes of different types of emotional symptoms and disorders, MS impairments (eg, physical, cognitive), and concurrent MS treatments; targeted comparative-effectiveness trials for commonly used types of nonpharmacologic interventions (eg, CBT, psychotherapy) and different approaches (eg, individual vs. group, telephone vs. in-person); systematic examinations of combinations of pharmacologic and nonpharmacologic therapies (and combinations within modalities). Other treatment studies could include replication of findings of safety and efficacy of DM/Q for PBA in individuals with MS and head-to-head comparisons with other currently used therapies; assessments of treatment options for euphoria, apathy, and emotional dysregulation; evaluations of health-care services for individuals with MS designed to optimize identification and treatment of mental disorders; appraisals of telemedicine technologies among individuals with MS who are housebound, have difficulty traveling, or live in remote communities. Areas for which there were no studies of sufficient quality to produce recommendations included those related to effective treatments for psychotic disorders in individuals with MS. Clinical evaluation procedures and screening and diagnostic instruments can be used to accurately distinguish between MS fatigue and depression in individuals with MS. What are the effects of disease-modifying agents (DMAs) on mood and affect in individuals with MS? What are the effects of steroids on mood and affect in individuals with MS? What are the effects of symptomatic treatments on mood and affect in individuals with MS? What are the risk factors for suicidal thinking and behavior among individuals with MS? We included these questions at the outset because they are clinically relevant: Individuals with MS may have psychotic disorders and require treatment. Clinicians may have difficulty determining whether fatigue, for example, is due to MS or depressed mood and therefore selecting appropriate treatment. Individuals with MS may experience emotional symptoms while taking DMAs, steroids, and symptomatic agents, and may become suicidal. We reviewed studies on these issues, but none met criteria to support recommendations. Neurorologists, individuals with MS, and families would welcome well-designed investigations of the effects of interferons on mood. They would also benefit from knowing whether particular characteristics of individuals with MS might predict suicide. Cognitive and emotional disorders co-occur, and it can be difficult to determine the source of inattention, distractibility, slowed thought processing, and difficulty concentrating. Further research is needed on screening, diagnosing, and distinguishing these disorders and on effective treatments when they co-occur. We reviewed only studies of adults with MS. Future research should address emotional disorders in children and adolescents with MS, including comparisons with adults with MS and children and adolescents without MS.

Supported by: None


Keywords: Comprehensive care and MS, Psychological issues and MS

(CG31) SYMBOL DIGIT MODALITIES TEST IS MORE SENSITIVE THAN PASAT TO DEMONSTRATE THE CORRELATION BETWEEN COGNITIVE IMPAIRMENT AND WALKING DISABILITY

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Background: Cognitive deficit can be an early feature in the course of multiple sclerosis (MS). One of the most common cognitive impairments documented based on neuropsychological testing in MS involves cognitive processing speed. The Multiple Sclerosis Walking Scale–12 (MSWS-12) has been a commonly used patient-reported outcome for measuring walking impairment in research involving MS, based on the strength and breadth of evidence for the construct validity of its scores. The evidence for its construct validity is largely based on associations with other ambulatory-based outcomes such as the Timed 25-Foot Walk (T25FW) and Expanded Disability Status Scale (EDSS). Performance on measures of processing speed, particularly the Symbol Digit Modalities Test (SDMT) and Paced Auditory Serial Addition Test (PASAT), has been associated with walking outcomes in MS patients.

Objectives: The aim of the present study was to investigate the relationship between cognitive impairment and walking disability.

Methods: 71 MS patients (54 female) who completed the MSWS-12 underwent a neurologic examination and completed the SDMT, PASAT, and T25FW.

Results: The SDMT was significantly correlated with MSWS-12 scores (r = −0.602, P = .002), T25FW (r = −0.512, P = .016), and EDSS (r = −0.368, P = .042). The PASAT was also significantly correlated with the MSWS-12 (r = −0.455, P = .008) and T25FW (r = −0.360, P = .045). There was no significant correlation between the PASAT and EDSS (P = .0124, P = .074). There were statistically significant correlations between the MSWS-12 and the T25FW (r = 0.690, P = .001) and
EDSS ($r = 0.896$, $P = .000$). Conclusions: Our results demonstrated that both the SDMT and PASAT were correlated with walking impairment. The SDMT seems to be more sensitive than the PASAT regarding demonstration of the correlation between cognitive impairment and walking disability.

Supported by: None

Keywords: Psychological issues and MS

(CG32) ARTS FOR HEALTH: VISUAL PERSPECTIVES IN MULTIPLE SCLEROSIS
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Background: In 2013, the John Hunter Hospital Multiple Sclerosis (MS) Clinic in Australia facilitated an alternative type of support group, an art workshop. The theme for the workshop was Emerging Images. Objectives: The poster will discuss using art as a means to health and wellness, review the literature about art in the health arena, and illustrate the benefits of this alternative type of support group. This project also draws on the personal experience of participating in the workshop, in a small thematic analysis. Methods: People who attended the MS Clinic were invited to participate in the workshop, a program that lasted 6 weeks and culminated in the creation of personal and collaborative pieces of art. The weekly sessions were facilitated by an established artist who encouraged the small group to draw on their experience of having MS in creating their pieces. The works were exhibited in the annual Arts for Health MS Awareness Exhibition. Conclusions: This poster will describe a unique support program and discuss using art and creating art for wellness. More primary health facilities use art to promote health issues and encourage an illuminating, diverting, and soothing environment. In the MS arena, it provides an opportunity to share artful ideas, to be socially connected, and to support one another in their experience of MS.

Supported by: Genzyme
Disclosure: Bayer, Biogen Idec, BioCSL, Genzyme, Novartis, Merck Serono (MS Clinic support); Novartis (consulting fees)

Keywords: Psychological issues and MS, Support network in MS

DISEASE MANAGEMENT, MECHANISMS, AND TREATMENT

(DX07) GOOD TREATMENT ADHERENCE IS MAINTAINED IN MULTIPLE SCLEROSIS PATIENTS USING REBISMA: ASSESSMENT OF THE MEASURE PRIMARY ENDPOINT

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Background: Poor treatment adherence in patients with multiple sclerosis (MS) may be associated with increased risk of severe relapse. RebiSmart® is the first electronic autoinjector for subcutaneous interferon beta-1a (IFN) treatment of relapsing MS (RMS) and was designed to reduce several barriers to optimal treatment adherence. Objectives: We evaluated adherence over 24 weeks to a regimen of subcutaneous IFN, self-injected thrice-weekly by treatment-naive patients with RMS. Here we present the final analyses of the MEASURE study primary and secondary endpoints at week 24. Methods: MEASURE (NCT01128075) was a multicenter, two-arm, noncomparative, observational, 96-week phase 4 study. Data from only the treatment-naive arm are presented here. The primary endpoint was the proportion of treatment-naive subjects at week 24 who were adherent to treatment, defined as having administered ≥80% of scheduled injections, as recorded in the RebiSmart injection log. Treatment adherence was calculated as 100 x the number of administered injections, divided by the expected number of injections (72 injections). Subjects who discontinued treatment before week 24 were included in the analyses of 24-week adherence, with all injections scheduled after discontinuation considered missed injections. A cutoff of ≥80% was defined as good adherence to treatment. Treatment compliance, persistence, and fear of injection were also assessed to week 24. Fear of injection was measured on a scale of 1 (not fearful) to 5 (greatly fearful). Subjects were considered less fearful if their score declined by 1 point or more. Results: Final results show that 82.9% (95% confidence interval [CI], 76.2-88.0%) of patients (n = 158) were ≥80% adherent at 24 weeks. The proportion of patients with ≥80% compliance to treatment was 92.4% at week 24, and the mean (±SD) compliance rate was 95.2 ± 9.7 at week 24. Only 22 (13.9%) patients discontinued treatment by the 24th week. At baseline, 48.3% of patients reported at least a moderate fear (score of 3 on a scale of 1 to 5) of injection. By week 24, 69.9% of patients became less fearful of injection, compared to baseline. The proportion of patients who were ≥80% adherent at week 24 was similar for patients with and without injection fear at baseline (81.5% vs. 84.2%, respectively; $P = .678$). Conclusions: RebiSmart® is an effective device to maintain good adherence, compliance, and persistence on treatment.

Supported by: EMD Serono

Keywords: Adherence, Interferon beta

(DX08) REBISMA PRESSURE PROFILE ACCESSORIES CAN REDUCE INJECTION-SITE PAIN

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Background: Injection pain may compromise treatment adherence in patients with multiple sclerosis (MS). RebiSmart® is the first electronic autoinjector for subcutaneous interferon beta-1a (IFN) treatment of relapsing MS and was designed to reduce several barriers to optimal treatment adherence. However, a minor proportion of patients still experience injection pain. The RebiSmart® electronic autoinjector is not currently approved by the US Food and Drug Administration.
Background: The BENEFIT study examined the effects of early versus delayed treatment with interferon beta-1b (IFNβ-1b) for patients with clinically isolated syndrome (CIS). In prior analyses, dichotomized 25-hydroxyvitamin D (25[OH]D) classes contributed to the prediction of rate of conversion to clinically definite multiple sclerosis (CDMS), MS activity, and rate of progression up to 5 years after CIS in patients starting IFNβ-1b treatment at the CIS or after conversion to CDMS. Objectives: To examine the predictive effects of continuous 25[OH]D concentrations on conversion to CDMS, conversion to McDonald MS (MDMS), rate of newly active lesions, relapse rate, T2 volume, and brain volume by assessing changes in these variables from year 1 to year 5. Results: 216 patients had 25(OH)D measurements at both 6 and 12 months. Each 50 nmol/L (20 ng/ ml) increase in 25(OH)D led to a lower probability of conversion to MDMS (hazard ratio [HR], 0.43; 95% confidence interval [CI], 0.22-0.84; P = .01), with a trend toward lower probability of conversion to CDMS (HR, 0.48; 95% CI, 0.22-1.04; P = .06). Rates of newly active lesions (rate ratio [RR], 0.31; 95% CI, 0.15-0.61; P = .0008) and relapses (RR, 0.38; 95% CI, 0.14-0.99; P = .048) also decreased with increasing 25(OH)D levels. Annual percent change in T2 volume (−26%; 95% CI, −39% to −12%; P = .0007) and brain volume (0.64%; 95% CI, 0.08%-1.2%; P = .02) were lower with each incremental increase in 25(OH)D. Conclusions: Among patients who started IFNβ-1b treatment right after CIS, incremental increases in 25(OH)D levels were associated with reduction of long-term MS activity and severity. These findings suggest a potential benefit of monitoring and managing vitamin D levels (eg, through supplementation) in early MS patients treated with IFNβ-1b.

Supported by: Bayer HealthCare Pharmaceuticals

Disclosure: Alberto Ascherio, Almirall, Roche, Sanofi-Aventis, Serono (consulting fees); Kassandra Munger, Kelly C. Simon: Nothing to disclose. Richard A. White: Bayer Schering Pharma (consulting fees). Karl Köchert: Bayer Pharma AG (consulting fees). Chris H. Polman: Biogen Idec; Bayer Schering Pharma AG, Teva Pharmaceutical Industries, Merck Serono, MorphoSys, Novartis Pharmaceuticals Corporation, GlaxoSmithKline, Actelion Pharmaceuticals Ltd, UCB, ReceptoRoche (consulting fees); Bayer Schering, Biogen Idec, Merck Serono, Teva, Novartis, GSK, Roche (grant/research support). Mark S. Freedman: Actelion, Bayer HealthCare, Biogen Idec, Celgene, EMD Canada, Genzyme, Glycominds, Hoffmann-LaRoche, Merck Serono, Novartis, Opera, Sanofi-Aventis, Teva Canada Innovation (consulting fees); Bayer HealthCare, Genzyme (grant/research support); Genzyme (speaking fees). Hans-Peter Hartung: Bayer Pharma AG, Biogen Idec, Genzyme, Merck Serono, Novartis, Roche, Teva, Sanofi-Aventis (consulting fees, speaking fees). David H. Miller: Biogen Idec, GlaxoSmithKline, Novartis, Merck, Chugai, Mitsubishi Pharma Europe, Bayer Pharma AG (consulting fees); GlaxoSmithKline, Biogen Idec, Novartis, Merck (grant/research support). Xavier Montalbán: Bayer, Biogen Idec, EMD, Genentech, Genzyme, Merck Serono, Neurotec, Novartis, Sanofi-Aventis, Teva Pharmaceuticals, Almirall (consulting fees, speaking fees, travel expenses).

Gilles Edan: Bayer Pharma AG, Biogen Idec, Merck Serono, Sanofi-
Aventis (consulting fees, speaking fees); Serono, Teva (grant/research support); Frederik Barkhof; Bayer Pharma AG, Biogen Idec, Merck Serono, Novartis, Sanofi-Aventis, Genzyme, Roche, Teva (consulting fees); Dutch Foundation for MS Research (grant/research support). Dirk Pleines, Rupert Sandborn; Christoph Podl; Bayer AG, the owner of Bayer Pharma AG/Bayer HealthCare Pharmaceuticals (ownership interest). Dirk Pleines; Bayer Pharma AG/Bayer HealthCare Pharmaceuticals (consulting fees); Ernst W. Radus; Actelion, Basel Pharma Research Ltd, Biogen Idec, Merck Serono, Novartis (grant/research support); Novartis, Biogen Idec, Merck Serono, Bayer Schering (consulting fees; speaking fees). Ludwig Kappos; Actelion, Bayer HealthCare, Bayer Schering, Biogen Idec, BioMarin, C.L.C. Behring, Eli Lilly, Genentech, Genmab, GlaxoSmithKline, Lilly, Merck Serono, Novartis, Novo Nordisk, Peptimmune, Sanofi-Aventis, Santhera, Roche, Teva, UCB, Wyeth (consulting fees, grant/research support).

Keywords: Disease-modifying treatments in MS, Vitamin D

**(DX10) TERIFLUNOMIDE AFFECTS THE IMMUNE SYSTEM AND DOES NOT IMPAIR PROTECTIVE RESPONSES: PRECLINICAL AND CLINICAL DATA**

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1 Aventis (consulting fees, speaking fees); Serono, Teva (grant/research support); 2 Bayer Pharma AG, Biogen Idec, Merck Serono, Novartis, Sanofi-Aventis, Genzyme, Roche, Teva (consulting fees); Dutch Foundation for MS Research (grant/research support). 3 Dirk Pleines, Rupert Sandborn; Christoph Podl; Bayer AG, the owner of Bayer Pharma AG/Bayer HealthCare Pharmaceuticals (ownership interest). 4 Dirk Pleines; Bayer Pharma AG/Bayer HealthCare Pharmaceuticals (consulting fees); Ernst W. Radus; Actelion, Basel Pharma Research Ltd, Biogen Idec, Merck Serono, Novartis (grant/research support); Novartis, Biogen Idec, Merck Serono, Bayer Schering (consulting fees; speaking fees). Ludwig Kappos; Actelion, Bayer HealthCare, Bayer Schering, Biogen Idec, BioMarin, C.L.C. Behring, Eli Lilly, Genentech, Genmab, GlaxoSmithKline, Lilly, Merck Serono, Novartis, Novo Nordisk, Peptimmune, Sanofi-Aventis, Santhera, Roche, Teva, UCB, Wyeth (consulting fees, grant/research support).

**Background:** Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing-remitting multiple sclerosis (MS). Teriflunomide inhibits the enzyme dihydroorotate dehydrogenase, required for de novo pyrimidine synthesis in rapidly dividing lymphocytes, thereby limiting proliferation of stimulated T and B cells. **Objectives:** To present preclinical and clinical evidence supporting preservation of protective immunity under teriflunomide treatment. **Methods:** We summarize preclinical and clinical data related to the selective mechanism of action (MoA) of teriflunomide and its effect on immune responses. In vitro murine T-cell proliferative responses to cognate peptides of various affinities were measured. In vivo primary and memory anti-viral antibody responses were evaluated in teriflunomide-treated animals inoculated with adenovirus. Immune response to seasonal flu vaccine and to rabies vaccination was measured in human subjects treated with teriflunomide. **Results:** Teriflunomide most strongly inhibited the proliferation of murine T cells stimulated with high-affinity peptides. Teriflunomide-treated mice effectively mounted specific primary and memory antibody responses to adenovirus, with only a slight delay in response. In clinical trials of patients with MS, therapeutic doses of teriflunomide showed no clinical evidence of immunosuppression. Incidences of infection, serious opportunistic infection, and malignancy were comparable to placebo. Mean leukocyte counts were reduced (<15% from baseline), but remained within the normal range. Open-label extension study patients have received teriflunomide for up to 12 years. In healthy volunteers, teriflunomide did not impair development of seroprotective immune responses to rabies vaccine neoantigen, although antibody titers were lower in subjects receiving teriflunomide than in those receiving placebo. Patients with MS treated with teriflunomide for >6 months mounted effective memory immune responses to seasonal influenza vaccination (NCT01403376). **Conclusions:** Therapeutic teriflunomide doses demonstrating consistent, beneficial effects on relapses and disability progression in phase 3 MS clinical trials do not appear to compromise protective immunity or antibody responses to either recall or neoantigen vaccines. Combined with preclinical data, these findings confirm teriflunomide has a selective immunomodulatory MoA that preserves protective immune responses.

**Supported by:** Genzyme, a Sanofi company

**Disclosure:** Amit Bar-Or: AmPhimmune, Aventis, Bayhill Therapeutics, Berlex/Bayer, Biogen Idec, BioMS, Diogenes, Eli Lilly, EMD Serono, Genentech, Genzyme-Sanofi, GlaxoSmithKline, Gatsby-Jackson Good Foundation, MedImmune, Mitsubishi Pharma, Novartis, Ono Pharmacica, Recepto (consulting fees, grant/research support). Johanne Kaplan, Andrea Edling, Philippe Truffinet: Genzyme, a Sanofi company (employer). Françoise Menguyc-Vacheron: Teva (employee). Heinz Wiendl: Bayer HealthCare, Biogen Idec, EMD Serono, Merck Serono, Novartis, Sanofi-Aventis, Sanofi/Genzyme, Teva (consulting fees); German Research Foundation (DFG), Interdisciplinary Center for Clinical Research (IZKF) Muenster, German Ministry of Education and Research (BMBF) (grant/research support), pending patent on CD62-L risk prediction (receipt of intellectual property rights/payments).

**Keywords:** Disease-modifying treatments in MS, Immunology and MS

**International Journal of MS Care**
this post hoc subgroup analysis based on three pooled fingolimod phase 3 trials, Hispanic patients with RRMS treated with fingolimod had less relapse activity than those receiving placebo or IFNβ-1a IM, confirming efficacy of fingolimod in this subgroup. The efficacy and safety profiles were consistent with those of the overall study population.

Supported by: Novartis Pharmaceuticals Corporation
Keywords: Fingolimod, Hispanic patients, Treatment efficacy

(FX12) FINGOLIMOD FIRST-DOSE EFFECTS IN HISPANIC PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS
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Background: A transient decrease in heart rate (HR) and typically asymptomatic atrioventricular (AV) conduction delays in a small minority of patients are well-characterized pharmacologic effects of fingolimod treatment initiation. A previous in-clinic study demonstrated the safety profile of fingolimod on initiation of therapy in Hispanic patients. Data provided here expand on those findings. Objectives: To evaluate the first-dose effects of fingolimod in Hispanic patients with relapsing-remitting multiple sclerosis (MS), using a large, integrated, clinical trial data set. Methods: The data set included all patients randomized to receive fingolimod (0.5 mg or 1.25 mg once daily), placebo, or intramuscular interferon beta-1a (IFNβ-1a IM; 30 µg weekly) in the core, controlled phases of all phase 2 and 3 fingolimod studies, comprising FREEDOMS, FREEDOMS II, TRANSFORMS, and a phase 2 study. In the Hispanic subgroup, vital signs, including HR, were recorded hourly for 6 hours; electrocardiogram (ECG) readings were obtained on day 1 pre-dose and 6 hours post-dose. Here, results are reported only for fingolimod 0.5 mg, placebo, and IFNβ-1a IM. Results: At treatment initiation, 89 Hispanic patients were receiving fingolimod 0.5 mg, compared with 27 receiving placebo and 65 receiving IFNβ-1a IM. A maximum mean decrease in HR of 8.1 beats per minute (bpm) occurred after 5 hours in the fingolimod group. During the first 6 hours, 79.8% of patients in the fingolimod group had an HR of at least 55 bpm, 20.2% had an HR of 45 to 54 bpm, and no patient had an HR lower than 45 bpm. No adverse events of symptomatic bradycardia were reported. Transient, newly occurring post-dose ECG abnormalities were reported in 11.4% (10/88) of patients receiving fingolimod, 3.8% (1/26) receiving placebo, and 9.4% (6/64) receiving IFNβ-1a IM. The incidence of first-degree AV block was low, occurring in 4.5% of those receiving fingolimod, compared with 3.8% receiving placebo and 3.1% taking IFNβ-1a IM. One patient treated with fingolimod had a Mobitz type I AV block. Conclusions: The effects of fingolimod initiation on HR and AV conduction in Hispanic patients were as expected, benign, and similar to those in the general treated population.

Supported by: Novartis Pharmaceuticals Corporation
Keywords: Fingolimod, Hispanic patients, First-dose observation

(DX13) ALOPECIA BARBAE AFTER LONG-TERM NATALIZUMAB THERAPY
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Background: Natalizumab is a standard disease-modifying medication for patients with multiple sclerosis (MS). It has been commercially available for over 7 years. Most of the side effect information is focused on progressive multifocal leukoencephalopathy (PML). However, patients may present with other unusual side effects. We provide the first report of alopecia barbae associated with long-term natalizumab therapy. Objectives: To report an unusual autoimmune disorder in a patient with MS treated with natalizumab.

Methods: Case report and literature review. Results: A 39-year-old highly functioning Indo-Canadian male presented to the MS Clinic with optic neuritis in early 2008. After confirmation of a diagnosis of relapsing-remitting MS, the patient started natalizumab in September 2008 at Expanded Disability Status Scale (EDSS) score of 2.0. The EDSS score decreased to 0.0 by June 2009 and recently increased to 1.0 in September 2013. He had no prior therapies or underlying illnesses. There have been no relapses on natalizumab. His biannual MRI scans were stable until June 2013, with one new lesion evident at that time; the most recent MRI is again stable. CD4/CD8 ratios were performed at baseline and monthly throughout the course of therapy. Of note, this ratio was abnormally low prior to treatment initiation, measuring 0.74 (normal, 1.05-3.62). An immunologic review concluded that it was safe for the patient to start therapy. In February 2013, the patient reported a small area of alopecia barbae on his right chin. He received local steroid (triamcinolone) injections from the dermatology department, which deemed it an autoimmune process. Assessment in the MS Clinic in April 2013 showed the alopecia increasing in size. By September, two more spots were evident. It was decided to wean the patient off natalizumab. He was given a 3-day PULSE steroid for prevention of a rebound phenomenon as well as continued regular steroid injections from the dermatology department for the alopecia. His last dose of natalizumab was August 2013, and by late September the alopecia was significantly improved. He was started on BG-12 in early October 2013. The patient reported increased fatigue and leg numbness in mid-October, and a second course of IV steroids was administered. Assessment in late December revealed no new neurologic events, but two small alopecia spots had appeared since he was seen 1 month previously but were healing. His CD4/CD8 tested in November was the lowest seen since starting testing in 2008, but more recent testing reveals the ratio to be in the normal range. Conclusions: A literature review shows no cases of alopecia with natalizumab therapy. The medical information officer of Biogen reviewed resources and did not find anything suggesting a relation between natalizumab and facial alopecia. It is interesting that a patient on natalizumab developed an unusual autoimmune disorder, which improved after discontinuation of natalizumab. It is possible that the low pretreatment CD4/CD8 ratio predisposed the patient to such a response.

Supported by: None
Disclosure: Jill R. Nelson: Biogen Idec, EMD Serono, Genzyme Canada, Novartis, Teva Innovation Canada (consulting fees). Anna
(DX14) RETROSPECTIVE CHART REVIEW OF MULTIPLE SCLEROSIS PATIENTS RECEIVING LOW-DOSE NALTREXONE TO ASSESS SAFETY, TOLERABILITY, AND EFFECT ON FATIGUE

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Background: A significant but unknown number of patients in the United States with multiple sclerosis (MS) have been using low-dose naltrexone (LDN) prepared by compounding pharmacies. The exact number of individuals using the LDN has never been established, but there are numerous websites that have established a subculture of patients with MS who have claimed its benefits. LDN’s transient blockade of the opioid receptors upregulates the production of both endogenous opioids and the classical and nonclassical opioid receptors. The nonclassical opioid receptor enhances the body’s ability to regulate cell proliferation, specifically T cells and B cells causing autoimmune damage to the central nervous system (CNS). In a recently published preclinical experiment, met-enkephalin, also known as opioid growth factor (OGF), was shown to be the peptide upregulated by the LDN’s transient blockade of the receptor. OGF demonstrated a significant biological and clinical effect on murine experimental autoimmune encephalitis (EAE) models. This EAE model is the industry standard for evaluating preclinical effectiveness of potential MS therapies. If proven effective in delaying the progression of MS in the clinical setting, LDN would change the paradigm of MS treatment in terms of mode of delivery, cost, and safety. Objectives: This study investigated the safety, tolerability, and benefits to fatigue of LDN in patients with MS. It will focus on the number of patients who stopped taking LDN and the reasons why they stopped the drug. It also studies the frequency and variety of side effects that were reported to be specific to their LDN use. Methods: A retrospective review was performed on 435 patient charts seen in an outpatient MS clinic between 1/1/2005 and 5/31/2012. There were 215 MS patients having exposure to LDN, and they served as the study group. LDN was offered as an adjunctive therapy to patients who reported significant fatigue as an MS symptom (no other medical cause), were not interested in any of the injectable MS treatments, or reported severe needle phobia. Several patients were diagnosed as having a clinically isolated syndrome, by the 2001 McDonald criteria in place at that time, and were offered LDN after declining injectable therapies. Patients were offered the LDN with the understanding that they could stop the medication if they felt little benefit or experienced side effects. Results: Results of the study supported LDN as a safe, well-tolerated, and inexpensive therapy when either used alone or added to existing modes of MS treatment. Conclusions: This retrospective chart review may offer support for a future prospective double-blind placebo study or potential studies of combination LDN + disease-modifying therapy (DMT) versus DMT.

Disclosure: Nothing to disclose.

Keywords: Disease-modifying treatments in MS, Natalizumab

(IX15) PERSISTENCE, ADHERENCE, AND QUALITY OF LIFE IN PATIENTS TREATED WITH AN INTRAMUSCULAR INTERFERON BETA-1A AUTOInjector IN A REAL-WORLD CLINICAL SETTING

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Background: The intramuscular interferon beta-1a (IM IFNβ-1a) autoinjector (AVONEX PEN®) was approved for the treatment of multiple sclerosis (MS) in Europe in 2011 and in the United States in 2012. Objectives: To describe the results of the PERSIST study, which prospectively evaluated once-weekly use of the IM IFNβ-1a autoinjector over 12 months in patients with MS in a real-world clinical setting. Methods: PERSIST was a global, prospective, observational, 12-month, open-label, phase 4 study of MS patients self-administering IM IFNβ-1a therapy by autoinjector. Outcomes evaluated included physician-reported persistence and patient-reported compliance, tolerability, quality of life, ease of use, and satisfaction. Preliminary 12-month data for the preplanned analysis are reported. Results: Of the 274 MS patients (mean age 43.0 years; 75.8% female) enrolled, 219 were included in the intent-to-treat population and 158 patients have completed the 12-month visit and contribute to the interim dataset. Among completers, 92.4% of patients (146/158) persisted in using the autoinjector through month 12; contributors to nonpersistence included adverse events, disease progression, and loss to follow-up. Based on all available data over 12 months, overall compliance (not missing any injections) was 75.4% (150/199) and the proportion of patients missing <20% of injections was 97.0% (193/199). From baseline to 12 months, the proportion of patients requiring injection assistance from a caregiver decreased from 10.0% to 5.2%. Similarly, fear of injection was reduced from 17.5% (baseline) to 2.4% (month 12). Among patients who completed their injection-related questionnaires, 75.4% (92/122) reported injection-site pain levels ≤2 (0 = no pain; 10 = extremely painful) and 74.4% (93/125) reported no injection-site reactions at month 12. At month 12, almost all patients (96.0% [119/124]) reported being satisfied or very satisfied with the autoinjector. Final 12-month results will be presented. Conclusions: In this real-world setting, patients reported that the IM IFNβ-1a autoinjector was well tolerated, easy to use, and associated with high levels of compliance, reduced need for injection assistance, and reduced fear of injection; physician-reported persistence was also high. Potential study limitations related to patient-reported outcomes will be further explored in the final results.

Supported by: Biogen Idec Inc.

(DX16) ACUTE LIVER FAILURE AFTER NATALIZIMAB INFUSION: CASE REPORT AND REVIEW OF LITERATURE
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Background: Natalizumab is a recombinant monoclonal antibody against α4 integrin for treatment of relapsing-remitting forms of multiple sclerosis (RRMS). In the post-marketing setting, cases of hepatotoxicity including severe liver injury have been described. The etiology of liver dysfunction is unknown but postulated to be unmasking autoimmune hepatitis. Objectives: To present a case of a young woman with RRMS who developed acute liver dysfunction after second infusion of natalizimab and review of the literature. Methods: Case report. Results: A 26-year-old woman with no significant past medical history or toxic habits was diagnosed with an aggressive form of RRMS; a year after diagnosis, her relevant clinical manifestations were severe truncal ataxia and prominent gait difficulty. Magnetic resonance imaging (MRI) of the brain showed T1-enhancing lesions of the subcortical white matter as well as FLAIR/T2 lesions in periven-tricular areas, brainstem, and cerebellum. Due to the severity of her disease, she received 5 days of plasma exchange followed by maintenance treatment with natalizumab 300 mg every 28 days with good response to this therapy; 2 weeks after her second infusion she developed nausea, vomiting, severe jaundice, and choloria. Her liver function tests showed AST 1076 (15–56), ALT 856 (11–50), alkaline phosphatase 165 (39–117), total bilirubin 24.9 (0–1), conjugated bilirubin 15.7 (0–0.3). Antimitochondrial and antinuclear antibodies were negative, but anti-smooth muscle antibodies were weakly positive 1:20 (<1:20). Liver ultrasound ruled out biliary obstruction. Follow-up studies continued to show significant elevation of her liver enzymes and bilirubin. Full results and outcomes will be revealed at the CMSC conference. Review of literature demonstrates at least 11 cases of severe natalizumab-associated liver injury. In a post-marketing study four out of six patients developed significant liver dysfunction after the first infusion. The mechanism of lesion is unknown, but in some cases pathological reports suggest immune mediation. Conclusions: Natalizumab can precipitate severe liver dysfunction, often after the first or second infusion; the exact mechanism of injury is unknown but possibly immune mediated. Clinical implications and recommendations will be provided.

Supported by: None
Disclosure: Nothing to disclose

Keywords: Natalizumab, Liver injury, Autoimmune hepatitis

(DX17) PATIENT- AND PHYSICIAN-REPORTED OUTCOMES AFTER THERAPY SWITCH FROM INTERFERONS OR GLATIRAMER ACETATE TO FINGOLIMOD
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Background: Patients with relapsing multiple sclerosis (MS) who had received continual disease-modifying therapy (DMT) for ≥6 months were enrolled in the phase 4, open-label, 6-month Evaluate Patient Outcomes, Tolerability, and Safety of Fingolimod (EPOC) study and randomized 3:1 to fingolimod 0.5 mg once daily or standard-of-care DMT. Objectives: To assess patient- and physician-reported outcomes in patients receiving interferon (IFN) who stayed on IFN, patients receiving glatiramer acetate (GA) who stayed on GA, and patients receiving each agent who switched to fingolimod. Methods: Post hoc analyses determined least squares mean (LSM) changes from baseline (BL) to 6 months (last observation carried forward) in Treatment Satisfaction Questionnaire for Medication (TSQM; 0–100 scale, higher scores = greater satisfaction), Beck Depression Inventory–II (BDI-II), Fatigue Severity Scale (FSS), and physician-assessed Clinical Global Impression of Improvement (CGHI) scores. Results: 205 patients switched to fingolimod from intramuscular (IM) IFN beta-1a (IFNa), 196 from subcutaneous (SC) IFNa, and 125 from SC IFN beta-1b (IFNb), while 48, 58, and 39 patients stayed on IM IFNa, SC IFNa, and IFNb, respectively; 262 switched from GA to fingolimod, and 74 stayed on GA. LSM changes from BL to 6 months in TSQM Global Satisfaction scores favored switching to fingolimod versus remaining on IFN (17.57 vs. 2.10 [IM IFNa], 24.7 vs. 2.29 [SC IFNa], and 22.34 vs. 4.45 [IFNb; all P < .001]) or GA (17.08 vs. 0.81; P < .001). LSM changes from BL to 6 months in TSQM subscale scores for fingolimod versus IFN were: Effectiveness, 13.31 versus 1.37 (IM IFNa), 15.07 versus 1.62 (SC IFNa), 17.59 versus 0.68 (IFNb); Side Effects, 30.62 versus 6.56 (IM IFNa), 27.83 versus –0.42 (SC IFNa), 21.50 versus –1.24 (IFNb); Convenience, 43.83 versus 5.70 (IM IFNa), 42.36 versus 1.66 (SC IFNa), 41.57 versus 1.31 (IFNb; all P < .001). LSM changes from BL favored fingolimod versus GA for Effectiveness (12.16 vs. 0.62; P < .001) and Convenience (38.01 vs. 3.11; P < .001). A nonsignificant trend existed for the Side Effects subscale (9.25 vs. 4.47; P = .111). Changes in FSS and BDII favored switching to fingolimod versus remaining on IFN or GA, although not all differences were statistically significant. Changes in CGHI favored switching to fingolimod versus remaining on IFN or GA (all P < .001). Conclusions: Switching to fingolimod was associated with improved patient-reported treatment satisfaction and physician assessments relative to not switching from IFN or GA.

Supported by: Novartis
Disclosure: Bruce A.C. Cree: Biogen Idec, EMD Serono, Novartis, Teva Neurosciences (consulting fees). Keith R. Edwards: Biogen Idec, Novartis, Actelion, Genzyme, Genentech, Eli Lilly (grant/research support); Novartis Pharmaceuticals Corporation, Biogen Idec, Genzyme (scientific advisory boards and speaker fees); Acorda, EMD Serono (speaker fees, consulting fees). Kevin McCague, Luigi M. Barbato: Novartis Pharmaceuticals Corp. (employee).

Keywords: Disease-modifying treatments in MS, Fingolimod

(DX18) EFFECT OF BISMUTH SUBSALICYLATE ON GASTROINTESTINAL TOLERABILITY IN HEALTHY VOLUNTEERS RECEIVING DELAYED-RELEASE DIMETHYL FUMARATE
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1Posters: Disease Management, Mechanisms, and Treatment
2International Journal of MS Care
Background: Delayed-release dimethyl fumarate (DMF) demonstrated efficacy and safety in relapsing-remitting multiple sclerosis (RRMS) in the 2-year, phase 3 DEFINE and CONFIRM studies. Common adverse events associated with delayed-release DMF included flushing and gastrointestinal (GI)–related events. **Objectives:** In an 8-week, randomized, multicenter, double-blind, placebo-controlled, phase 1 study (PREVENT), we evaluated the effect of bismuth subsalicylate (Pepto-Bismol®) on GI-related events in healthy volunteers receiving delayed-release DMF. **Methods:** Subjects were randomized 1:1 to receive bismuth subsalicylate 524 mg or placebo 30 minutes prior to delayed-release DMF (weeks 1–4). Delayed-release DMF was dosed at 120 mg twice a day (week 1) and 240 mg twice a day (weeks 2–8). Subjects were instructed to take delayed-release DMF with or without approximately 60 minutes after a meal. Using an eDiary, subjects recorded information regarding GI-related events and flushing events on the Modified Overall Gastrointestinal Symptom Scale (MOSISS) and Modified Global Flushing Severity Scale (MGFSS) once daily for the previous 24 hours, and entered GI and flushing side effects using the Modified Acute Gastrointestinal Symptom Scale (MAGISS) and Modified Flushing Severity Scale (MFSS) after each administration of study drug. The primary endpoint was the time to first GI-related event. **Results:** PREVENT enrolled 175 subjects with a mean age of 37 years (range, 18–64 years). Approximately half (50.9%) were female, and a majority (67.4%) were white. PREVENT is ongoing; results will be reported. **Conclusions:** The PREVENT study will evaluate the effect of bismuth subsalicylate on GI-related events in healthy volunteers receiving delayed-release DMF.

Supported by: Biogen Idec

Disclosure: Carlo Tornatore: Biogen Idec (fees for non-CME services from commercial interests or their agents); Biogen Idec, Genzyme, Novartis (consulting fees); Tina S. Ma: PharmStaxs (employee). Jie Li, Christian von Hehn, John Waldt, Javier Zambrano: Biogen Idec (employee).

Keywords: Disease-modifying treatments in MS

**(DX19) TREATMENT-NAIVE RELAPSING-REMITTING MULTIPLE SCLEROSIS PATIENTS MORE LIKELY TO BE DISEASE ACTIVITY FREE WITH ALEMTUZUMAB THAN SUBCUTANEOUS INTERFERON BETA-1A ACROSS PATIENT SUBGROUPS**

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**Background:** In the phase 3 Comparison of Alemtuzumab and Rebif Efficacy in Multiple Sclerosis (CARE-MS) I study, alemtuzumab significantly improved relapse rate versus subcutaneous interferon beta-1a (SC IFNβ-1a) with a manageable safety profile in treatment-naive relapsing-remitting multiple sclerosis (RRMS) patients. Alemtuzumab patients were more likely to be free of detectable clinical disease activity, magnetic resonance imaging (MRI) activity, and MS (clinical or MRI) disease activity. **Objectives:** To compare odds of being clinical, MRI, and MS disease activity free after 2 years of treatment with alemtuzumab versus SC IFNβ-1a in subgroups stratified by baseline demographic or disease characteristics. **Methods:** CARE-MS I (NCT00530348) was a randomized, rater-blinded comparison of intravenous alemtuzumab (12 mg on 5 days at baseline and 3 days 12 months later) and SC IFNβ-1a (44 µg 3 times weekly) in treatment-naive patients for 2 years. Clinical disease activity (≥1 relapse or 6-month sustained accumulation of disability), MRI activity (≥1 new gadolinium [Gd]–enhancing lesion or new/enlarging T2-hyperintense lesion), and MS disease activity (clinical or MRI activity) were assessed at 24 months. Odds ratios (ORs) and P values were calculated from logistic regressions with covariate adjustment for baseline characteristics (Expanded Disability Status Score [EDSS] score, relapse in prior 2 years, disease duration, brain parenchymal fraction, T2 lesion volume, Gd activity, highly active disease).

**Results:** 376 alemtuzumab and 187 SC IFNβ-1a patients were included in this analysis. Alemtuzumab-treated patients were more likely to be free of clinical, MRI, and MS (clinical or MRI) disease activity. Alemtuzumab-treated patients had significantly greater odds (OR 1.59–4.74; P < .05) of being clinical disease activity free versus SC IFNβ-1a in all disease characteristic subgroups and being MRI activity free (OR, 1.89–3.23; P < .05) regardless of baseline EDSS, median disease duration, Gd activity, and disease severity. Freedom from MS (clinical or MRI) disease activity favored alemtuzumab (OR > 1.00) but did not reach statistical significance for all subgroups. **Conclusions:** Treatment-naive patients treated with alemtuzumab were more likely to be clinical, MRI, and MS (clinical or MRI) disease activity free versus SC IFNβ-1a patients regardless of baseline disease characteristics.

Supported by: Genzyme, a Sanofi company; Bayer Healthcare Pharmaceuticals


Keywords: Alemtuzumab, Disease-modifying treatments in MS
simplex virus encephalitis (HSE) in a patient with fulminant MS treated with natalizumab without prior IS or DMT exposure. **Methods:** Case report. **Results:** A 38-year-old man with fulminant MS was treated with natalizumab as initial therapy. He developed acute encephalitis after four monthly infusions of natalizumab. Brain MRI showed a new hemorrhagic left temporal lesion with associated focal edema. HSV type 1 DNA was detected in cerebrospinal fluid (CSF) by PCR. He responded well to 6 weeks of IV acyclovir therapy followed by 30 days of oral treatment, aside from continued neuropsychiatric symptoms, including severe anterograde amnesia and impaired executive function. Repeat CSF studies after completion of 6 weeks of IV antiviral therapy showed no detectable HSV DNA. **Conclusions:** Our case and the previously reported cases suggest that there is increased risk of CNS HSV infection with natalizumab therapy, even without prior IS exposure. Previous cases demonstrated apparent good response with early detection and appropriate treatment with antiviral agents. In addition to monitoring for PML, clinicians caring for patients treated with natalizumab should remain vigilant for other CNS infections.

**Supported by:** National Multiple Sclerosis Society Clinical Fellowship Award FP 1788-A-1

**Disclosure:** Carrie Hersh: National Multiple Sclerosis Society (grant research support); Jeffrey A. Cohen: Biogen Idec, Elan, Lilly, Novartis, Teva, Vaccinex (consulting fee).

**Keywords:** Disease-modifying treatments in MS, Herpes virus encephalitis (HSE), Imaging and MS

**(DX21) SAFETY AND EFFICACY OF TERIFLUNOMIDE IN PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS IN A COMMUNITY SETTING**

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**Background:** Teriflunomide is a new oral disease-modifying agent (DMA) recently approved for the treatment of relapsing-remitting multiple sclerosis (RRMS). It has demonstrated efficacy and safety in a number of large multicenter phase 3 clinical trials. However, its benefit in real-world MS patients is still not well known. **Objectives:** To report the efficacy and side effects of teriflunomide when used in MS patients followed in a community hospital MS center. **Methods:** We retrospectively reviewed the charts of all our RRMS patients treated with dimethyl fumarate since its approval in March 2013. The number of clinical relapses and potential side effects were studied. **Results:** We had 104 patients, 73 women (70.2%) and 31 men (29.8%), with a mean age of 50.3 years. Patients were followed for a mean of 4.5 months. Side effects from prior disease-modifying agents (46%) was the most common reason for starting dimethyl fumarate, followed by lack of efficacy (21%) of prior immunomodulators. The most common side effects were gastrointestinal (GI) symptoms, followed by flushing. GI side effects occurred in 56.5% of patients within the first month, but declined to 11% by the end of the third and sixth months. Twelve percent of those patients had a history of prior GI symptoms. The incidence of flushing was 50.6% in the first month, and decreased to 24.2% and 30% by the end of the third and sixth months, respectively. Leukopenia grade 2 or lymphopenia grade 3 or higher occurred in 3.1% of patients at month 3 and 25% of patients at month 6. Two patients with grade 3 lymphopenia developed an infection; one patient had cellulitis and the other one developed herpes zoster. Mild elevation of LFTs (less than 3x baseline) was seen in 14% of patients at month 3 and 27.3% of patients at month 6. Four patients had clinical exacerbations confirmed by imaging, all of them between months 3 and 5. Half of these patients had multiple enhancing lesions. Treatment was discontinued in 13 patients (12.5%), the vast majority due to the GI side effects, followed by clinical relapse in 3 patients.

**Conclusions:** In our study, the side effects from dimethyl fumarate were similar to those in phase 3 trials; however, the incidences of flushing and severe leukopenia or lymphopenia at 6 months were higher than previously reported. During this short follow-up, clinical exacerbations have occurred in approximately 4% of the patients.

**Supported by:** None

**Disclosure:** Nothing to disclose

**Keywords:** Disease-modifying treatments in MS

**(DX22) SAFETY AND EFFICACY OF DIMETHYL FUMARATE IN PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS IN A COMMUNITY SETTING**

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**Background:** Dimethyl fumarate is a new oral disease-modifying therapy approved in March 2013 to treat relapsing-remitting multiple sclerosis (RRMS). It has demonstrated efficacy and safety in a number of large multicenter phase 3 clinical trials. However, its benefit in real-world MS patients is still not well known. **Objectives:** To report the safety and efficacy of dimethyl fumarate when used in MS patients followed in a community hospital MS center. **Methods:** We retrospectively reviewed the charts of all our RRMS patients treated with dimethyl fumarate since its approval in March 2013. The number of clinical relapses and potential side effects were studied. **Results:** We had 104 patients, 73 women (70.2%) and 31 men (29.8%), with a mean age of 50.3 years. Patients were followed for a mean of 4.5 months. Side effects from prior disease-modifying agents (46%) was the most common reason for starting dimethyl fumarate, followed by lack of efficacy (21%) of prior immunomodulators. The most common side effects were gastrointestinal (GI) symptoms, followed by flushing. GI side effects occurred in 56.5% of patients within the first month, but declined to 11% by the end of the third and sixth months. Twelve percent of those patients had a history of prior GI symptoms. The incidence of flushing was 50.6% in the first month, and decreased to 24.2% and 30% by the end of the third and sixth months, respectively. Leukopenia grade 2 or lymphopenia grade 3 or higher occurred in 3.1% of patients at month 3 and 25% of patients at month 6. Two patients with grade 3 lymphopenia developed an infection; one patient had cellulitis and the other one developed herpes zoster. Mild elevation of LFTs (less than 3x baseline) was seen in 14% of patients at month 3 and 27.3% of patients at month 6. Four patients had clinical exacerbations confirmed by imaging, all of them between months 3 and 5. Half of these patients had multiple enhancing lesions. Treatment was discontinued in 13 patients (12.5%), the vast majority due to the GI side effects, followed by clinical relapse in 3 patients.

**Conclusions:** In our study, the side effects from dimethyl fumarate were similar to those in phase 3 trials; however, the incidences of flushing and severe leukopenia or lymphopenia at 6 months were higher than previously reported. During this short follow-up, clinical exacerbations have occurred in approximately 4% of the patients.

**Supported by:** None

**Disclosure:** Nothing to disclose

**Keywords:** Disease-modifying treatments in MS

**International Journal of MS Care**
(DX23) APPLICATION OF THE DELPHI TECHNIQUE FOR EVALUATION OF THE TOLERABILITY PROFILE OF PEGYLATED INTERFERON BETA-1A

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Background: The tolerability profile of multiple sclerosis (MS) treatments can have an impact on patient adherence and affect treatment outcome. Common adverse events (AEs) with investigational peginterferon beta-1a (PEG-IFN) are flu-like symptoms (FLS) and injection-site reactions (ISR). Objectives: Understand PEG-IFN-related FLS and ISR and identify effective management strategies for these AEs. Methods: ADVANCE is a 2-year, randomized, double-blind, placebo-controlled (year 1) phase 3 study evaluating the efficacy and safety of subcutaneous PEG-IFN 125 µg every 2 (Q2W) or 4 (Q4W) weeks. Investigators with a minimum number of enrolled patients in ADVANCE were offered the opportunity to participate in a consensus-generating exercise to identify best practices for management of FLS and ISR. A second questionnaire will be used to clarify best practices and generate consensus recommendations. Results: The mean (SD) number of patients enrolled at these sites for Q2W and Q4W dosing was 4.5 (4.2) and 4.3 (4.2), respectively. Based on data from year 1 of ADVANCE, the median time on PEG-IFN was 337 days for both Q2W and Q4W. The percentage of patients reporting FLS and ISR over 1 year for Q2W was 38.6% (59/153) and 64.1% (98/153), respectively, and 44.7% (68/152) and 69.1% (105/152) for Q4W, respectively. In year 1, 74.0% (94/127) of PEG-IFN patients experiencing FLS utilized symptomatic therapy for FLS; 6.4% (13/203) of PEG-IFN patients experiencing ISR utilized symptomatic therapy for ISR. At these sites 2.0% (3/153) and 0.7% (1/153) of Q2W patients discontinued PEG-IFN owing to FLS and ISR, respectively, and 2.0% (3/152) and 1.3% (2/152) of Q4W patients discontinued owing to FLS and ISR, respectively. Of the 83 eligible investigators, 36 from 13 countries agreed to participate. Results from both questionnaires will be reported. Conclusions: Data regarding patients enrolled by investigators agreeing to participate in the Delphi project are representative of the overall ADVANCE population. The recommendations of the panel based on the results of the Delphi process will reflect substantive experience with PEG-IFN, and may have an impact on patient adherence to therapy and ultimately influence patient outcomes.

Supported by: Biogen Idec


Keywords: Disease-modifying treatments in MS, Peginterferon beta-1a

(DX24) FEWER BLACK HOLE CONVERSIONS WITH ALEMTUZUMAB VERSUS SUBCUTANEOUS INTERFERON BETA-1A IN RELAPSING-REMITTING MULTIPLE SCLEROSIS PATIENTS WHO RELAPSED ON PRIOR THERAPY

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Background: In the phase 3 Comparison of Alemtuzumab and Rebif Efficacy in Multiple Sclerosis (CARE-MS) II trial, alemtuzumab significantly reduced risk of relapse and sustained accumulation of disability, reduced formation of T2, gadolinium (Gd)–enhancing, and T1-hypointense lesions, and slowed brain atrophy versus subcutaneous interferon beta-1a (SC IFNβ-1a) in relapsing-remitting multiple sclerosis (RRMS) patients who relapsed on prior therapy. Objectives: To compare efficacy of alemtuzumab and SC IFNβ-1a in preventing conversion of Gd-enhancing lesions (markers of active brain inflammation) to chronic T1-hypointense lesions or black holes (markers of permanent tissue destruction) on magnetic resonance imaging (MRI) in CARE-MS II patients. Methods: CARE-MS II (NCT00548405) was a 2-year, randomized (2:1), rater-blinded trial comparing alemtuzumab and SC IFNβ-1a in 798 RRMS patients who had relapsed while on disease-modifying therapy. Intravenous (IV) alemtuzumab 12 mg was administered on 5 days at study start and on 3 days 12 months later. SC IFNβ-1a 44 µg was administered 3 times weekly. T1-weighted MRI, with/without IV Gd contrast, was obtained at baseline and months 12 and 24 to assess conversions of Gd-enhancing lesions to chronic black holes (lesions with ≤85% signal hypointensity relative to surrounding normal-appearing white matter). T1-hypointense lesion numbers were assessed using negative binomial regressions. Odds ratios (ORs) and P values for percentages of T1-hypointense conversions were calculated using logistic regression with generalized estimating equations. Results: 426 and 202 patients treated with alemtuzumab and SC IFNβ-1a, respectively, were eligible for this analysis. Baseline Gd-enhancing lesions evolved similarly in alemtuzumab- and SC IFNβ-1a-treated patients (P = NS). Gd-enhancing lesions that formed on therapy, seen at month 12, were significantly less likely to convert to black holes by month 24 in alemtuzumab-treated than in SC IFNβ-1a-treated patients (10.7% vs. 27.3% [60.8% reduction]; OR, 0.33; 95% confidence interval, 0.15-0.75; P = .0078). Conclusions: Compared with SC IFNβ-1a, alemtuzumab significantly reduced the risk of conversion to chronic black holes for Gd-enhancing lesions that developed on therapy, suggesting that alemtuzumab reduces progression from active inflammation to irreversible tissue injury and axonal loss. Baseline Gd-enhancing lesions that developed before treatment did not benefit.

Supported by: Genzyme, a Sanofi company; Bayer HealthCare Pharmaceuticals

Disclosure: Douglas L. Arnold: Acorda, Bayer, Biogen Idec, Eli Lilly, EMD Serono, Merck Serono, Genentech, Genzyme, GSK, MedImmune, NeuroRx Research, Novartis, Opeca, Receptos, Roche, Sanofi-Aventis, Teva, Canadian Institute of Health Research, Multiple Sclerosis Society of Canada (consulting fees, grant/research support, honoraria, advisory board fees); NeuroRx Research (stock ownership). Jeffrey Palmer, David H. Margolin: Genzyme (employee).

Keywords: Alemtuzumab, Disease-modifying treatments in MS
(DX25) FINGOLIMOD: LONG-TERM (UP TO 4 YEARS) EFFICACY IN RELAPSING-REMITTING MULTIPLE SCLEROSIS PATIENTS IN FREEDOMS AND FREEDOMS II STUDY EXTENSIONS

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Background: In the 24-month FREEDOMS and FREEDOMS II core studies, oral, once-daily fingolimod (0.5 mg or 1.25 mg) showed beneficial effects on clinical and magnetic resonance imaging (MRI) endpoints versus placebo in patients with relapsing-remitting multiple sclerosis (RMS). Objectives: To report long-term (up to 4 years) efficacy outcomes of fingolimod in the FREEDOMS and FREEDOMS II extension studies. Methods: Patients treated with fingolimod (0.5 mg or 1.25 mg) in the core studies (months 0–24) continued the same dose (continuous group) in the extension studies, while those on placebo were rerandomized (1:1) to fingolimod (0.5 mg/1.25 mg; switch group). After study amendment, all patients received open-label fingolimod 0.5 mg until end of study (EOS). Comparisons were analyzed for continuously treated groups versus the merged 0.5 mg/1.25 mg switch group. Results: Of 1272 patients randomized in the FREEDOMS core study, 920 (72.3%) entered the extension, and of these 773 (84.0%) patients completed the study. In the core ITT, from month 0 to EOS, the annualized relapse rate (ARR) remained significantly lower in the continuous fingolimod groups (1.25 mg, 0.16; 0.5 mg, 0.19) versus the switch group (0.36, both P < .001). In the extension ITT, patients who switched from placebo to fingolimod had a 55% reduction in ARR (0.13 vs. 0.29 during the core phase, respectively; P < .001). MRI measures continued to show significantly reduced brain atrophy in the continuous fingolimod 0.5 and 1.25 mg groups versus the switch group (mean % change in brain volume –1.67% and –1.64% vs. –2.24%; both P ≤ .001) at EOS. Of 1083 patients randomized in the FREEDOMS II study, 632 (58.4%) entered the extension, and of these 529 (83.7%) patients completed the study. From month 0 to EOS, the ARR remained significantly lower in the continuous fingolimod groups (0.5 mg: 0.19; 1.25 mg: 0.18) versus the switch group (0.36), resulting in relative reductions of 47% and 50% (both P < .001). MRI measures continued to show significantly reduced brain atrophy in the continuous fingolimod groups (0.5 mg: -0.98%; 1.25 mg: -0.84%; both P ≤ .002) versus the switch group (-1.33%) at EOS. Within-group comparisons will be presented for both studies. Conclusions: Results from FREEDOMS and FREEDOMS II extension studies support long-term efficacy of fingolimod. In both studies, continuous fingolimod treatment maintained the low clinical and MRI disease activity seen in the core studies for up to 4 years. Benefits were also seen relative to core study results in patients switched from placebo to fingolimod.

Supported by: Novartis


Keywords: Disease-modifying treatments in MS, Fingolimod

(DX26) FINGOLIMOD EFFECT ON RELAPSE RATE IN YOUNG ADULT PATIENTS WITH MULTIPLE SCLEROSIS

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Background: Relapse frequency has been reported to be higher in multiple sclerosis (MS) patients with younger age. To date, no controlled studies have been completed to evaluate disease-modifying treatments in pediatric MS patients. Objectives: To estimate and compare annualized relapse rates (ARRs) for fingolimod 0.5 mg, placebo, or intramuscular interferon beta-1a (IFNβ-1a) in young adult MS patients from phase 3 pivotal studies, in order to inform sample size requirements for a study of fingolimod in pediatric MS patients. Methods: A post hoc analysis of ARRs was conducted in the ITT populations of FREEDOMS (2-year study vs. placebo) and TRANSFORMS (1-year study vs. IFNβ-1a). A negative binomial regression model with adjustments for treatment, age at baseline (continuous), and a treatment-by-age interaction estimated ARRs at age 20 years and at age 30 years. Results: Of all randomized patients in FREEDOMS and TRANSFORMS, respectively, 28/1272 (2.2%) and 40/1292 (3.1%) were aged 20 years or younger; 325/1272 (25.6%) and 355/1292 (27.5%) were aged 30 years or younger at baseline. The estimated ARRs in young patients treated with fingolimod 0.5 mg were lower irrespective of age and similar to those in the overall fingolimod 0.5 mg treatment groups (20 years, 30 years, overall: ARR = 0.16, 0.19, 0.18 in FREEDOMS; ARR = 0.14, 0.17, 0.16 in TRANSFORMS). The estimated ARRs in the control groups were higher in young patients compared with those in the overall control groups (20 years, 30 years, overall: ARR = 0.73, 0.57, 0.40 for placebo in FREEDOMS; ARR = 0.60, 0.48, 0.33 for IFNβ-1a in TRANSFORMS). The estimated relative reduction in ARR in patients aged 20 years, 30 years, and in the overall population, respectively, was 79%, 67%, and 54% versus placebo in FREEDOMS and 77%, 64%, and 52% versus IFNβ-1a in TRANSFORMS (all P < .001). Conclusions: ARRs in fingolimod 0.5 mg treated patients were low and independent of age. The relative treatment effects of fingolimod versus placebo or IFNβ-1a were higher in the young adult patients compared with the overall population in the fingolimod phase 3 studies. For a randomized, double-blind study to evaluate the efficacy of fingolimod versus IFNβ-1a in pediatric MS patients aged 10 to <18 years (PARADIGMS), a sample size of 190 patients in total was determined to be required to detect a 50% treatment effect on ARR for fingolimod versus IFNβ-1a. The PARADIGMS study is currently recruiting worldwide.

Supported by: Novartis Pharma AG, Novartis Pharmaceuticals Corporation

Disclosure: Görl Karlsson, Dieter A. Häring, Philipp von Rosenstiel, Gordon Francis, Peter Chin, Norman Putzki: Novartis (employee)

Keywords: Disease-modifying treatments in MS, Pediatric multiple sclerosis
**(DX27) CLINICAL MANAGEMENT OF HIGH-RISK PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS TREATED WITH NATALIZUMAB**

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**Background:** Progressive multifocal leukoencephalopathy (PML) is a rare opportunistic infection of the central nervous system that mainly occurs in the setting of immunosuppression. Natalizumab is an immunomodulatory agent indicated for the treatment of relapsing-remitting multiple sclerosis (RRMS) that is most often associated with the development of PML. There are three predictive risk factors for developing natalizumab-associated PML: JC virus (JCV) antibody status, history of immunosuppressant therapy, and duration of natalizumab treatment. The estimated risk of a JCV-positive person exposed to natalizumab for 25 to 48 months with no prior immunosuppressant use is 5/1000 and for those previously exposed to immunosuppressant use is 11/1000. Clinical management considerations in high-risk patients with two or more risk factors are important in the overall scope of treatment outcomes. **Objectives:** To describe the clinical management of high-risk patients with RRMS treated with natalizumab who have two or more risk factors. **Methods:** We review patient charts for 210 RRMS patients actively treated with natalizumab in our clinic. **Results:** Among the 210 patients, 27 patients have at least two risk factors: tested JCV-positive and were exposed to natalizumab for over 25 months. In addition, 5 of the 27 patients have all three risk factors, including prior exposure to immunosuppressants. According to our protocol, all MS patients actively treated with natalizumab are tested for the JCV twice a year. In addition, physicians clinically monitor high-risk patients with two or more risk factors every 6 months with magnetic resonance imaging (MRI) and scheduled office visits. All 27 patients are currently stable, and no confirmed cases of PML have been reported. **Conclusions:** Our experience indicates that a small population of high-risk RRMS patients treated with natalizumab may be managed and monitored safely and effectively. The US Food and Drug Administration (FDA) designates a black box warning regarding natalizumab increasing the risk of PML; therefore, the potential risks and benefits must be carefully assessed prior to maintaining high-risk patients on natalizumab therapy.

**Disclosure:** Nothing to disclose

**Keywords:** Comprehensive care and MS, Disease-modifying treatments in MS, Imaging and MS

**(DX28) TERIFLUNOMIDE MECHANISM OF ACTION: LINKING PRECLINICAL EVIDENCE TO CLINICAL ACTIVITY**

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**Background:** Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing-remitting multiple sclerosis (RRMS). Teriflunomide inhibits the mitochondrial enzyme dihydro-orotate dehydrogenase (DHODH), which is required for de novo pyrimidine synthesis in rapidly dividing lymphocytes. **Objectives:** To present the current understanding of teriflunomide’s mechanism of action (MoA) based on preclinical and clinical data. **Methods:** Several methodologies were used to study the proposed MoA of teriflunomide. We here summarize preclinical (impact on human lymphocyte proliferation/cell viability [in vitro]; impact on central nervous system [CNS] lymphocyte counts, disease severity, and neuronal conduction [in vivo in animal studies]) and clinical trial data (magnetic resonance imaging [MRI], relapse, disability outcomes) to further characterize the MoA of teriflunomide and its effects in patients with MS. **Results:** In vitro, teriflunomide inhibited proliferation of stimulated human T and B cells, an effect reversed by the addition of uridine, thereby confirming DHODH dependency, without affecting lymphocyte viability. In an experimental autoimmune encephalomyelitis (EAE) model, teriflunomide-treated EAE rats had significant reductions in T- and B-cell counts in the CNS at all disease stages. EAE rats also had reduced disease severity at attack, remission, and relapse when teriflu

**Disclosure:** Heinz Wiendl: Bayer HealthCare, Biogen Idec, EMD Serono, Merck Serono, Novartis, Sanofi-Aventis, Sanofi/Genvy, Teva (consulting fees); German Research Foundation (DFG), Interdisciplinary Center for Clinical Research (IZKF) Muenster, German Ministry of Education and Research (BMBF) (grant/research support), pending patent on CD62-L risk prediction (receipt of intellectual property rights/patents). Andrew R. Pachner: Biogen Idec, Novartis (funds for non-CME services from commercial interests or their agents); Biogen Idec, Novartis, Genvy (consulting fees); Sanofi (grant/research support). Johanne Kaplan: Genvy (employee). Françoise Menguy-Vacheron: Sanofi (employee). Philippe Truffinet: Genvy, a Sanofi company (employee). Amir Bar-On: Allogeneic, Aventis, Bayhill Therapeutics, Berlin/ Bayer, Biogen Idec, BioMS, Diogenix, Eli Lilly, EMD Serono, Genentech, Genvy-Sanofi, GLAXO SmithKline, Guthy-Jackson Greater Good Foundation, MedImmune, Mitsubishi Pharma, Novartis, Ono Pharma, Recepto (consulting fees, grant/research support).

**Keywords:** Disease-modifying treatments in MS, Immunology and MS

**Supported by:** Genvy, a Sanofi company

**(DX29) SAFETY PROFILE OF DELAYED-RELEASE DIMETHYL FUMARATE IN RELAPSING-REMITTING MULTIPLE SCLEROSIS: LONG-TERM INTERIM RESULTS FROM THE ENDORSE EXTENSION STUDY**

J. Theodore Phillips,1 Robert J. Fox,2 Krzysztof Selma,3 Ray Zhang,4 Mark Novas,5 Marianne Sweetser,6 Vissia Viglietto,3 Ralf Gold1

1International Journal of MS Care

**Disclosure:** J. Theodore Phillips: EMD Serono, Genzyme-Sanofi, Merck-Serono, Novartis, Sanofi-Aventis (employee).

**Conclusion:** Delayed-release dimethyl fumarate (DMF) was well tolerated in patients with RRMS in the long-term extension study of the ENDORSE trial. The incidence of adverse events was consistent with the known profile of DMF, and no new safety issues were identified.
Background: Delayed-release dimethyl fumarate (DMF) demonstrated significant efficacy and an acceptable safety profile in patients with relapsing-remitting multiple sclerosis (RRMS) in the phase 3 DEFINE and CONFIRM studies. ENDORSE is an ongoing, 5-year, dose-blind extension of DEFINE and CONFIRM. Objectives: To report long-term interim safety results from ENDORSE. Methods: Patients randomized to delayed-release DMF 240 mg twice (BID) or three times daily (TID) in DEFINE/CONFIRM continued the same dosing regimen in ENDORSE. Placebo (PBO; DEFINE/CONFIRM) and glatiramer acetate (GA; CONFIRM) patients were randomized 1:1 to delayed-release DMF BID or TID. Safety data were analyzed according to parent/extension study treatment: BID/BID, TID/TID, PBO/BID, PBO/TID, GA/BID, GA/TID. Results: As of the 12 June 2013 data cut, the overall incidences of adverse events (AEs) were: 89% BID/BID (n = 501), 90% TID/TID (n = 501), 93% PBO/BID (n = 249), 90% PBO/TID (n = 248), 86% GA/BID (n = 118), 84% GA/TID (n = 119). The incidences of serious AEs were: 18% BID/BID, 19% TID/TID, 22% PBO/BID, 15% PBO/TID, 13% GA/BID, 18% GA/TID. The incidence of discontinuations due to AEs was 4% to 6% (BID/BID, TID/TID) and 14% to 23% (PBO/BID, PBO/TID, GA/BID, GA/TID). The incidence of serious infections was ≤3% (all groups). There were no confirmed opportunistic infections and no new findings in hematologic outcomes compared with DEFINE/CONFIRM. Hepatic AEs occurred in ≤3% of patients in any treatment group. There was no evidence of increased risk of renal or urinary events. There were 20 malignancies in 19 patients (11 continuing and 8 new to delayed-release DMF). There were four deaths, none of which was considered related to study drug. Conclusions: The long-term safety profile of delayed-release DMF appears consistent with findings from DEFINE/CONFIRM. No new or worsening safety signals were observed.

Supported by: Biogen Idec

Disclosure: J. Theodore Phillips, Acorda, Biogen Idec, Genzyme, Novartis, Sanofi, Teva, Xenoport (consulting fees); Roche (grant/research support); Robert J. Fox: Allozyne, Avanir, Biogen Idec, Novartis, Questcor, Teva, Xenoport (consulting fees); Novartis (grant/research support). Krzysztof Selmaj: Biogen Idec (fees for non-CME services from commercial interests or their agents); Genzyme, Novartis, Ono, Roche, Synthanalysis, Teva (consulting fees); Ray Zhang, Mark Novak, Marianna Sawyer, Viscia Virginia: Biogen Idec (employee); Raif Gold: Bayer HealthCare, Biogen Idec; Merck Serono, Novartis, Genzyme, Teva Neuroscience (grant/research support, consulting fees); Sage (compensation for serving as editor of Therapeutic Advances in Neurological Disorders).

Keywords: Disease-modifying treatments in MS

(DX30) A DELPHI PANEL TO ADDRESS MANAGEMENT OF GASTROINTESTINAL SIDE EFFECTS OBSERVED WITH USE OF DELAYED-RELEASE DIMETHYL FUMARATE

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Background: Delayed-release dimethyl fumarate (DMF) is an oral therapy approved in the United States and Australia for treatment of relapsing forms of multiple sclerosis (MS) and in Canada for treatment of relapsing-remitting MS (RRMS). In placebo-controlled clinical trials of DMF, events associated with gastrointestinal (GI) tolerability (eg, nausea/vomiting, abdominal pain, diarrhea) were reported in 40% of patients treated with DMF (240 mg twice a day) compared with 31% of placebo-treated patients. An expert panel of investigators with substantial experience in the phase 3 DMF clinical trial program previously provided insight into characterization and management of GI events associated with DMF, but real-world experience with respect to their severity, impact on daily activities, and management strategies is limited. Objectives: To gain further insight into GI events associated with DMF from clinicians with experience managing patients treated with DMF and who experience GI events, to obtain consensus on the most effective strategies to manage side effects, and to obtain consensus on setting appropriate expectations for patients with GI events. Methods: The Delphi method, a process of achieving consensus from an experienced panel, has been initiated in the United States and Canada, and will use two or more rounds of questionnaires. A steering committee was convened to design and conduct surveys of health-care professionals who have MS patients receiving treatment with DMF. Each questionnaire includes questions relating to clinician experience with GI events associated with DMF treatment. Results from each questionnaire will be used to develop the subsequent questionnaire of the Delphi process. A summary of the results will be provided to respondents with the subsequent questionnaire, which is designed to narrow the range of responses as a means of trying to obtain consensus on the management of each specific GI event. Results: The approach to obtaining consensus on managing DMF-associated GI events will be presented. These results of the Delphi process are intended to provide clinicians with strategies for managing DMF-associated GI events and to set appropriate expectations in patients based on real-world experience with DMF treatment. Conclusions: Strategies and techniques to manage DMF-associated GI events based on real-world experience are important in clinical practice to improve tolerability and compliance.

Supported by: Biogen Idec

Disclosure: J. Theodore Phillips: Acorda, Biogen Idec, Genzyme, Novartis, Teva (honoraria); Biogen Idec, Roche (grant/research support). April Erwin: Biogen Idec ( speakers’ bureau), Novartis ( speakers’ bureau, consulting fees); Jeanine Agrella: Acorda, Avanir, Genzyme-Sanofi, Novartis, EMD Serono, Pfizer, Teva (fees for non-CME services from commercial interests or their agents); Acorda, Biogen Idec, Genzyme-Sanofi, Novartis, Teva (consulting fees). Marcelo Kremenchutzky: Bayer, Biogen Idec, Serono, Genzyme, Novartis, Teva (consulting fees); MS Society of Canada, Canadian Institute of Health Research, Bayer, Biogen Idec, Serono, Genzyme, Novartis, Sanofi, Teva (grant/research support). John Kramer: Avanir, Bayer, Biogen Idec, Teva (honoraria); Biogen Idec, Novartis (consulting fees). Robert J. Fox: Allozyne, Avanir, Biogen Idec, Novartis, Questcor, Teva, Xenoport (consulting fees); Novartis (grant/research support).

Keywords: Disease-modifying treatments in MS, Management of treatment side effects
(DX31) LYMPHOCYTE COUNT REDUCTIONS IN RELAPSING-REMITTING MULTIPLE SCLEROSIS PATIENTS TREATED WITH DELAYED-RELEASE DIMETHYL FUMARATE: INTEGRATED ANALYSIS OF THE PLACEBO-CONTROLLED STUDIES

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Background: Delayed-release dimethyl fumarate (DMF) demonstrated significant efficacy and an acceptable safety profile in placebo-controlled clinical trials, including a phase 2b trial and the phase 3 DEFINE and CONFIRM studies. The most common adverse events (AEs) with delayed-release DMF were flushing and GI events, but delayed-release DMF was also associated with a reduction in lymphocyte counts.

Objectives: To describe the clinical relevance of lymphocyte count reductions with delayed-release DMF, based on an integrated analysis of the placebo-controlled phase 2b, DEFINE, and CONFIRM studies. Methods: The analysis comprised 2428 relapsing-remitting multiple sclerosis (RRMS) patients who received placebo (n = 836) or delayed-release DMF 240 mg twice daily (BID; n = 769) or three times daily (TID; n = 823) for up to 96 weeks. CONFIRM included a glatiramer acetate reference comparator arm (n = 351; results not shown). Results: In delayed-release DMF-treated patients, mean white blood cell and lymphocyte counts decreased by approximately 11% and 30%, respectively, through week 48, then plateaued, but remained within normal limits throughout the observation period. Percentages of patients with worst post-baseline Common Terminology Criteria (CTC) grades 1, 2, or 3, respectively, were higher in the BID (10%, 22%, 6%) and TID (8%, 18%, 3%) groups than in the placebo group (2%, 2%, <1%). Percentages of patients with >1 grade 3 or 4 lymphocyte count were 0% (placebo), 3% (BID), and 1% (TID), and with consecutive grade 3 or 4 lymphocyte counts were 0% (placebo), 2% (BID), and 1% (TID). The incidence of grade 3 or 4 lymphopenia increased through week 48, then stabilized. There was no clear pattern of increased incidence of infections or serious infections with increasing post-baseline lymphocyte CTC grade. No patients discontinued study drug due to lymphopenia. Four weeks after stopping delayed-release DMF, mean lymphocyte counts increased but did not return to baseline. Conclusions: Treatment with delayed-release DMF was associated with decreased lymphocyte counts but no overall increased risk of infection.

Supported by: Biogen Idec

Disclosure: J. Theodore Phillips: Acorda, Biogen Idec, Genzyme, Novartis, Sanofi, Teva, Xenoport (consulting fees); Roche (grant/research support); Robert J. Fox: Alleleon, Avanir, Biogen Idec, Novartis, Questcor, Teva, Xenoport (consulting fees); Novartis (grant/research support); Ralf Gold: Bayer HealthCare, Biogen Idec, Merck Serono, Novartis, Genzyme; Teva Neuroscience (grant/research support, consulting fees); Sage (compensation for serving as editor of Therapeutic Advances in Neurological Disorders). Krzysztof Selmaj: Biogen Idec (fees for non-CME services from commercial interests or their agents); Genzyme, Novartis, Ono, Roche, Synthon, Teva (consulting fees). Kartik Raghupathi, Huixing Yuan, John O’Gorman, Mark Novas, Vissia Viglietta, Nuwan C. Kurukulasuriya: Biogen Idec (employee).

Keywords: Disease-modifying treatments in MS

(DX32) MANAGEMENT OF REPORTED SIDE EFFECTS OF PATIENTS INITIATING THERAPY ON DIMETHYL FUMARATE

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Background: Dimethyl fumarate is an oral medication approved by the US Food and Drug Administration (FDA) in April 2013 for the treatment of relapsing-remitting multiple sclerosis (RRMS). Phase 3 pivotal clinical trials revealed common adverse events related to dimethyl fumarate (previously designated as BG-12), including flushing, diarrhea, nausea, abdominal pain, and itching. In an attempt to proactively manage these well-recognized and not infrequently limiting side effects, providers recommended pretreatment with a variety of medications including aspirin, antihistamines, and anticholinergic agents, and bismuth salicylate. Objectives: To characterize patient-reported side effects in patients with MS treated with dimethyl fumarate, and to ascertain whether preemptive symptom management strategies could affect side effect profiles and successfully lengthen duration of treatment. Methods: The Clinical Center for MS at University of Texas Southwestern Medical Center followed 66 MS patients treated with dimethyl fumarate. Patients were systematically evaluated for treatment-associated symptoms, subsequent symptom management, and duration of treatment. Patients were followed via telephone and secure electronic messages. Additionally, data were collected at a clinical follow-up visit 3 months after initiating treatment with the new disease-modifying therapy. Results: Regardless of the symptom being reported, patients most commonly reported side effects during titration from the initial dose of 120 mg twice daily to the maintenance dose of 240 mg twice daily. Similar to the phase 3 clinical findings, patients most commonly reported flushing (35%), abdominal pain (12%), diarrhea (15%), nausea/vomiting (11%), and itching (9%). Low-dose aspirin (81 mg) was prescribed for flushing. Diphenhydramine or cetirizine was recommended for patients who experienced itching or rash. For diarrhea and abdominal discomfort, loperamide or bismuth salicylate was recommended. In rare instances, providers extended the length of time on 120 mg twice daily dosing before increasing to the 240 mg twice daily maintenance dose. Conclusions: In a real-world environment, patients experience symptoms including flushing, abdominal pain, diarrhea, and itching. These common side effects can be managed in the majority of patients if pretreated with aspirin, diphenhydramine, cetirizine, loperamide, or bismuth salicylate.

Supported by: None


Keywords: Disease-modifying treatments in MS
Delayed-release dimethyl fumarate (DMF) has shown promise as a drug with possible immune-modulating and independent neuroprotective qualities. However, there are a major cause of MS-related disability. Despite advances in the treatment of relapsing MS, progressive MS remains refractory to existing disease-modifying therapies (DMTs). Lithium has shown promise as a drug with possible immune-modulating and independent neuroprotective qualities. However, its safety, tolerance, and efficacy have not been previously demonstrated in an MS cohort. Objectives: Demonstrate the feasibility of using lithium carbonate to treat subjects with progressive MS. Present baseline characteristics of enrolled subjects and preliminary data on lithium tolerance. Methods: Subjects with >1 year of progressive disease were recruited from MS clinics at the Birmingham VA and the University of Alabama at Birmingham. Consenting subjects who completed screening were enrolled in a 2-year crossover study. Subjects were randomly assigned to take fixed-dose lithium in either year 1 or year 2. Comprehensive evaluations at baseline and at years 1 and 2 include magnetic resonance imaging (MRI), Expanded Disability Status Scale (EDSS), Multiple Sclerosis Functional Composite, and scales to assess mood, fatigue, and quality of life. Paired comparisons between on- and off-lithium periods will be used to assess clinical and MRI outcomes. The primary outcome measures for the study are 1) safety and tolerance of lithium, as evidenced by adverse events (AEs), side effects, and study withdrawals; and 2) evidence of disease progression, as evidenced by intra-individual changes in brain atrophy rates. Secondary outcomes include changes in MRI lesion burden, relapses, and changes in disability, fatigue, mood, and quality of life. Results: We obtained consent from 24 subjects, of whom 23 successfully completed screening. The cohort is 62.5% male, with a mean age of 51.5 (SD 7.5) years at enrollment and mean disease duration of 14.8 (SD 10.4) years. Subjects are 87.5% secondary progressive and 12.5% primary progressive. Median EDSS score is 4.0 (interquartile range [IQR], 3.5-6). Nineteen subjects are taking a DMT. Of the 17 subjects exposed to lithium to date, 8 have completed a full year of lithium, 4 are currently taking lithium, and 5 have discontinued the study, 3 due to AEs (worsening gait) and 2 for personal reasons. One subject on lithium has experienced a relapse requiring outpatient steroids, but remains enrolled and on lithium. Cumulative lithium exposure to date for all subjects is 141 months. After study initiation, maximum daily lithium was reduced from 600 to 300 mg due to frequent side effects, which improved overall tolerance. The most common AEs reported to date have all been mild and include increased thirst (11/17), polyuria (9/17), and fatigue (7/17). Efficacy endpoints will be analyzed upon study completion in 2015. Conclusions: Low-dose lithium is safe and well tolerated in this cohort of progressive MS patients. Major changes in disease activity, mood, and fatigue have not been noted to date. Deterioration in gait may limit lithium treatment in a subset of MS patients.

Background: As therapy for multiple sclerosis (MS) becomes more complex, many treatments require close monitoring. Monitoring is essential for patient safety. This involves a concerted effort involving prescribing physicians and patients. There are many barriers, including limited resources, costs for education, and costs for monitoring. Failure to comply with monitoring protocols by either party can lead to serious, life-threatening complications. Objectives: Two of the more recently available therapies include Aubagio and Gilenya. Aubagio requires blood monitoring every month for the first 6 months. Gilenya requires blood monitoring every 3 months, and patients are required to have baseline and follow-up eye examinations. The purpose of the monitoring is to evaluate for liver disease and, in the case of Gilenya, macular edema. Methods: All patients at the MS Center of Atlanta who were prescribed Aubagio or Gilenya were educated on the benefits and risks of treatments, given a written protocol, and given required laboratory tests and eye examination prescriptions. We performed a retrospective chart review for the first 6 months of therapy. For Aubagio, we looked at the percentage of patients who complied with required monthly blood testing. For Gilenya, we looked at the percentage of patients who complied with the blood testing at months 3 and 6 and the percentage who went for their 4-month follow-up eye examination. Results: Adherence to monitoring protocol will be presented, with numerical data showing a troubling low adherence rate despite a rigid protocol and patient education. For Gilenya, 81% of patients received the required blood testing, but only 38% received the required follow-up eye examination. For Aubagio, only 42% of patients received over half of the required blood tests, whereas 58% performed three or fewer of the required six tests. Conclusions: Patient adherence to monitoring protocols was poor. As therapies become more effective, complex safety monitoring protocols also increase patient risk.

Support by: None

Disclosure: Jeffrey B. English: Biogen Idec, Genzyme, Questcor, Teva (consulting fees); Novartis (grant/research support). Katie E. English: Nothing to disclose.

Keywords: Complementary/alternative therapies in MS, Disease-modifying treatments in MS, Economic issues and MS

(Oral) Delayed-release dimethyl fumarate (DMF) as add-on therapy to interferon beta or glatiramer acetate in relapsing-remitting multiple sclerosis: safety and tolerability

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Background: Progressive forms of multiple sclerosis (MS) are a major cause of MS-related disability. Despite advances in the treatment of relapsing MS, progressive MS remains refractory to existing disease-modifying therapies (DMTs). Lithium has shown promise as a drug with possible immune-modulating and independent neuroprotective qualities. However, its safety, tolerance, and efficacy have not been previously demonstrated in an MS cohort.

Objectives: Demonstrate the feasibility of using lithium carbonate to treat subjects with progressive MS. Present baseline characteristics of enrolled subjects and preliminary data on lithium tolerance.

Methods: Subjects with >1 year of progressive disease were recruited from MS clinics at the Birmingham VA and the University of Alabama at Birmingham. Consenting subjects who completed screening were enrolled in a 2-year crossover study. Subjects were randomly assigned to take fixed-dose lithium in either year 1 or year 2. Comprehensive evaluations at baseline and at years 1 and 2 include magnetic resonance imaging (MRI), Expanded Disability Status Scale (EDSS), Multiple Sclerosis Functional Composite, and scales to assess mood, fatigue, and quality of life. Paired comparisons between on- and off-lithium periods will be used to assess clinical and MRI outcomes. The primary outcome measures for the study are 1) safety and tolerance of lithium, as evidenced by adverse events (AEs), side effects, and study withdrawals; and 2) evidence of disease progression, as evidenced by intra-individual changes in brain atrophy rates. Secondary outcomes include changes in MRI lesion burden, relapses, and changes in disability, fatigue, mood, and quality of life.

Results: We obtained consent from 24 subjects, of whom 23 successfully completed screening. The cohort is 62.5% male, with a mean age of 51.5 (SD 7.5) years at enrollment and mean disease duration of 14.8 (SD 10.4) years. Subjects are 87.5% secondary progressive and 12.5% primary progressive. Median EDSS score is 4.0 (interquartile range [IQR], 3.5-6). Nineteen subjects are taking a DMT. Of the 17 subjects exposed to lithium to date, 8 have completed a full year of lithium, 4 are currently taking lithium, and 5 have discontinued the study, 3 due to AEs (worsening gait) and 2 for personal reasons. One subject on lithium has experienced a relapse requiring outpatient steroids, but remains enrolled and on lithium. Cumulative lithium exposure to date for all subjects is 141 months. After study initiation, maximum daily lithium was reduced from 600 mg to 300 mg due to frequent side effects, which improved overall tolerance. The most common AEs reported to date have all been mild and include increased thirst (11/17), polyuria (9/17), and fatigue (7/17). Efficacy endpoints will be analyzed upon study completion in 2015.

Conclusions: Low-dose lithium is safe and well tolerated in this cohort of progressive MS subjects. Major changes in disease activity, mood, and fatigue have not been noted to date. Deterioration in gait may limit lithium treatment in a subset of MS patients.

Support by: Department of Veterans Affairs CSR D Career Development Award

Disclosure: Nothing to disclose.

Keywords: Disease-modifying treatments in MS, Lithium
profile in patients with relapsing-remitting multiple sclerosis (RRMS) in placebo-controlled clinical trials. **Objectives:** To describe the safety and tolerability of delayed-release DMF as add-on therapy to interferon beta (IFNβ) or glatiramer acetate (GA) in the phase 2, open-label EXPLORE study. **Methods:** Eligibility criteria included age 18 to 55 years, RRMS diagnosis (McDonald criteria), Expanded Disability Status Scale (EDSS) score 0 to 5.0, established therapy with the same dose of IFNβ or GA for ≥12 months, and ≥1 relapse within 12 months or gadolinium-enhancing lesion(s) on magnetic resonance imaging (MRI) within 6 weeks prior to enrollment. Patients continued on their prescribed MS therapy for 2 months (monotherapy period), then received delayed-release DMF 240 mg three times daily in addition to their prescribed MS therapy for 6 months (add-on therapy period). **Results:** During the add-on therapy period, in the delayed-release DMF/IFNβ (n = 57) and delayed-release DMF/GA (n = 47) groups, the overall incidence of AEs was 95% and 100%; the most common AEs were flushing (42% and 53%), diarrhea (32% and 15%), and abdominal pain (21% and 6%). Most AEs were reported as mild or moderate in severity. There was no overall increased risk of infection. No malignancies were reported. At week 24, mean percentage decrease of lymphocyte counts from baseline was 22% (delayed-release DMF/IFNβ) and 7% (delayed-release DMF/GA). There was a transient increase in liver transaminases; no case fulfilled Hy’s law. There were no deaths. **Conclusions:** The safety profile of delayed-release DMF in combination with IFNβ or GA was similar to the known safety profile of delayed-release DMF monotherapy. There were no unexpected safety signals.

**Supported by:** Biogen Idec

**Disclosures:** Jonathan Calkwood: Acorda, Bayer HealthCare, Biogen Idec, EMD Serono, Genzyme, Novartis, Questcor, Teva (consulting fees); Biogen Idec, Novartis, Roche, Xenoport (grant/research support). Timothy Vollmer: Biogen Idec, Teva Pharmaceutical Industries, Genzyme, Ono Pharmaceuticals, Elan Pharmaceuticals, Novartis, National Institutes of Health, Avanir Pharmaceuticals, Janssen Research & Development (grant/research support); Sanofi, Novo, Novartis Japan, Teva, Teva Canada Innovations, Roche, Biogen Idec, Xenoport, University of Florida PeerView, Krog & Partners, National Multiple Sclerosis Society, University of St. Louis, Acorda, Mylan, Genzyme, Deloitte Consulting (consulting fees); Vianna Viogletta, Ray Zhang, Mark Novas, Sarah L. Sheikly; Biogen Idec (employee). Robert J. Fox: Allozyne, Avanir, Biogen Idec, Novartis, Questcor, Teva, Xenoport (consulting fees); Novartis (grant/research support).

**Keywords:** Disease-modifying treatments in MS, Natalizumab

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**Posters:** Disease Management, Mechanisms, and Treatment

**(DX37) TREATMENT EFFECT ON T1-HYPOINTENSE LESIONS: EVALUATION OF TWO DIFFERENT METHODOLOGIES IN RELAPSING-REMITTING MULTIPLE SCLEROSIS SUBJECTS FROM THE GALA STUDY**

Robert Zivadinov,1 Omar Khan,2 Michael G. Dwyer,3 Deepa P. Ramasamy,3 Hadas Barkay,4,5 Abi Vainstein-Haras,6 Joshua R. Steinerman,1 Volker Knappertz,*6

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**Background:** When evaluating treatment effects on T1-hypointense lesions (T1H) in multiple sclerosis (MS) clinical trials, there is no guideline whether to assess all active T1H on pre-contrast magnetic resonance imaging (MRI) scans (T1H-total) or just those T1H on pre-contrast MRI scans that are simultaneously nonenhancing on post-contrast scans (T1H-nonenhancing). **Objectives:** To examine new/enlarging T1H-total and T1H-nonenhancing between 0–6 and 6–12 months in the Glatiramer Acetate Low-frequency Administration (GALA) study. **Methods:** GALA was a phase 3 trial that randomized 1404 relapsing-remitting MS subjects to receive glatiramer acetate (GA) 40 mg/1 mL three times a week or placebo for 12 months. MRI was performed at baseline and months 6 and 12. Cumulative numbers of T1H-total and of T1H-nonenhancing were calculated and analyzed using an adjusted negative binomial regression model. **Results:** Overall, 1325 patients were included in the analysis of T1H-total, and 1323 were included in the analysis of T1H-nonenhancing. Analyses of T1H-total revealed that 884 GA-treated patients developed a mean of 1.7 versus 2.6 lesions in the 441 placebo arm patients (risk ratio [RR], 0.67; 95% confidence interval [CI], 0.55-0.81; P < .0001). Analysis of T1H-nonenhancing revealed that GA-treated patients developed a mean of 1.3 versus 1.9 lesions in the placebo arm patients [RR, 0.71; 95% CI, 0.57-0.87; P = .0009]. **Conclusions:** Results using the two methodologies are comparable. However, T1H-nonenhancing lesions may represent a distinct stage of lesion evolution, potentially showing a more advanced pathological substrate of tissue damage compared with T1H-total. On the other hand, T1H-total may capture

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**(DX36) BETTER CHARACTERIZING THE NATALIZUMAB “WEARING-OFF” PHENOMENON**

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**Background:** Multiple sclerosis (MS) patients treated with natalizumab often report a “wearing-off effect,” described as worsening MS symptoms or various constitutional symptoms, most often prior to their next dose. **Objectives:** We sought to better characterize the “wearing-off” phenomenon in our patient population and compare the intensity, onset, and duration of symptoms in patients on a 4-week dosing cycle to those on a 6- or 8-week dosing cycle. **Methods:** We performed a prospective observational study on all of our MS patients being treated with natalizumab for 3 months or longer, using a questionnaire to evaluate the prevalence and severity of constitutional symptoms, and temporal relationship to their dose. **Results:** 83 patients were surveyed. 63% of patients noted symptoms prior to their dose of natalizumab, the most prominent being fatigue. The majority experienced symptoms 4 to 9 days prior to each dose, regardless of the dosing interval. Symptoms typically resolved within 1 day of their infusion. **Conclusions:** Our data suggest that approximately two-thirds of patients experience the “wearing-off effect,” predominantly characterized by fatigue and myalgias. Additionally, there was no significant difference in intensity, onset, or duration of symptoms in patients on a 4-week dosing cycle compared to those on a 6- or 8-week dosing cycle, suggesting that patients acclimate to their prescribed dosing cycle.

**Supported by:** None

**Disclosure:** Nothing to disclose

**Keywords:** Disease-modifying treatments in MS, Natalizumab

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additional aspects of lesion evolution, such as remyelination, thus obscuring mechanistic interpretation. This study is relevant to future clinical trials aiming to clarify mechanisms of treatment effect.

Supported by: Teva Pharmaceutical Industries

Disclosures: Robert Zivadinov: Biogen Idec, Bracco, EMD Serono, Sanofi-Genzyme, Questcor, Teva (grant/research support); Biogen Idec, EMD Serono, Novartis, Sanofi-Genzyme, Teva (consulting fees); Omar Khan: Biogen Idec, Genzyme, National Institutes of Health, National Institute of Neurological Disorders and Stroke, National Multiple Sclerosis Society, Novartis, Roche, Teva (grant/support); Biogen Idec, Genzyme, Novartis, Teva (consulting fees); Michael G. Dwyer: EMD Serono, Inc. (consulting fees); Deepa P. Ramasamy: Nothing to disclose.

Keywords: Disease-modifying treatments in MS, Glutamatergic imaging and MS

(DX38) SWITCHING FROM NATALIZUMAB TO TERIFLUNOMIDE IN MULTIPLE SCLEROSIS PATIENTS WHO HAVE RECEIVED NATALIZUMAB FOR MORE THAN 12 MONTHS

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Background: Teriflunomide is an oral immunomodulator approved for use in multiple sclerosis (MS) patients with relapsing forms of MS. In order to reduce the risk of progressive multifocal leukoencephalopathy (PML), a need exists for the safe transition to another disease-modifying therapy for certain patients who have received natalizumab (NAT) for more than 12 months. Many MS patients have significant exacerbations after stopping NAT. Objectives: To review the efficacy and safety in 30 consecutive patients who have been switched from NAT to teriflunomide and have received teriflunomide for at least 6 months. Methods: This study is a retrospective data review of 30 MS patients who had received at least 12 NAT treatments; all were clinically stable while on NAT. The patients usually were able to begin teriflunomide within 4 weeks of their last NAT treatment. Clinical examination and cranial magnetic resonance imaging (MRI) were obtained at time of last NAT treatment and at 3 and 6 months after last NAT treatment for evaluation of possible PML and for any new MS activity. ALT values were measured monthly for 6 months after starting teriflunomide. Side effects were recorded. Results: Of the 30 patients regarding their risk for PML, 11 were triple positive (for receiving more than 24 NAT treatments, having prior immunosuppression, and being positive for anti-JCV-antibody), 13 were positive for anti-JCV-antibody, and 6 tested negative for anti-JCV-antibody. The mean number of NAT treatments was 39 (range, 14–81), and mean age of patients was 52 years (range, 28–70 years). Seventy-six percent were female. Mean duration of teriflunomide treatment after NAT discontinuation was 9 months (range, 6–13). Of the 30 patients evaluated, 25 are still on teriflunomide. No patients developed PML. One patient discontinued teriflunomide due to a significant exacerbation, and 3 others had minor exacerbations responding to IVMP and continued teriflunomide. Two other patients discontinued due to persistent diarrhea and abdominal cramps, and 1 discontinued because of hair thinning. Minor diarrhea and transient hair thinning occurred in 7 and 5 patients, respectively. There were no LFTs abnormalities. Conclusions: Teriflunomide may be an effective and safe alternative for patients switching from NAT. A reduced “washout” period after NAT may be important to lessen breakthrough disease.

Supported by: None

Disclosure: Keith R. Edwards: Acorda, Biogen Idec, EMD Serono, Genzyme, Novartis Pharmaceutical (speakers’ bureau); Biogen Idec, Genzyme, Novartis Pharmaceutical (scientific advisory board, consulting fees); Actelion, Biogen Idec, Eli Lilly, Genentech, Genzyme, Novartis (grant/research support). Vineetha Kamath, Judy O’Connor: Nothing to disclose.

Keywords: Disease-modifying treatments in MS

(DX39) OPSOCONUS-MYOCOLONUS IN A 14-YEAR-OLD MULTIPLE SCLEROSIS PATIENT RECEIVING NATALIZUMAB

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Background: Opsoclonus-myoclonus syndrome (OMS) is a rare neurologic disorder most commonly diagnosed in very young pediatric patients. Paraneoplastic (especially neuroblastoma and neoplasms of reproductive organs), viral infections, and idiopathic etiologies are most common. The clinical features of OMS include rapid, conjugate, and random saccadic eye movements. Myoclonus is most often reported in the head, neck, and limbs. Treatment is focused on symptom responsiveness. Therapy with acetylcholine, steroids, and/or immunoglobulin (Ig) has proven most beneficial. Objectives: To describe the disease course and treatment of OMS in a multiple sclerosis (MS) patient receiving natalizumab.

Methods: A 14-year-old MS patient with severe clinical and radiologic disease had fewer relapses and stable radiographic findings during treatment with natalizumab. She is JC virus (JCV) antibody (Ab) negative. After her 23rd dose, the patient developed visual disturbances, ataxia, and vertigo. These symptoms began after recovery from 2 weeks of intermittent vomiting and diarrhea. Upon examination, her eye movements were saccadic in all directions, but conjugate; gait was wide-based and ataxic with infrequent limb myoclonus. Romberg test was positive. Results: Magnetic resonance imaging (MRI) showed a slight increase in small plaques, but no enhancing lesions or other abnormalities inconsistent with MS. Remarkable findings on lumbar puncture included an elevated protein and oligoclonal bands. These data led to the conclusion that the patient had OMS. Conclusions: OMS is a rare disorder, most commonly occurring in children. This study is unique because the patient had received natalizumab and OMS cannot be drawn. Watchful management of MS patients switching from NAT is necessary.

Supported by: None

Disclosure: None

Keywords: Disease-modifying treatments in MS

International Journal of MS Care

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Supported by: EMD Serono, Inc., Rockland, MA (a subsidiary of Merck KGaA, Darmstadt, Germany)

Disclosure: Kelley Lehan, Nothing to disclose. Sibyl Wray: Acorda, BioMarin, Genentech (consulting fees); Bayer, Biogen Idec, EMD Serono, Inc., Novartis, Roche, Sanofi-Aventis, Teva Neuroscience (consulting fees, grant/research support); Genzyme, Ono (grant/research support).

Keywords: Disease-modifying treatments in MS

(DX40) CLINICAL EXPERIENCE WITH TECFIDERA
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Background: Tecfidera® (dimethyl fumarate) was approved by the US Food and Drug Administration (FDA) for use in people with multiple sclerosis (MS) in April 2013, making it the newest oral disease-modifying agent (DMA) for MS. There are over 100,000 patient years of experience with a compound of dimethyl fumarate and its esters (Fumaderm®) used in Europe to treat psoriasis.

Objectives: To describe management of individuals with MS on Tecfidera in a post-marketing outpatient clinic setting.

Methods: Patients were placed on Tecfidera if therapy with conventional DMAs resulted in failure. Failure was defined as increase in clinical relapses, increase in radiologic disease activity, or intolerability of DMA side effects. Two people with new diagnoses of MS were started on Tecfidera because of their refusal to take injectable agents. Patients had a comprehensive metabolic panel, complete blood count with differential, platelet count, and urine analysis at baseline and then every 2 months for the first 6 months, and then every 3 to 4 months thereafter.

Results: Thirty patients began therapy with Tecfidera between April 2013 and January 2014. Five patients discontinued therapy (16.67% dropout rate). The primary reason for dropout for all five patients was intolerable gastrointestinal (GI) side effects; additionally, one of these patients developed splenomegaly, which occurred just over a week after starting Tecfidera and resolved after the drug was stopped. We instituted a slower titration than recommended by the manufacturer, which appeared to lessen symptoms for some patients. Other strategies that seemed to ameliorate side effects included taking the medication with fat-containing food; use of yogurt and probiotics, anticholinergic medications for GI symptoms, simethicone for gas pain, antiemetics for nausea, and baby aspirin for flushing. Twenty-five patients completed at least one set of laboratory tests after initiation. Laboratory data are available for four out of the five patients who discontinued the medication due to GI side effects and revealed eosinophilia in all four patients. None of the other 21 patients showed eosinophilia.

Conclusions: Our results in a real-world setting are similar to those of the clinical trials in terms of adverse events, tolerability, and dropout rate. In our small sample size, eosinophilia appeared only in the patients with GI side effects severe enough to necessitate discontinuation of Tecfidera.

Supported by: None


Keywords: Disease-modifying treatments in MS, Nursing management in MS

(DX41) PREGNANCY OUTCOMES IN PARTNERS OF MALE STUDY PARTICIPANTS TREATED WITH TECFIDERA

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Background: Teriflunomide is a once-daily oral immuno-modulator approved for treatment of relapsing-remitting multiple sclerosis. Embryo-fetal toxicity and teratogenicity occur when teriflunomide is administered to pregnant rats and rabbits, but not when treated male rats are bred to untreated females. Teriflunomide is present in seminal fluid, although the estimated plasma exposure in females from semen transfer from a male patient is expected to be ≥100 times lower than exposure following oral dosing of teriflunomide 14 mg.

To date, there is no signal for teratogenicity in humans for teriflunomide or its parent compound, leflunomide (in patients with rheumatoid arthritis [RA]).

Objectives: To report pregnancy outcomes in partners of male study participants in the teriflunomide clinical program, with reference to preclinical genotoxicity studies.

Methods: Participants in teriflunomide studies were required to use effective contraception; despite this, pregnancies occurred in teriflunomide-exposed women and partners of male study participants. Pregnancy outcomes through October 2013 will be reported. Preclinical genotoxicity tests and tissue distribution studies were performed in support of the clinical program.

Results: Across teriflunomide clinical trials, 22 pregnancies were reported in partners of male study patients (teriflunomide, n = 19; placebo, n = 3). There were 18 live births, 16 to partners of patients who had been exposed to teriflunomide. Newborns were healthy and free from structural and functional abnormalities. Two induced abortions and one spontaneous abortion were reported in the teriflunomide group; one induced abortion was reported in the placebo group. No induced abortions were performed for defects or malformations. Additionally, there is no preclinical evidence that teriflunomide would directly damage DNA in vivo, as indicated by negative in vitro mutagenicity and in vivo clastogenicity assays. The drug was undetectable in rat sperm within 14 days following a single oral dose, suggesting that it does not bind irreversibly to sperm.

Conclusions: Data from the clinical program have shown no teratogenic signal for teriflunomide. These outcomes are supported by preclinical data and are consistent with findings of over 2.5 million patient-years of post-marketing exposure to leflunomide in patients with RA. Additional information will be provided by prospective data from teriflunomide pregnancy registries.

Supported by: Genzyme, a Sanofi company

Disclosure: Lily Jung Henson: Biogen Idec, Genzyme, Novartis, Pfizer, Questcor, Sanofi, Teva (consulting fees); Biogen Idec, Genzyme, Opeoa, Novartis, Sanofi (grant/research support). Lynn Davenport, Myriam Benamar, Andreas Czich, Sandrine Turpault: Sanofi (employee).

Keywords: Disease-modifying treatments in MS

(DX42) CARDIAC-RELATED INFUSION-ASSOCIATED REACTIONS IN RELAPSING-REMITTING MULTIPLE SCLEROSIS PATIENTS TREATED WITH ALEMTUZUMAB
Lise Casady,1 Cathy Meyer,2 Stanley Krakczyk,2 Pedro Oyuela,3 Jeffrey Palmer,4 David H. Margolin3

Supported by: EMD Serono, Inc., Rockland, MA (a subsidiary of Merck KGaA, Darmstadt, Germany)

Disclosure: Kelley Lehan: Nothing to disclose. Sibyl Wray: Acorda, BioMarin, Genentech (consulting fees); Bayer, Biogen Idec, EMD Serono, Inc., Novartis, Roche, Sanofi-Aventis, Teva Neuroscience (consulting fees, grant/research support); Genzyme, Ono (grant/research support).

Keywords: Disease-modifying treatments in MS, Nursing management in MS

International Journal of MS Care
Dimethyl fumarate is the most recently approved oral disease-modifying therapy (DMT) in the United States. The safety profile of dimethyl fumarate is considered benign compared with that of natalizumab. Natalizumab, although a highly effective DMT for multiple sclerosis (MS), carries a serious risk of progressive multifocal leukoencephalopathy (PML), although this risk may be stratified based on certain patient characteristics. Many MS health-care providers planned to switch their natalizumab patients with high risk to dimethyl fumarate once it became available. Patients with injection fatigue or with insufficient disease control on the interferons or glatiramir acetate were also considered good candidates for dimethyl fumarate. Objectives: To summarize cardiac-related alemtuzumab IARs in RRMS patients in a phase 3 clinical program. Methods: In 36-month, phase 2 CAMMS223 (NCT00050778) and 24-month, phase 3 CARE-MS I (NCT00303348) and CARE-MS II (NCT00548405) core studies, RRMS patients received alemtuzumab intravenously 12 or 24 mg/day (only 12 mg/day in CARE-MS I) on 5 consecutive days at baseline and 3 consecutive days 12 or 24 months later. All studies included an extension (NCT00930553) with as-needed alemtuzumab retreatment. For IAR mitigation during and after infusions, methylprednisolone premedication (and optional treatment with antipyretics, antihistamines, and anti-emetics) and infusion management strategies were implemented. IARs were defined as AEs beginning during or within 24 hours after any alemtuzumab infusion. Serious IARs were identified by standard ICH criteria. All IAR SAEs in cardiac disorders were reported. Results: Incidence of any IAR cardiac event was 12.5% among alemtuzumab-treated patients (n = 1485), most frequently tachycardia (6.7%), bradycardia (2.8%), and palpitations (2.6%). Serious cardiac-related IARs occurred in 0.5% (n = 8): bradycardia (2), sinus bradycardia (1), atrial fibrillation (3), and sinus tachycardia (2). Other serious IARs included hypotension (3) and hypertension (2), and 1 anaphylaxis event (investigator later characterized as nonanaphylactoid hypotension). Risk of event was not increased with course number/repetition. Events were most frequent on day 1. All events resolved with treatment. All patients continued on study; however, 2 (0.1%) discontinued alemtuzumab treatment. Conclusions: Cardiac symptoms, most commonly tachycardia, can occur with alemtuzumab infusions. In studies, symptoms resolved and did not preclude further alemtuzumab treatment. SAEs were uncommon. Given the potential for these symptoms, it is important to be aware of patients' cardiac history prior to first infusion.

Support by: Genzyme, a Sanofi company; Bayer HealthCare Pharmaceuticals


Keywords: Disease-modifying treatments in MS

(DX44) A CASE OF MISTaken Identity: Natalizumab, Dermatographia, AND INFUSION REACTION

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Background: Natalizumab is an available and effective disease-modifying therapy (DMT) to treat relapsing forms of multiple sclerosis (MS). Natalizumab discontinuation can occur due to infusion reactions. Objective: To describe the appearance of dermatographia (dermatographic urtication) that occurred during the course of natalizumab infusions and was mistaken for an infusion reaction. Case Report: A 58-year-old female with relapsing-remitting multiple sclerosis (RRMS) developed a rash starting at the site of the intravenous (IV) access for natalizumab during the second infusion. It was diagnosed as an infusion reaction and described as an erythematous macular pruritic rash at the site of the IV access. The infu...
Bullous pemphigoid is an uncommon autoimmune skin disorder seen in <0.001% of the population. In this condition, autoantibodies directed against the cell surface of keratinocytes produce acantholysis that leads to intraepithelial blisters in the skin and/or mucous membranes. The disorder can occur independently of other disorders. It has been related to medications and several autoimmune disorders and has occasionally been reported in patients with MS. The underlying cause of bullous pemphigoid is unknown. Treatment can be helpful, but the disorder can result in increased morbidity and mortality. Conclusions: Not all skin reactions that occur during or after natalizumab infusion are allergic and related to therapy. Serious skin reactions may necessitate therapy discontinuation due to the need to initiate other treatments. Vigilance as well as prompt and accurate identification of skin reactions occurring during infusion or thought to be related to infusion is needed to determine the appropriate course of treatment. Differentiating serious skin reactions from nonserious or unrelated reactions is important to ensure appropriate treatment and infusion care.

Supported by: None

Disclosure: Marijke Buhse, Barbara Bumstead, Myassar Zarif, Mark Gudesblatt, Biogen Idec (consulting fees); Lori Fafard: Biogen Idec (grant/research support).

Keywords: Disease-modifying treatments in MS, Nursing management in MS

(DX46) EARLY AND CONSISTENT BENEFITS OF SUBCUTANEOUS INTERFERON BETA-1A IN RELAPSING MULTIPLE SCLEROSIS: POST HOC ANALYSIS OF PRISMS MRI DATA

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Background: In results of the 2-year PRISMS-2 study (Lancet. 1998;352:1498–1504), interferon beta-1a given subcutaneously (IFNβ-1a SC) reduced disease activity on magnetic resonance imaging (MRI) scans versus placebo among patients with relapsing multiple sclerosis (RMS). Objectives: Investigate monthly differences in active lesions and MRI scans in patients with RMS receiving placebo or IFNβ-1a SC over 9 months. Methods: 560 adults with RMS having had ≥2 relapses over 2 years, with Expanded Disability Status Scale score of 0 to 5.0, were randomized to receive placebo or IFNβ-1a SC 22 or 44 µg, three times a week for 2 years. A cohort (n = 198) underwent monthly MRI scans for the first 9 months. Post hoc analysis of this cohort determined mean number of combined unique (CU) active lesions [combined count of proton density (PD)/T2 and T1 gadolinium-enhanced (Gd+) new and recurring lesions; unique means an active lesion on both PD/T2 and T1 Gd+ scans was only counted once] per patient per scan, and percentages of combined active scans (scans with CU active lesions) per patient. For each monthly point, pairwise between-treatment comparisons including all scans up to that point were assessed using analysis of variance (ANOVA) models on ranks adjusting for number of CU active lesions at baseline and study center. Percentages of patients with no active scans at each month were calculated. Results: As early as up to 2 months (including 4–8 weeks titration), for mean CU active lesions/patient/...
scan, means (medians) were 1.92 (0.75), 1.40 (0.25), and 0.77 (0.00) for placebo (n = 66) and IFNβ-1a SC 22 µg (n = 64) and 44 µg (n = 67), respectively (P < .01 for 22 and 44 µg vs. placebo). Among scans up to 2 months, mean (median) percentages of combined active scans/patient were 55.3% (50%), 36.7% (25%), and 32.1% (0%) for placebo, 22 µg, and 44 µg groups, respectively (P < .01 for 22 and 44 µg vs. placebo). Differences between each IFNβ-1a SC group and placebo in mean CU active lesions and percentage of combined active scans were significant at subsequent monthly points up to 9 months (P = NS for 22 vs. 44 µg). At month 2, 42.9%, 67.2%, and 78.1% of placebo, 22 µg, and 44 µg patients, respectively, had no active scans. This rose to 49.2%, 84.4%, and 88.2% at month 9 (in 65, 64, and 68 placebo; 22 µg, and 44 µg patients with valid scans). **Conclusions:** Results support an early (2 months) and consistent treatment-associated reduction of CU active lesions and combined active scans among patients with RMS receiving IFNβ-1a SC versus placebo.

**Supported by:** EMD Serono, Inc., Rockland, MA (a subsidiary of Merck KGaA, Darmstadt, Germany)

**Disclosure:** Mark Cacchione: Accera, Avanir, Eisai, Eli Lilly, Tau (grant/research support); Acorda, Bayer HealthCare, Biogen Idec, EMD Serono, Inc., Genentech, Genzyme/Sanofi, Novartis, Pfizer, Roche, Teva (consulting fees, fees for non-CME services from commercial interests or their agents, grant/research support); Questor (consulting fees).

Carol Gaines, Jianzhi Fang, Fernando Danoup: EMD Serono, Inc. (employee).

Aaron Miller: Acorda Therapeutics Inc., CVS Caremark, EMD Serono, Inc., GlaxoSmithKline, Novartis, Nuron Biotech Inc., Ono (consulting fees, fees for non-CME services from commercial interests or their agents; Acorda, Genentech, Roche (grant/research support); Biogen Idec, Genzyme/Sanoft-Aventis, Questcor (consulting fees, fees for non-CME services from commercial interests or their agents, grant research support).

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

**DX47** **CONSISTENT TREATMENT EFFECT OF TERIFLUNOMIDE IN SUBGROUPS BASED ON PRETRIAL THERAPY: POOLED ANALYSES OF TEMSO AND TOWER

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**Background:** Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing-remitting multiple sclerosis (RRMS). Phase 3 trials TEMSO (NCT00134563) and TOWER (NCT00751881) had similar designs and patient demographics, allowing for pooling of data. In the pooled analyses, teriflunomide 14 mg significantly reduced annualized relapse rate (ARR) and disability progression; teriflunomide 7 mg significantly reduced ARR. Both doses had similar, manageable safety profiles. Pre-trial use of disease-modifying therapies (DMTs) or steroids (to treat attacks) and their subsequent discontinuation could imply more active or severe forms of MS; herein we present the pooled subgroup analysis from TEMSO-TOWER by pretrial therapy. **Objectives:** To assess the consistency of the teriflunomide effect on ARR and disability progression across subgroups based on pretrial MS therapy. **Methods:**

**TEMPSO and TOWER enrolled patients with relapsing forms of MS, aged 18 to 55 years, with Expanded Disability Status Scale (EDSS) score ≤5.5, and ≥1 or ≥2 relapses in the 12 or 24 months before study entry, respectively. Patients were randomized 1:1:1 to once-daily teriflunomide 14 mg (n = 728) or 7 mg (n = 772), or placebo (n = 751) for 108 weeks (TEMPSO) or 48 weeks after last patient randomized (TOWER). Post hoc analyses of ARR and 12-week confirmed disability progression were performed on pooled subgroups defined by pretrial therapy: >1 prior DMT, 1 prior DMT, prior steroids only, and no prior MS treatment in the previous 2 years. **Results:** Baseline disease characteristics were generally well balanced across subgroups, with differences reflecting varying stages of disease. Mean time since diagnosis of MS and most recent relapse varied (3.9 years [steroids only] to 7.3 years [≥1 prior DMT]; 4.8 months [steroids only] to 6.4 months [≥1 prior DMT], respectively). Efficacy of 14 mg was consistent across the subgroups defined by pretrial MS therapy for ARR and disability progression, with all estimates of treatment effect favoring teriflunomide versus placebo and no statistically significant (P > .05) treatment-by-subgroup interaction. Similar results were observed for 7 mg for ARR. **Conclusions:** Pooled subgroup analyses show consistent treatment effect of teriflunomide across subgroups defined by pretrial DMT or prior use of steroids, including efficacy in patients with more active or severe disease activity at baseline.

**Supported by:** Genzyme, a Sanofi company

**Disclosure:** Mark S. Freedman: Bayer HealthCare, Biogen Idec, Merck Serono, Novartis, Opea (board of directors); Sanofi-Aventis (fees for non-CME services from commercial interests or their agents); Bayer HealthCare (grant/research support); Bayer HealthCare, Biogen Idec, EMD Canada, Novartis, Sanofi-Aventis, Teva Canada Innovation (consulting fees). Deborah Dukovic, Myriam Benamor: Sanofi (employee), Philippe Truffinet: Genzyme, a Sanofi company (employee). Ludwig Kappos: Actelion, Allozyne, Bayer HealthCare Pharmaceuticals, Bayer Schering Pharma, Bayhill, Biogen Idec, CLC Behring, GeNeuro SA, Genmab, Genzyme, GlaxoSmithKline, Lilly, Merck Serono, Mitsubishi Pharma, Novartis, Novonordisk, Peptim (grant/research support).

**Keywords:** Disease-modifying treatments in MS

**DX48** **HIGH CONTINUATION RATE, GOOD DISEASE CONTROL AFTER SWITCHING FROM NATALIZUMAB TO FINGOLIMOD

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**Background:** Gilenya® (fingolimod) is approved in Canada for the treatment of relapsing-remitting multiple sclerosis (RRMS). The Gilenya Go Program™ was launched in March 2011 to provide patient support services, reinforce patient adherence to recommended monitoring, and coordinate first-dose observation (FDO) at specialized FDO centers. **Objectives:** The present analysis evaluated the adherence and tolerability of fingolimod in the subset of patients who were previously treated with natalizumab. The objective was to assess the continuation rate on fingolimod after natalizumab withdrawal. **Methods:** Data were collected and analyzed.
for patients enrolled in the Canadian Gilenya® Go Program™ from the time of first patient enrollment in March 2011 to October 2013. **Results:** At data cutoff, 243/1989 fingolimod-treated patients reported prior natalizumab as their most recent treatment. Duration on natalizumab was not obtained. 70% were female; mean age was 42 years. Patient-reported reasons for discontinuing natalizumab (n = 171) were unspecified adverse effects (35%), anti-JCV antibody positivity (18%), lack of efficacy (18%), infusion-related (12%), adverse effects (allergic reaction, shingles, other, 9%), concerns about progressive multifocal leukoencephalopathy (PML) risk (5%), neutralizing antibodies (2%), and other (1%). During the 33-month observation period, the continuation rate on fingolimod was 83.0%. Mean time to withdrawal of fingolimod (n = 40) was 225 days. Reasons for withdrawal were adverse events (AEs) (22/40, 55%), physician or patient request (20%), lack of efficacy (17.5%), and no reason given (7.5%). Women were more likely than men to discontinue fingolimod (19% vs. 10%). There was one withdrawal at first dose due to AV block. AEs associated with fingolimod discontinuation after the first dose included palpitations (n = 4), low lymphocyte count (n = 4), headache/migraine (n = 2), oral herpes infection (n = 2), and other infections (n = 3). Three patients withdrew due to MS-related symptoms (relapse, optic neuritis, incontinence). **Conclusions:** Oral fingolimod is associated with good tolerability in patients discontinuing natalizumab. 83% of patients are successfully maintained on fingolimod in clinical practice. The high continuation rate is comparable to the 1-year continuation rate in TRANSFORMS (89%) and the 2-year continuation rate in FREEDOMS (81%).

Supported by: Novartis

**Disclosure:** Mark S. Freedman; Bayer HealthCare (advisory board, consulting fees, grant/research support); Biogen Idec, Novartis, Sanofi-Aventis (advisory board, consulting fees); EMD Serono, Teva Canada Innovation (consulting fees); Genzyme (consulting fees, grant/research support, speakers’ bureau); Hoffmann-La Roche, Merck Serono, Opeca (advisory board). Paul O’Connor; Biogen Idec, Celgene, Genzyme, Hoffmann-La Roche, Novartis, Teva Neuroscience (grant/research support). Pierre Duguet; Biogen Idec, EMD Serono (grant/research support, investigator-initiated trial grant); Canadian Institutes of Health Research, Genzyme, MS Society of Canada, Novartis, Teva Neuroscience (grant/research support). Robyn Schecter; Novartis (employee).

**Keywords:** Disease-modifying treatments in MS

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**POSTERS: DISEASE MANAGEMENT, MECHANISMS, AND TREATMENT**

**(DX50) THE PREFERMS STUDY: EVALUATING REAL-WORLD PATIENT RETENTION ON ORAL FINGOLIMOD COMPARED WITH INJECTABLE DISEASE-MODIFYING THERAPIES IN RELAPSING-REMITTING MULTIPLE SCLEROSIS**

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**Background:** The efficacy and safety of fingolimod in relapsing-remitting multiple sclerosis (RRMS) has been well established in controlled clinical trials and the postmarketing setting. However, real-world patient retention on injectable disease-modifying therapies (iDMTs) and related clinical and magnetic resonance imaging (MRI) outcomes have not been evaluated for fingolimod versus iDMTs. Understanding the impact of patient retention in early RRMS could have important implications for treatment decision-making during the initial stages of the disease. **Objectives:** To conduct a randomized, prospective, real-world study of patient retention on once-daily oral fingolimod (0.5 mg) compared with retention on first-line iDMTs in the course of RRMS. **Methods:** PREFERMS is a 12-month, phase 4, open-label, active-
controlled, randomized, multicenter study enrolling ~850 patients, mostly in the early stages of RRMS, who either are treatment-naïve or have been treated with one class of iDMT (interferon or glatiramer acetate) or dimethyl fumarate (<2 months’ exposure). Patients are in the process of being randomized 1:1 to receive fingolimod or iDMT; those who have previously been treated with iDMT will receive an alternative iDMT class during the study if randomized to iDMT. The primary endpoint is the rate of retention on randomized treatment. Secondary endpoints include reasons for treatment discontinuation, occurrence and persistence of drug-related adverse events, cognitive impairment, percentage change in brain volume, and medication satisfaction. Comprehensive MRI, optical coherence tomography, Multiple Sclerosis Functional Composite, and quality of life assessments are exploratory parameters. Results: Enrollment started in June 2012; approximately 140 investigational sites across the United States have met more than 60% of the recruitment target as of 28 October 2013. Study results are expected in 2015.

Conclusions: PREFERMS will evaluate patient retention on fingolimod compared with retention on iDMT, and if this impact may have on key clinical and MRI outcomes in RRMS. Moreover, this study will provide important real-world clinical evidence and patient-reported outcomes of relevance to early fingolimod therapy.

Supported by: Novartis Pharmaceuticals Corporation

Disclosure: Nadia Tenenbaum, Lesley Schofield, Xiangyi Meng, Ralph Kern: Novartis (employee).

Keywords: Fingolimod, Patient retention, Real-world evidence

(DX51) IMPROVED ESTIMATION OF TREATMENT EFFECTS: ANALYSIS OF TIME TO RECURRENT RELAPSE WITH FINGOLIMOD OR INTERFERON BETAL-1A USING PROPORTIONAL MEANS MODEL

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Background: Many statistical comparisons of treatment effects on relapse outcomes in patients with multiple sclerosis (MS) do not use all available relapse information recorded during a study. TRANSFORMS, a 12-month, randomized, double-blind, phase 3 study, showed the superior efficacy of fingolimod over intramuscular interferon beta-1a (IFNβ-1a IM), with respect to relapses and magnetic resonance imaging outcomes, in patients with relapsing-remitting MS (RRMS). Primary analyses used the Cox regression model to identify a reduction in the risk of experiencing a first relapse in patients receiving fingolimod compared with those receiving IFNβ-1a IM. Here, we use multiple relapses to assess time to recurrent confirmed relapse using the proportional means model proposed by Lin, Wei, Yang, and Ying (LWYY).

Objectives: To analyze further the effects of oral fingolimod (0.5 mg once daily) or IFNβ-1a IM (30 µg weekly) treatment in order to assess alternative methods of analyzing recurrent confirmed relapses in patients with RRMS.

Methods: The LWYY model was employed to assess treatment effect on time to recurrent confirmed relapse. This model is an extension of the proportional hazards model, which accounts for recurrent events within the model using robust variance estimation. Treatment group, number of relapses in the previous 2 years, and baseline Expanded Disability Status Scale score are included as covariates.

Results: The Cox regression model prospectively estimated a 49.2% risk reduction (hazard ratio [HR], 0.51; 95% confidence interval [CI], 0.38-0.68), whereas the LWYY model estimated a 53.1% risk reduction (HR, 0.47; 95% CI, 0.35-0.62) for patients treated with fingolimod relative to those receiving IFNβ-1a IM, with better accuracy than the Cox regression model.

Conclusions: The additional relapse data accounted for by the LWYY model enables a more robust estimation of the HR for treatment effects, yielding narrower CIs, than the Cox regression model.

Supported by: Novartis Pharmaceuticals Corporation

Disclosure: Xiangyi Meng, Zahur Islam, Peter Chin, Nadia Tenenbaum: Novartis (employee). Gary Cutter: Alexion, Allozyne, Consortium of Multiple Sclerosis Centers (grant support); Diagnexus, Klein-Buendel Incorporated, Genzyme, MedImmune, Novartis, Nurion Biotech, Receptos, Spiniflex Pharmaceuticals, Somahultion, Teva Pharmaceuticals, Xenoport (consulting fees); Apotek, Biogen Idec, Cleveland Clinic, GlaxoSmithKline Pharmaceuticals, Gilead Pharmaceuticals, Medigeneethe/Prolor, Merck/Ono Pharmaceuticals, Merck, Neuren, PCT Bio, Reslesio, Sanofi-Aventis, Teva, Viroq, National Heart, Lung, and Blood Institute (protocol review committee), National Institute for Neurological Disorders and Stroke, NMS (data and safety monitoring committees); Pythagoras, Inc (president of a private consulting company).

Keywords: Fingolimod, Disease relapses, Proportional means model

(DX52) RELAPSE OUTCOMES IN FINGOLIMOD-TREATED PATIENTS PREVIOUSLY EXPOSED TO NATALIZUMAB, INTERFERON, OR GLATIRAMER ACETATE: RESULTS FROM THE FIRST STUDY

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Background: The Fingolimod Initiation and Cardioiac Safety Trial (FIRST) was a phase 3b, single-arm, open-label, multicenter, 4-month study of fingolimod 0.5 mg in patients (N = 2417) with relapsing multiple sclerosis (MS) in 23 countries. In addition to treatment-naïve patients, the study population included patients who had been treated with natalizumab, interferon beta (IFNβ), or glatiramer acetate (GA) prior to enrollment.

Objectives: To determine relapse outcomes with fingolimod in patients previously treated with natalizumab, IFNβ, or GA.

Methods: Post hoc analyses of data from patients who received natalizumab >6 months (n = 135) and 3 to 6 months (n = 119) prior to baseline and from patients who received IFNβ (n = 1040) or GA (n = 432) within 6 months prior to baseline were carried out. Pre- and on-study annualized relapse rates (ARRs) and proportions of patients who were relapse free during the trial were analyzed. ARR was calculated as the total number of relapses divided by the total duration (in days) of fingolimod exposure for all patients in that group multiplied by 365.25. The ARR for the 1 year before the study was calculated as the total number of retrospectively reported relapses divided by the number of patients in the group.

Results: Prior to the study, ARR at year -1 was 1.52 in patients who discontinued natalizumab >6 months before the study, 1.08 in patients who discontinued natalizumab 3 to 6 months before the study, 1.13 in patients who discontinued GA before the study, and 1.01 in patients who discontinued IFNβ before the study. During 4 months of fingolimod therapy, ARR was 0.85 in the natalizumab >6 months group, 0.97 in the natalizumab 3 to 6 months group, and 0.97 in the natalizumab 3 to 6 months group.
group, 0.51 in the GA group, and 0.45 in the IFN\(\beta\) group. The proportions of patients who were relapse free after 4 months of fingolimod therapy were 76.1% in the natalizumab >6 months group, 74.8% in the natalizumab 3 to 6 months group, 85.9% in the GA group, and 87.3% in the IFN\(\beta\) group. **Conclusions:** Results of these analyses indicate that patients with relapsing MS who recently discontinued natalizumab, GA, or IFN\(\beta\) had improvement in ARR with fingolimod treatment.

**Supported by:** Novartis  
**Disclosure:** Philipp von Rosenstiel, Erik Burton: Novartis Pharmaceuticals Corporation (employee)  
**Keywords:** Disease-modifying treatments in MS, Fingolimod

**(DX53) SWITCH ANALYSIS OF TERIFLUNOMIDE FROM OTHER MULTIPLE SCLEROSIS DISEASE-MODIFYING THERAPIES**  
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**Background:** Teriflunomide is an oral immunomodulatory agent that blocks the proliferation of activated B and T lymphocytes. Although the effects of teriflunomide on relapse-related neurologic sequelae are known, there is no published study evaluating the effectiveness and safety of teriflunomide when switched from other multiple sclerosis (MS) disease-modifying therapies (DMTs). **Objectives:** Evaluate the effectiveness and safety of teriflunomide in the first switch analysis study. **Methods:** Subjects included MS patients \(n = 87\) who had been treated with other DMTs and switched to teriflunomide for at least 6 months. Prior DMTs included glatiramer acetate \(n = 70\), interferon beta-1a IM \(n = 7\), natalizumab \(n = 8\), and fingolimod \(n = 2\). No “washout” period was used for conversion from natalizumab to teriflunomide, and no immune inflammatory reconstitution syndrome was noted in any of those patients. Analysis included reasons for switching, side effects, relapse rate, MS disease activity-free (absence of relapse, 12-week SAD, and MRI changes), and discontinuation rate on teriflunomide. **Results:** Over 80% of patients were female, age ranged from 24 to 80 years, and baseline Expanded Disability Status Scale (EDSS) scores ranged from 2.0 to 7.0. Reasons for switching to teriflunomide included injection exhaustion (predominant factor), injection-site reactions, lipoatrophy, JC virus ELISA positivity, increase in relapse rate on prior DMT, NABS to interferon and natalizumab, and preference for an oral agent. Nine patients (10.3%) reported side effects early in the treatment course (within 2 months). Of these, 5 (5.7%) required discontinuation and resumed prior DMT: nausea (2), hypotension (1), anxiety (1), and elevated liver function tests (1). Side effects in the other 4 patients resolved while remaining on teriflunomide. Four patients (4.6%) experienced relapses (2 pseudo and 2 required methylprednisolone treatment), and all returned to baseline while remaining on teriflunomide. Ninety-five percent of patients were free of MS disease activity. **Conclusions:** Teriflunomide is a well-tolerated oral medication for the management of MS. Side effects were mild and rarely led to medication discontinuation (only 5.7% discontinued and returned to their prior DMT). A 95% MS disease activity-free rate during the first year of treatment with teriflunomide compares favorably to other DMTs in our clinical practice and makes it a logical choice for first-line switch therapy in the management of MS.

**Supported by:** None  
**Disclosure:** Ronald O. Bailey: Teva, Genzyme, Biogen (speaker honoraria). Nader M. Gemayel, Vu A. Nguyen, Carina G. Sprague: Nothing to disclose.  
**Keywords:** Comprehensive care and MS, Disease-modifying treatments in MS, Teriflunomide

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**Posters: Disease Management, Mechanisms, and Treatment**

**(DX54) THE STRIVE STUDY OF NATALIZUMAB IN PATIENTS WITH EARLY MULTIPLE SCLEROSIS: BASELINE CHARACTERISTICS**

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**Background:** Initiating natalizumab treatment early in the course of disease may improve long-term outcomes for relapsing-remitting multiple sclerosis (RRMS) patients. However, the effects of natalizumab on patients with early-stage RRMS have not been systematically studied. **Objectives:** To report baseline patient characteristics in the ongoing STRIVE study. **Methods:** STRIVE is a prospective, multicenter, single-arm study of outcomes and predictors of treatment response in patients initiating natalizumab early in RRMS. Target enrollment is approximately 300 patients, 18 to 50 years of age, with Expanded Disability Status Scale (EDSS) score ≤4.0, who initiated natalizumab treatment ≤3 years after MS diagnosis. Patients must test negative for anti–JC virus antibodies ≤6 months before initiation. Prior treatment with disease-modifying therapy for a total of ≤36 months is permitted. Primary endpoints are the proportion of patients free of measured disease activity (no 24-week confirmed EDSS progression, no relapses, no gadolinium-enhancing lesions, and no new or enlarging T2-hyperintense lesions) at years 1 and 2 and the proportion of patients free of measured clinical disease activity at years 3 and 4. Additional endpoints include 24-week confirmed EDSS progression, relapse rate, magnetic resonance imaging (MRI) measures, cognitive function using the Symbol Digit Modalities Test (SDMT), and quality of life assessments. In approximately 100 patients, the visual system will be assessed with optical coherence tomography (OCT) and low-contrast visual acuity testing. Baseline characteristics of enrolled patients were assessed using descriptive statistics. **Results:** As of August 23, 2013, 120 patients were enrolled. At baseline, mean age was 32.6 years, 78% were female, mean EDSS score was 2.0, mean time since RRMS diagnosis was 0.6 years, mean number of relapses within the past year was 1.5, and mean SDMT score was 53.0. Of enrolled patients, 51% were treatment-naïve; 28% had received prior interferon treatment, 23% had received glatiramer acetate, and 2% had received teriflunomide. Baseline OCT was performed in 40 patients (33%); macular measurements will be presented. **Conclusions:** Enrollment is ongoing. STRIVE will provide long-term data on the effectiveness of natalizumab as measured by MRI and clinical parameters in patients initiating treatment in the early stages of RRMS.

**Supported by:** Biogen Idec Inc.  
**Disclosure:** Roumen Balabanov: Biogen Idec (fees for non-CME services
(DX55) EARLY ADOPTERS OF TECFIDERA: PRELIMINARY CHARACTERISTICS AND PATIENT-REPORTED OUTCOMES FROM THE NARCOMS REGISTRY

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Background: Oral disease-modifying therapies (DMTs) offer a convenient treatment option for people with relapsing-remitting multiple sclerosis (RRMS). Several factors are associated with a decision to start a new treatment, such as anticipated efficacy, potential adverse effects, and cost. Little is known about the real-world patient experience following initiation of recently approved therapies. The April 2013 introduction of Tecfidera (oral dimethyl fumarate, DMF) to the growing number of US Food and Drug Administration (FDA)-approved DMTs provided an opportunity to assess the initial experiences of early adopters. Objectives: To compare groups of DMF users based on their current and past treatment history. Methods: Respondents to the NARCOMS Fall 2013 update survey who completed DMT and functionality questions were included. Functionality was assessed using the Patient-Determined Disease Steps (PDDS). We conducted non-parametric Wilcoxon rank and chi-square tests for comparisons as applicable and used covariate adjusted analysis of variance (ANOVA) for change in PDDS. A P value < .05 was considered meaningful. Results: Of the 8284 respondents to the NARCOMS Fall 2013 update survey, 8093 (97.7%) completed the DMT questions: 449 (5.5%) of them reported using DMF in the past 6 months; 366 (81.5%) indicated current use. Of the 52 (11.6%) who stopped using DMF and 31 (6.9%) not indicating a current status, only 6 (7.2%) reported a switch to another DMT. As expected in an MS population, DMF users were predominantly female (83.0%) and white or white/mixed (82.4%); 63 (14.0%) were diagnosed within the past 5 years. The median (range) age of all users was 53.4 (25.5–79.8) and disease duration was 14 (2–45) years, both slightly lower than in the registry overall, with 98.8% reporting having health insurance. At enrollment, participants reported a median (range) PDDS of 3 (0–7). “Gait Disability,” with an increase in PDDS of 1 (5–7) points at update survey, adjusted for starting PDDS, age at survey, and time of follow-up (no difference by status of DMT use). Conclusions: Since FDA approval, 5.5% of NARCOMS survey responders reported taking DMF, with a higher adoption rate observed in the younger segment of the registry population. Current and past users had similar demographics and disability level. No significant differences in disability progression emerged between the groups, potentially due to the brief post-change follow-up period. Reasons for DMF usage, as well as disability and medication history, will be reported.

Supported by: Biogen Idec; NARCOMS is supported in part by the CMSC and its Foundation.


Keywords: Disease-modifying therapies in MS

(DX56) ALEMTUZUMAB PATIENT-REPORTED QUALITY OF LIFE: RECALL-BASED STUDY OF EXPERIENCED SUBJECTS

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Background: A cohort of alemtuzumab-treated, refractory, high-disability [mean Expanded Disability Status Scale (EDSS) score 5.5–6.0] multiple sclerosis (MS) patients has reported a favorable subjective experience. Prior reports showed that alemtuzumab provides improvement and/or temporary stabilization of EDSS score. How do these patients perceive their physical and mental experience with alemtuzumab? Objectives: Retrospectively assess patient-reported outcome (PRO) changes after alemtuzumab of quality of life with the 36-item Short Form Health Status Survey (SF-36) and a modified, retrospective SF-36 instrument. Methods: The SF-36v2 is a standardized, validated, norm-based instrument for collecting PRO perceptions of health. Both physical (PH) and mental health (MH) components are determined. Declines in health are indicated by decreases in the normalized scale, with a norm of 50 and SD of 10. We used both the SF-36v2 for current health status and a novel, modified SF-36 that collects retrospective quality of life measures. This retrospective instrument queried alemtuzumab-experienced subjects regarding life experience in the 2-year period preceding alemtuzumab. The questionnaires were scheduled near entry to an open-label phase I trial for alemtuzumab treatment (clinicaltrials.gov NCT01624714). 23 subjects had available data. The global question regarding health status was not collected retrospectively, but other items of the SF-36 were collected by recall for comparative purposes. Results: At the time of first scheduled assessment, nearly all alemtuzumab-experienced subjects reported scores ≥1 SD from commercial interests or their agents); Biogen Idec Inc., Teva Pharmaceutical, Questcor (consulting fees); Biogen Idec, Teva Pharmaceutical (grant/research support). Tai Perumal: Biogen Idec, Teva, Genzyme (consulting fees). Robert J. Fox: Allozyne, Avanir, Biogen Idec, Novartis, Questcor, Teva, Xenoport (consulting fees); Biogen Idec, Novartis (advisory committees); Novartis (grant/research support). Denise Campagna: Biogen Idec (employee, stock ownership). Ernest Diam, Stefan Lanker, Mary-Jean Fanelli: Biogen Idec (employee).
below norm for PH (21/23), but only a minority reported ≥1 SD below norm for MH (10/23). Measured as a change from first alemtuzumab cycle with retrospective recall, PH was improved in 48% of subjects; however, mean score was essentially unchanged (−3.1 ± 1.5; 95% confidence interval [CI], −0.1 to −6.1). This possibly correlates with the perceived need for additional alemtuzumab treatment and progressive disability of some in the cohort. However, 2/23 subjects reported dramatic PH improvements (18 and 20 points). MH improved in 70% (mean improvement, 20.9 ± 2.4; 95% CI, 18.1-23.3); no subjects had major declines in MH, but 9/23 reported major (≥1 SD) improvements. Conclusions: Dramatic changes in SF36v2 scales are possible using this exploratory retrospective technique. In this high-disability cohort, it is not surprising that recall over several years perceived little change in physical function. Indeed, function fluctuates in this cohort. Many participate in the trial due to wearing off of prior perceived beneficial alemtuzumab effects on disability. PRO stability of physical measures over years in a high-disability population is encouraging. Significant improvement in perception of mental health was unexpected and apparent, and marked in magnitude in many subjects’ recall. Serial data collection to assess the benefit of more regular alemtuzumab treatment and prospective changes in SF-36 should continue, and may be helpful in validating the retrospective collection of these data.

Supported by: Genzyme-Sanofi

Disclosure: Samuel F. Hunter: AbbVie, Roche, Synthon (grant/research support); Acorda, Avanir, Novartis, Osmotica, Questcor (consulting fees); Bayer HealthCare (fees for non-CME services from commercial interests or their agents); Biogen Idec, Genzyme-Sanofi, Teva (consulting fees, grant/research support). Daniel Kanator: Acorda, Avanir, Biogen Idec, Novartis, Teva (consulting fees, grant/research support); Allergan, Depomed, Questcor (consulting fees).

Keywords: Disease-modifying treatments in MS, Patient-reported outcomes

**[(DX57)] EFFICACY AND SAFETY OF PEGINTERFERON BETA-1A IN RELAPSING-REMITTING MULTIPLE SCLEROSIS: 2-YEAR DATA FROM THE ADVANCE STUDY**

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Background: At year 1 of ADVANCE, subcutaneous peginterferon beta-1a (PEG-IFN; 125 μg every 2 [Q2W] or 4 [Q4W] weeks) significantly reduced annualized relapse rate (ARR; primary endpoint), risk of relapse, risk of 12-week confirmed disability progression, and the number of new or newly enlarging T2 lesions versus placebo. Safety profiles were similar for Q2W and Q4W treatment arms, and consistent with established interferon beta-1a therapies.

Objectives: To further evaluate the efficacy and safety of investigational PEG-IFN in patients with relapsing-remitting multiple sclerosis (RRMS) in the ongoing phase 3 ADVANCE study. We present 24-week confirmed disability progress-

sion data at year 1 and interim 2-year efficacy and safety data. Methods: Year 1 data were analyzed post hoc to determine the proportion of patients with disability progression (defined by a ≥1.0- or ≥1.5-point increase in Expanded Disability Status Scale score, from a baseline score of ≥1.0 or 0.0, respectively) sustained over 24 weeks. During year 2, all patients received dose-blinded PEG-IFN (at the end of year 1 patients on placebo were re-randomized to PEG-IFN 125 μg Q2W or Q4W). Interim 2-year analyses of efficacy and safety were conducted for patients with 2 years of data at cutoff. Post hoc analyses compared the efficacy of Q2W versus Q4W regimens. Results: In the intent-to-treat population (placebo n = 500; PEG-IFN Q2W n = 512; PEG-IFN Q4W n = 500), 24-week confirmed disability progression data at year 1 reflected the significantly reduced risk of 12-week confirmed disability progression observed for PEG-IFN Q2W versus placebo at year 1. For patients continuing PEG-IFN in year 2, ARR was maintained (for Q4W) or further numerically reduced (for Q2W) relative to year 1. New or newly enlarging T2 lesions were numerically lower in year 2 versus year 1 for patients continuing Q2W and Q4W. Over 2 years, versus those originally assigned to placebo, reductions in ARR, risk of relapse, and risk of 12-week confirmed disability progression were seen for patients on PEG-IFN during both years 1 and 2. PEG-IFN Q2W provided numerically larger treatment effects over 2 years versus Q4W. Over 2 years, PEG-IFN was well tolerated, with a safety profile consistent with year 1 of ADVANCE and other beta interferons. Conclusions: Results for 24-week confirmed disability progression at year 1 and interim 2-year data support the maintained benefits of PEG-IFN Q2W in RRMS.

Supported by: Biogen Idec Inc.


Keywords: Disease-modifying treatments in MS

**[(DX58)] PEGINTERFERON BETA-1A MAY IMPROVE RECOVERY FOLLOWING RELAPSES IN THE ADVANCE RELAPSING-REMITTING MULTIPLE SCLEROSIS STUDY**

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Background: In relapsing-remitting multiple sclerosis (RRMS) study populations on placebo, approximately 30% of all relapses have been reported to lead to confirmed disability progression (DP). Given the 36% and 28% reductions in annualized relapse rate (ARR) seen for investigational sub-
cutaneous peginterferon beta-1a (PEG-IFN; 125 µg) every 2 (Q2W) or 4 (Q4W) weeks, respectively, versus placebo, at year 1 of the ADVANCE study, this treatment effect is unlikely to provide the only explanation for the relative 38% reduction in risk of 12-week confirmed DP seen for Q2W and Q4W.

**Objectives:** To determine whether PEG-IFN improved recovery following relapses (RRR) versus placebo in RRMS patients, and to examine the relationship between change in individual functional systems scores (FSS) during a relapse and following sustained DP. **Methods:** Post hoc analyses were conducted using data from patients randomized and dosed in ADVANCE (n = 1512). DP due to incomplete RR was defined as onset of 3-month sustained DP ≥1.0- or ≥1.5-point increase in Expanded Disability Status Scale score, from respective baseline scores of ≥1.0 or 0.0, confirmed after 12 weeks) within 180 days of a relapse. Simultaneous worsening of FSS was defined as a ≥1-point change in FSS caused by a relapse, with the same FSS being part of the sustained DP. **Results:** Overall, n = 55 experienced DP associated with relapses; n = 57 experienced DP not associated with relapses (numerically fewer on PEG-IFN vs. placebo). Relapse severities were not different between groups. Approximately 90% with sustained DP had ≥1 FSS that had simultaneous worsening during the preceding relapse; this was evident in 87% within 15 days of the most recent relapse (most frequent in pyramidal [55.3–55.7%]). PEG-IFN Q2W and Q4W reduced the proportion of patients experiencing sustained DP due to incomplete RR versus placebo by 56% (P = .012) and 41% (P = NS), respectively. Following a recent relapse, a lower proportion receiving PEG-IFN Q2W (13.6%) and Q4W (15.2%) had sustained DP versus placebo (19.6%), indicating relative reductions in risk of DP following any relapse of 30% and 22%, respectively. **Conclusions:** PEG-IFN, compared with placebo, significantly improved RRR. Approximately half of patients with sustained DP in year 1 of ADVANCE did not have an associated relapse. Simultaneous worsening of pyramidal FSS accounted for the majority of sustained DP, which occurred less frequently in PEG-IFN-treated patients.

**Supported by:** Biogen Idec Inc.


**Keywords:** Disease-modifying treatments in MS

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**(DX60) AUTOINJECTOR EASE-OF-USE IN PATIENTS WITH MULTIPLE SCLEROSIS TREATED WITH INTERFERON BETA-1A SUBCUTANEOUSLY: REDEFINE STUDY DESIGN**

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**Background:** In the use of injectable disease-modifying drugs, such as interferon beta-1a given subcutaneously (IFNβ-1a SC), for the treatment of relapsing-remitting multiple sclerosis (RRMS), limited information is available about which device characteristics may make a particular device more desirable for self-injection. **Objectives:** To determine the REDEFINE (Rebif® vs. Rebiject II™ autoinjector trial DEFIN- ing patient reported Ease-of-use) study is a crossover study designed to advance scientific knowledge of the Rebif® Rebi- dose and Rebiject II injection devices and demonstrate association between device characteristics and ease-of-use. The primary objective is to compare relative patient-assessed ease-of-use in a study of the two devices. Secondary objec-
The safety and efficacy of fingolimod in patients with IFN-β1a treatment, were analyzed post hoc using t-tests. Results: At baseline, interleukin (IL)-21/IL-4 and IL-22/IL-4 expression ratios in CD4+ T cells were significantly higher in RRMS patients than in HCs (fold difference of 1.6–4.6; P < .05). IL-17F/IL-4 gene expression ratio was also higher (5-fold) in RRMS patients than in HCs (P = .005). In RRMS patients, after 6 months of IFNβ-1a SC treatment, protein and gene expression ratios for IL-17F/IL-4, protein expression for IL-22/IL-4, and gene expression for IL-21/IL-4 decreased significantly (P < .005) to HC baseline values. Although T-bet/GATA-3 gene expression ratios did not differ between RRMS patients and HCs, this ratio in patients decreased 40-fold after IFNβ-1a SC (P = .0002).

Conclusions: Reduction of ratios of pro-inflammatory to anti-inflammatory cytokine expression, and of Th1 to Th2 transcription factor gene expression, in CD4+ T cells in RRMS patients following 6 months’ IFNβ-1a SC treatment suggests that they could be used as potential biomarkers of the therapeutic efficacy of IFNβ-1a in RRMS patients.

Supported by: EMD Serono, Inc., Rockland, MA (a subsidiary of Merck KGaA, Darmstadt, Germany); Pfizer Inc, New York, NY

Disclosure: Silva Markovic-Plese: Biogen Idec (grant/research support); EMD Serono, Inc., Genzyme Inc. (consulting fees, grant/research support); Yazhong Tao, Xin Zhang: EMD Serono, Inc. (consulting fees). Bianca Weinstock-Guttman: Acorda, Biogen Idec, EMD Serono, Inc., Novartis, Pfizer, Teva Pharmaceuticals (consulting fees, fees for non-CME services from commercial interests or their agents, grant/research support); Cyberonics (grant/research support). Robert Zivadinov: Biogen Idec, EMD Serono, Inc., Novartis, Sanofi-Aventis, Teva Pharmaceticals (consulting fees, fees for non-CME services from commercial interests or their agents, grant/research support); Clarlet (consulting fees, fees for non-CME services from commercial interests or their agents). Brooke Hayward, Fernando Dangond: EMD Serono, Inc. (employee).

Keywords: Disease-modifying treatments in MS, Interferon beta

(DX61) CHANGES IN IMMUNOLOGIC BIOMARKERS IN PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS TREATED WITH INTERFERON BETA-1A

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Background: Shifting from a Th17- or Th1- to a Th2-cytokine profile may ameliorate relapsing-remitting multiple sclerosis (RRMS) disease activity. Objectives: Compare percentages of CD4+ T cells producing Th17/Th2 and Th1/Th2 cytokines and transcription factor gene expression ratios in RRMS patients versus healthy controls (HCs); measure changes in these biomarkers following 6 months’ treatment with interferon beta-1a (IFNβ-1a) subcutaneously (SC). Methods: Blood samples were collected from 15 HCs at baseline, and from 23 RRMS patients at baseline and after 6 months’ treatment with IFNβ-1a SC three times weekly (NCT01085318).

The percentage of CD4+ T cells expressing a cytokine protein of interest was determined by flow cytometry (FACS); relative gene expression, normalized against 18S rRNA, was measured by quantitative real-time polymerase chain reaction (qRT-PCR). Differences in immunologic biomarker ratios between RRMS patients and HCs at baseline, and changes over 6 months in RRMS patients after IFNβ-1a treatment, were analyzed post hoc using t-tests. Results: At baseline, interleukin (IL)-21/IL-4 and IL-22/IL-4 expression ratios in CD4+ T cells were significantly higher in RRMS patients than in HCs (fold difference of 1.6–4.6; P < .05). IL-17F/IL-4 gene expression ratio was also higher (5-fold) in RRMS patients than in HCs (P = .005). In RRMS patients, after 6 months of IFNβ-1a SC treatment, protein and gene expression ratios for IL-17F/IL-4, protein expression for IL-22/IL-4, and gene expression for IL-21/IL-4 decreased significantly (P < .005) to HC baseline values. Although T-bet/GATA-3 gene expression ratios did not differ between RRMS patients and HCs, this ratio in patients decreased 40-fold after IFNβ-1a SC (P = .0002).

Conclusions: Reduction of ratios of pro-inflammatory to anti-inflammatory cytokine expression, and of Th1 to Th2 transcription factor gene expression, in CD4+ T cells in RRMS patients following 6 months’ IFNβ-1a SC treatment suggests that they could be used as potential biomarkers of the therapeutic efficacy of IFNβ-1a in RRMS patients.

Supported by: EMD Serono, Inc., Rockland, MA (a subsidiary of Merck KGaA, Darmstadt, Germany); Pfizer Inc, New York, NY

Disclosure: Silva Markovic-Plese: Biogen Idec (grant/research support); EMD Serono, Inc., Genzyme Inc. (consulting fees, grant/research support); Yazhong Tao, Xin Zhang: EMD Serono, Inc. (consulting fees). Bianca Weinstock-Guttman: Acorda, Biogen Idec, EMD Serono, Inc., Novartis, Pfizer, Teva Pharmaceuticals (consulting fees, fees for non-CME services from commercial interests or their agents, grant/research support); Cyberonics (grant/research support). Robert Zivadinov: Biogen Idec, EMD Serono, Inc., Novartis, Sanofi-Aventis, Teva Pharmaceuticals (consulting fees, fees for non-CME services from commercial interests or their agents, grant/research support); Clarlet (consulting fees, fees for non-CME services from commercial interests or their agents). Brooke Hayward, Fernando Dangond: EMD Serono, Inc. (employee).

Keywords: Disease-modifying treatments in MS, Interferon beta

(DX62) STUDY DESIGN OF TRANSITION: AN OBSERVATIONAL STUDY TO EVALUATE THE SAFETY PROFILE OF FINGOLIMOD IN PATIENTS SWITCHED FROM NATALIZUMAB

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Background: The safety and efficacy of fingolimod in relapsing multiple sclerosis (MS) have been successfully demonstrated in the phase 3 clinical program and various post-marketing studies. However, very limited longer-term data are available on the safety and disease activity in MS patients switched from natalizumab to fingolimod in routine medical practice. Objectives: The TRANSITION study evaluates, over 2 years, the overall safety profile of fingolimod and the incidence of selected safety outcomes in patients switched from natalizumab to fingolimod in routine medical practice.

Methods: This is a 2-year, prospective, observational, mul-
licenter, single-cohort, global study in up to 1500 patients with relapsing MS, previously treated with natalizumab and switched to fingolimod within 12 months prior to study entry or currently transitioning to fingolimod. Specific safety events will be monitored during the trial, including opportunistic infections such as progressive multifocal leukoencephalopathy (PML), cardiac and vascular events, macular edema, liver events, malignancies, and atypical MS relapses. MS disease activity using Expanded Disability Status Scale (EDSS) score and number of recorded relapses will be documented. The effect of switch from natalizumab to fingolimod on health-related quality of life will be explored as part of an optional substudy using the Multiple Sclerosis Impact Scale (MSIS-29). Treatment Satisfaction Questionnaire for Medication (TSQM-9), and a questionnaire to assess medication preference. Adherence of patients to fingolimod treatment will be assessed based on treatment discontinuation, overall study retention, and compliance data. **Results:** Study design will be presented at the congress. First descriptive summary of the study data will be compiled when approximately 500 patients complete 6 months’ follow-up and thereafter on a yearly basis. **Conclusions:** TRANSITION is the first large prospective observational study that aims to describe safety and disease activity in MS patients treated with fingolimod after natalizumab discontinuation in routine medical practice, over 2 years.

**Supported by:** Novartis Pharma AG

**Disclosure:** Stanley Cohen: Novartis, Biogen Idec, Providence St. Vincent Foundation, Sanoﬁ-Genzyme, Opera, Roche (grant/research support); Novartis, Biogen Idec, Sanoﬁ-Genzyme (consulting fees); Novartis, Biogen Idec, Sanoﬁ-Genzyme, Acorda (support for lectures). Maria Trojano: Merck Serono, Biogen, Novartis (grant/research support); Novartis, Biogen, Sanoﬁ-Genzyme, Merck Serono (consulting fees). Arjita Sinha, Mamuniar Patterdahy: Novartis Healthcare Pvt Ltd (employee). Davorka Tomic: Novartis Pharma AG (employee).

**Keywords:** Disease-modifying treatments in MS, Fingolimod, Natalizumab

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**(DX63) FINGOLIMOD TITRATION IS AN OPTION TO MANAGE SIDE EFFECTS EFFECTIVELY, REDUCE PATIENT TREATMENT WITHDRAWAL, AND ACHIEVE A FULL THERAPEUTIC DOSE REGIMEN**

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**Background:** Fingolimod is reported to have an acceptable safety profile; however, unwanted side effects result in a portion of patients withdrawing from treatment. A major teaching hospital that is supported by multiple sclerosis (MS) nursing expertise experimented with side effect management and dose titration strategies. This personalized approach resulted in the majority of patients remaining on treatment and tolerating the full recommended therapeutic dose. **Objectives:** To reduce and eliminate treatment side effects, reduce patient treatment withdrawal, and achieve the full therapeutic dose regimen. **Methods:** In collaboration with the neurologist, MS nurses were engaged to manage side effects and titrate the fingolimod dose as required. Patients who chose to withdraw from fingolimod were given the option of a personalized management plan. The program offered regular monitoring, side effect management, and fingolimod dose adjustments as required. Ongoing consultation with the neurologist by the nursing staff was maintained, and supportive medication prescribed as needed. Services were delivered via phone consultation, email, fax, mail, clinic visits, and the patient’s general physician. **Results:** In total 209 patients were treated with fingolimod. Clinically significant adverse events such as lymphopenia, herpes zoster, malignancy, headache, ophthalmic symptoms, gastrointestinal disturbance, and a general feeling of being unwell were reported by n = 51 (24.4%). From this group of patients n = 24 (47%) were offered a side effect management and drug titration plan; n = 16 (66.7%) agreed to participate in the treatment approach. Patients diagnosed with malignancy, ophthalmic symptoms, and opportunistic infections were excluded from the invitation. By providing an option to this selected patient group and adopting a “go slow” approach, n = 10 (62.5%) were able to reach the full recommended therapeutic dose and remain on treatment, n = 2 (12.5%) patients discontinued treatment due to poor tolerance, and n = 4 (25%) continue to remain on drug titration. **Conclusions:** An individualized side effect management and titration dose plan that is supported by MS nursing expertise can reduce patient treatment withdrawal and substantially increase full-dose medication tolerance.

**Supported by:** None

**Disclosure:** Nothing to disclose

**Keywords:** Fingolimod, Titration, Treatment withdrawal

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**(DX64) A PHASE 2 DOUBLE-BLIND PLACEBO CROSSOVER CLINICAL TRIAL IN SECONDARY PROGRESSIVE MULTIPLE SCLEROSIS**

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**Background:** Hyperimmune caprine serum (HICS) containing a stabilized neuropeptide may play a role in the treatment of secondary progressive multiple sclerosis (SPMS). **Objectives:** The objective of this phase 2 clinical trial was to determine whether HICS can exhibit measurable efficacy in patients with SPMS. **Methods:** The phase 2 double-blind, placebo-controlled (DBPC) crossover clinical trial in 20 patients with magnetic resonance imaging (MRI)– and clinically confirmed SPMS was undertaken with ethical approval in the United Kingdom. The mean age of the cohort was 50.3 years, and the male:female ratio was 1:4. The mean time since onset of MS symptoms was 18.7 years and since onset of SPMS was 5.7 years. 90% of patients used walking aids at enrollment. Patients were randomized and treated twice weekly with either 4.5 mg/mL subcutaneously (SC) [1 mL] of HICS or placebo for 4 weeks. Following a 6-week washout period, the reverse treatment was administered for 4 weeks (crossover). After 14 weeks, patients entered the open-label (OL) phase, with twice-weekly HICS administered up to 12 months. **Results:** HICS was safe and well tolerated in all phases of the trial. No treatment-related severe adverse events were recorded. HICS was not associated with a significant difference in bladder function in the DBPC phase. In the OL phase, HICS significantly decreased the mean urinary frequency (P < .0001) and mean urinary incon-
Posters: Disease Management, Mechanisms, and Treatment

(DX65) INCIDENCE OF LIPOTROPHY ASSOCIATED WITH AUTOINJECTION VERSUS MANUAL SUBCUTANEOUS INJECTION OF GLATIRAMER ACETATE

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Background: The incidence of lipoatrophy occurring as a consequence of subcutaneous (SC) injection of glatiramer acetate (GA) has been reported as 2% in the GA package label. The prevalence and severity of lipoatrophy with long-term GA therapy for multiple sclerosis (MS) are largely unknown. The exact cause of lipoatrophy is unknown, but it is thought to result from an adverse immunologic side effect of the injection. It has also been proposed that local elevated production of tumor necrosis factor–alpha leads to the dedifferentiation of adipocytes in the SC tissue. Objectives: Compare the incidence of lipoatrophy associated with long-term use of autoinjection versus manual SC injection of GA in a clinical practice population of MS patients. Methods: Seventy-three MS patients maintained on GA (mean 36 months) had been given the option of use of autoject 2 versus manual SC injection. Forty patients (54.8%) employed the autoinjection and the remaining 33 patients (45.2%) opted for manual SC injections. Both groups were followed with clinical examinations and serial photographic analysis every 3 months. All patients were counseled on proper injection-site rotation and methods on each visit. (The autoject 2 apparatus was provided through Shared Solutions.) Results: A total of 46 patients (63%) taking GA developed lipoatrophy over a 3-year interval. Of this number, the overwhelming majority, 35 patients (76%), developed it with the use of autoject 2. Lipoatrophy occurred predominantly in women and was noted at multiple injection sites in the same patient. In some patients, lipoatrophy developed within the first 3 months of injection initiation and was severe enough to necessitate switching to another MS disease-modifying therapy (DMT). Upon GA treatment discontinuation, lipoatrophy remained permanent. Serial photographs of individual patient lipoatrophy will be presented. Conclusions: Of the side effects of SC GA, lipoatrophy is the most disfiguring and is invariably permanent. Our clinical experience with GA showed that 63% of patients developed lipoatrophy. This occurrence (greatest in the autoinjection group) was substantially higher than previously reported and was often the sole factor prompting patients to switch to another MS DMT. Our data also suggest that a heightened risk of lipoatrophy is an inherent autoimmune problem and is not necessarily mitigated by vigilant injection-site rotation irrespective of the methodology of GA administration.

Supported by: None

Keywords: Disease-modifying treatments in MS

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(DX66) STUDY DESIGN OF A PHASE 3 TRIAL EVALUATING TERIFLUNOMIDE IN CHILDREN AND ADOLESCENTS WITH RELAPSING MULTIPLE SCLEROSIS

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Background: Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing-remitting multiple sclerosis (RRMS). Teriflunomide showed consistent significant positive effects on annualized relapse rate and disability progression in the phase 3 TEMSO (NCT00134563) and TOWER (NCT00751881) studies, with a manageable safety profile in adult patients. Studies have not yet been performed in pediatric patients, who represent approximately 5% of MS cases. Objectives: To report the design of TERIKIDS, a study planned to evaluate the efficacy, safety, and pharmacokinetics (PK) of teriflunomide compared with placebo in pediatric patients with relapsing forms of MS. Methods: TERIKIDS is a 2-year, phase 3, multicenter, randomized, double-blind, placebo-controlled study to be conducted in patients (target N = 165) aged 10 to 17 years who satisfy McDonald criteria for MS (2010) and International Pediatric Multiple Sclerosis Study Group criteria for pediatric MS (2013). In addition, patients should have ≥1 or ≥2 relapses in the 12 or 24 months preceding randomization, respectively. Patients will be randomized (2:1) to once-daily teriflunomide or placebo for 96 weeks. The teriflunomide dose will correspond to the adult 14 mg dose, after an
supported by: Genzyme, a Sanofi company

Disclosure: Tanuja Chitnis: Nothing to disclose. Brenda Banwell: Biogen Idec, Sanofi, Teva Neurosciences (consulting fees); Canadian Multiple Sclerosis Foundation, Dairy Farmers of Ontario (grant/research support); Douglas L. Arnold: Acorda Therapeutics, Bayer HealthCare, Biogen Idec, Coronado Biosciences, EMD Serono, Genentech, Genzyme, GlaxoSmithKline, MedImmune, NeuroRx Research, Novartis, Oplex Therapeutics, Roche, Merck Serono, Mitsubishi, StemmCells, Inc., Teva, XenonPort (consulting fees); Bayer HealthCare (grant/research support); NeuroRx Research Inc (ownership interest). Philippe Truffert, Michael A. Penzarelli: Genzyme, a Sanofi company (employee); Deborah Dubowick: Sanofi (employee). Ludwig Kappa: Actelson, Alzhey, Bayer HealthCare Pharmaceuticals, Bayer Schering Pharma, Bayhill, Biogen Idec, CLC Behring, GenNeuro SA, Genmab, Genmark, Genzyme, GlaxoSmithKline, Lilly, Merck Serono, Mitsubishi Pharma, Novartis, Novo Nordisk, Pepsin (grant/research support).

Keywords: Disease-modifying treatments in MS

(DX67) WEIGHT AND BODY-MASS INDEX CHANGES OVER 7 YEARS IN CombiRx

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Background: The CombiRx trial was a double-blind, multicenter randomized clinical trial involving 1008 individuals with relapsing-remitting multiple sclerosis (RRMS), comparing 50% of participants on interferon beta-1a (IFN) and glatiramer acetate (GA) treatment versus 25% on each of the single-agent arms with matching placebo. Entry criteria include Expanded Disability Status Scale (EDSS) score ≤ 5.5, RRMS diagnosed by Poser or McDonald criteria, 18 to 60 years of age, at least 2 relapses in the prior 3 years, and no prior use of either medication. Participants were followed for up to 7 years with both clinical and magnetic resonance imaging (MRI) measures. Objectives: Describe changes in weight and body-mass index (BMI) in CombiRx over 7 years.

Methods: Participants were randomized and followed with quarterly visits, including vital signs, through month 42 and every 6 months from month 48 for up to 7 years. The trial concluded in March 2012 with 80.1% (814/1008) completing 3 years and 84.4% (687/814) entering with 85.0% (584/687) completing the extension phase. Results are reported as mean (SD) change from baseline assessed by covariate adjusted analysis of variance (ANOVA) with Tukey adjustment for multiple comparisons and logistic regression; a P value of <.05 was considered meaningful. BMI was calculated from weight at each visit and baseline height. Results: The baseline weight was 180.4 (46.0) pounds and BMI was 28.7 (6.8), with no differences by treatment group. Males and females had similar BMI (P = .98), with African Americans having higher weight (P = .043) and BMI (P = .040) compared with whites. With an average follow-up of 3.9 (1.6) years, change in weight was related to starting weight, age, and years of follow-up; those on GA alone had a significant mean increase of 2.4 pounds, compared with a nonsignificant loss of 1.9 for IFN alone (GA vs. IFN; P = .023) or significant gain of 1.3 for IFN + GA vs. IFN + GA; P = .75). Similarly, change in BMI was related to starting BMI; GA had a greater increase compared with IFN (0.5 vs. −0.4, P = .0496) but not IFN + GA (0.5 vs. 0.3, P = .09). On GA alone 53.7% gained more than 1 pound (53.7%) compared with IFN (42.9%, P = .029) but similar to IFN + GA (53.7%, P = .57). There were no gender or race differences in changes in weight or BMI during the study. Conclusions: Growing interest in MS comorbidities makes weight changes important to understand and investigate. There was differential weight gain based on treatment received. A higher proportion of participants gained weight on GA compared with IFN. More detailed exploration of weight changes and reasons for weight gain will be presented.

Supported by: National Institutes of Health/National Institute of Neurological Disorders and Stroke (1R01NS050156-01A1)

Disclosure: Tarah Gustafson, Jerry S. Wolinsky, Robin Conwit: Nothing to disclose. Fred D. Lublin: Acorda Therapeutics, Inc., Biogen Idec, Novartis Pharmaceuticals Corp, Teva Neurosciences, Inc., Genzyme, Sanofi, Celgene, National Institutes of Health, National Multiple Sclerosis Society (grant/research support); Bayer HealthCare Pharmaceuticals, Biogen Idec, EMD Serono, Inc, Novartis, Teva Neurosciences, Actelion, Sanofi-Aventis, Acorda, Questcor, Roche, Genentech, Celgene, Johnson & Johnson, Revalste, Coronado Bioscience, Genzyme, MedImmune, Bristol-Myers Squibb, Xenoport, Receptos, Forward Pharma (consulting fees); Cognition Pharmaceuticals, Inc. (current financial interest/stock ownership); Multiple Sclerosis and Related Diseases (co-chief editor). Gary Cutter: Alexion, Alzhey, Consortium of Multiple Sclerosis Centers (grant support); Diogenix, Klein-Buendel Incorporated, Genzyme, MedImmune, Novartis, Nuron Biotech, Receptos, Spiniflex Pharmaceuticals, Somahltion, Teva Pharmaceuticals, Xenoport (consulting fees); Apotek, Biogen Idec, Cleveland Clinic, GlaxoSmithKline Pharmaceuticals, Gilead Pharmaceuticals, Medigenetech/Prodir, Merck/Onc Pharmaceuticals, Merck, NeuroSpin, PET Bio, Revalste, Sanofi-Aventis, Teva, Viva, National Heart, Lung, and Blood Institute (protocol review committee), National Institute of Neurological Disorders and Stroke, NNS (data and safety monitoring committees); Pythagoras, Inc (president of a private consulting company). Stacey S. Coffield: American Shoulder and Elbow Society, Teva Neurosciences (consulting fees); Medimmune, OrthoBiotech Biotech (DSMB).

Keywords: Comorbidities, Disease-modifying treatments in MS

(DX68) INCREASED RELAPSE FREQUENCY IN FEMALES WITH PEDIATRIC-ONSET MULTIPLE SCLEROSIS

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Supported by: National Institute of Neurological Disorders and Stroke (5U01NS045719)

Disclosure: Yolanda C. Harris, Sarah M. Dowdy, Jayne Ness: Nothing to disclose. Jerry S. Wolinsky, Robin Conwit: Nothing to disclose. Fred D. Lublin: Acorda Therapeutics, Inc., Biogen Idec, Novartis Pharmaceuticals Corp, Teva Neurosciences, Inc., Genzyme, Sanofi, Celgene, National Institutes of Health, National Multiple Sclerosis Society (grant/research support); Bayer HealthCare Pharmaceuticals, Biogen Idec, EMD Serono, Inc, Novartis, Teva Neurosciences, Actelion, Sanofi-Aventis, Acorda, Questcor, Roche, Genentech, Celgene, Johnson & Johnson, Revalste, Coronado Bioscience, Genzyme, MedImmune, Bristol-Myers Squibb, Xenoport, Receptos, Forward Pharma (consulting fees); Cognition Pharmaceuticals, Inc. (current financial interest/stock ownership); Multiple Sclerosis and Related Diseases (co-chief editor). Gary Cutter: Alexion, Alzhey, Consortium of Multiple Sclerosis Centers (grant support); Diogenix, Klein-Buendel Incorporated, Genzyme, MedImmune, Novartis, Nuron Biotech, Receptos, Spiniflex Pharmaceuticals, Somahltion, Teva Pharmaceuticals, Xenoport (consulting fees); Apotek, Biogen Idec, Cleveland Clinic, GlaxoSmithKline Pharmaceuticals, Gilead Pharmaceuticals, Medigenetech/Prodir, Merck/Onc Pharmaceuticals, Merck, NeuroSpin, PET Bio, Revalste, Sanofi-Aventis, Teva, Viva, National Heart, Lung, and Blood Institute (protocol review committee), National Institute of Neurological Disorders and Stroke, NNS (data and safety monitoring committees); Pythagoras, Inc (president of a private consulting company). Stacey S. Coffield: American Shoulder and Elbow Society, Teva Neurosciences (consulting fees); Medimmune, OrthoBiotech Biotech (DSMB).

Keywords: Comorbidities, Disease-modifying treatments in MS

8-week titration and adaption process. The primary objective is to evaluate the effect of teriflunomide compared with placebo on disease activity, as measured by time to first clinical relapse after randomization. Secondary outcomes include proportion of patients who are relapse-free; brain magnetic resonance imaging (MRI) parameters (number of new/newly enlarged T2, T1 gadolinium-enhancing, and new T1-hypointense lesions, volume of T2 and T1-hypointense lesions, and brain atrophy); cognitive function; safety and tolerability of teriflunomide; and PK evaluation of teriflunomide. During the study, it will be possible to switch to open-label teriflunomide in case of a confirmed relapse (after 8 weeks) or if the number of new/enlarged T2-hyperintense lesions is above a predetermined threshold; however, core study treatment will remain blinded. Results: Results will be reported after completion of the study. Conclusions: Results from the study will provide important data on the use of teriflunomide in children and adolescent patients with relapsing forms of MS.
Background: Pediatric-onset multiple sclerosis (POMS) has been increasingly recognized over the last 15 years. The Center for Pediatric Onset Demyelinating Disease (CPODD) at the University of Alabama at Birmingham was established in 2006 to provide long-term follow-up for children and adolescents with POMS and related demyelinating disorders. Objectives: Characterize POMS patients evaluated at CPODD from January 1, 2006, to December 31, 2013. Methods: CPODD patients (n = 359) were categorized using the 2012 International Pediatric MS Study Group diagnostic criteria. POMS patients were analyzed with respect to age at onset, race/ethnicity, sex, initial symptoms, and number of exacerbations within 2 years of initial presentation and disease-modifying therapy (DMT). Results: Nearly one-third of the CPODD cohort developed POMS (n = 114, 31%). POMS patients were predominantly female (65%) and disproportionately African American (43%); <2% were Hispanic or Asian, and the remainder were white. Mean age at symptom onset was 13.1 ± 4 years, with 22% being ≤10 years old, 41% from 11 to 14 years, and 37% from 15 to 18 years. The majority of POMS patients presented with clinically isolated syndrome (CIS) (89%, n = 101); symptoms were characterized as pyramidal (n = 45, 39%), brainstem/cerebellar (n = 34, 30%) or optic neuritis [ON] (n = 18, 16%). A minority presented with acute disseminated encephalomyelitis (ADEM) (n = 7, 6%), radiologically isolated syndrome (n = 5, 4%), paroxysmal dysarthria (n = 2, 2%), behavioral symptoms (n = 1, 1%), or seizures (n = 2, 2%). Over two-thirds of POMS patients had follow-up of ≥2 years (n = 78, 68%). All POMS patients were started on DMT, most within 12 months of symptom onset. Of those patients with follow-up >2 years, nearly half had 0 exacerbations (n = 37, 47%), nearly one-third had 1 exacerbation (n = 23, 30%), 13% had 2 exacerbations (n = 10), and 10% had between 3 and 6 exacerbations. Females had significantly more relapses than males (chi-square test, P < .001), but there was no correlation between the number of relapses and age at onset or race. Conclusions: People with POMS in this southern US cohort were predominantly female and >11 years old at symptom onset. Similar to adults, the typical presentation is CIS, with ON being relatively infrequent. Over 75% experienced ≤1 relapse within the first 2 years after symptom onset; however, females had a higher number of relapses than males.

Supported by: None


Keywords: Disease-modifying treatments in MS, Epidemiology of MS

(DX69) THE EFFECT OF GLATIRAMER ACETATE TREATMENT ON MITOCHONDRIAL FISSION/FUSION IN EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS

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Background: The approved disease-modifying therapies (DMTs) for multiple sclerosis (MS) primarily target inflammation rather than neurodegeneration, even though the latter is more closely linked to disability. Some MS DMTs, such as glatiramer acetate (GA), may reduce neurodegeneration in MS, but the mechanism for that effect is not fully understood. Mitochondrial dysfunction appears to play a key role in other neurodegenerative conditions and could play a role in MS. One indicator of mitochondrial stress and dysfunction is changes in mitochondrial fission and fusion. Objectives: Determine the effect of GA treatment on mitochondrial stress as evidenced by changes in fission and fusion. Methods: Experimental autoimmune encephalomyelitis (EAE) was induced in C57Bl/6 female mice by immunization with myelin oligodendroglial glycoprotein peptide 35-55. GA (150 μg/mouse/day) was administered intraperitoneally starting at disease onset. Mice were euthanized on day 20 of GA treatment and brains and spinal cords were examined histologically. Results: Perivascular cell infiltration and demyelination, which were present in the spinal cords of the untreated EAE mice, were reduced by GA treatment. Mitochondrial Fis1 (a key regulator of mitochondrial fission) was increased in untreated EAE mice but not in GA-treated EAE mice, and Mito fusion -2 (a key regulator of fusion) was reduced in untreated EAE mice but not in GA-treated EAE mice. Conclusions: These results suggest a GA-mediated increase in mitochondrial fission and reduced fusion that could be due to reduced inflammation, resulting in reduced mitochondrial stress.

Supported by: Teva

Disclosure: Vamsi Nimmagadda: Teva (grant/research support). Christopher T. Bever Jr.: Department of Veterans Affairs, National Multiple Sclerosis Society, Teva (grant/research support); Department of Veterans Affairs, University of Maryland (employee). Rupal Jain, Susan I. Judge, David Trisler: Nothing to disclose. Tapas K. Makar: Teva, Department of Veterans Affairs, National Multiple Sclerosis Society (grant/research support); University of Maryland School of Medicine (employee).

Keywords: CNS repair, Disease-modifying treatments in MS, Immunology and MS

EPIDEMIOLOGY

(EP01) COMPARING DISABILITY OF MULTIPLE SCLEROSIS COHORT IN A TERTIARY CLINIC AND VOLUNTEER NARCOMS REGISTRY USING PATIENT-DERIVED MULTIPLE SCLEROSIS SEVERITY SCORE

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Background: Patient-Determined Disease Steps (PDDS) is a validated, patient-reported disability measure used in the ~36,000-enrollee-strong NARCOMS (North American Research Committee on Multiple Sclerosis) Registry. We recently introduced the Patient-Derived Multiple Sclerosis Severity Score (P-MSSS), which represents disease duration-adjusted mean ranks of PDDS among NARCOMS registrants. P-MSSS is calculated based exclusively on information provided by patients. P-MSSS is an easy-to-use tool for comparing disease severity in different patient populations and for tracking disease progression. Objectives: To com-
pare disease severity of multiple sclerosis (MS) patients in the NARCOMS Registry and NYU Multiple Sclerosis Care Center using the novel P-MSSS. Methods: We collected PDSS and disease duration on consecutive MS patients evaluated in the NYU Multiple Sclerosis Care Center. The P-MSSS values of our cohort were calculated using a published reference table (Kister et al., Neurology. 2013;80:1) and compared to the reference values. Results: 102 out of 108 MS patients completed the PDSS and provided their disease duration (completion rate >94%). Mean ± SD age was 45.0 ± 11.9 years and disease duration 13.3 ± 8.5 years. The mean P-MSSS of 4.1 ± 2.8 was significantly lower than the NARCOMS mean P-MSSS of 5.0 (P < .0001, Mann-Whitney U test). Conclusions: Although self-referred volunteer registrants might have been expected to have milder disease course compared with tertiary clinic patients, our preliminary results led to the opposite conclusion. This finding could be due to a variety of factors, including more aggressive treatment of clinic patients and overrepresentation of ambulatory patients in our cohort. We plan to present results of analysis extended to the entire clinic population seen over a 6-month period. P-MSSS was easy to use and quick to administer except in those with considerable cognitive deficits. P-MSSS is a promising new tool for tracking disease progression in a busy MS clinic.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Multiple sclerosis, Patient-Determined Disease Steps, Patient-Derived Multiple Sclerosis Severity Score

(Posters: Epidemiology)

(EPO2) CHARACTERISTICS OF THE 15-YEAR LONGITUDINAL MULTIPLE SCLEROSIS PATIENT REGISTRY OF THE NEW YORK STATE MULTIPLE SCLEROSIS CONSORTIUM
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Background: The New York State Multiple Sclerosis Consortium (NYSMSC), an alliance of MS care centers across the state, was founded in 1996 to develop a long-term clinical database and advance collaborative and multidisciplinary research in MS. A profile of the registry was published in 1999 (n = 3109). In 2009, Kister et al. published findings of a significant trend in lower MS severity scores over 10 years coinciding with an increase in relapsing-remitting disease type at enrollment, decrease in Expanded Disability Status Scale (EDSS) score at enrollment, and increase in disease-modifying therapy (DMT) use. Objectives: With inclusion of data through June 2013, we aimed to differentiate data between a cohort profile published in 1999 of the NYSMSC and a profile of the current registry. Methods: Data on 9261 subjects with MS were analyzed. Proportions and means were calculated to characterize the sample, and independent-sample t tests and chi-square tests were performed to investigate cohort differences. Results: As of June 2013, females comprised 74.3% of the NYSMSC sample. Whites made up 92.3% of the registry, with 6.2% of subjects being African American. The mean (SD) age at enrollment was 43.8 (11.3) years, and the mean age at symptom onset was 32.7 (9.9) years, while the mean age at diagnosis was 36.9 (10.3) years. Mean disease duration from symptom onset to most recent follow-up was 15.7 (10.1) years. In comparison between the two time cohorts, no significant difference was found in the sex ratio. The biggest differences were found in MS type; before 1999, 44.7% of subjects had a progressive disease type versus 25.5% in later years (P < .001). Subjects who registered before 1999 had higher EDSS scores at study enrollment, with a mean of 4.1 (2.4) versus 3.2 (2.1) (P < .001). The proportion of DMT use increased as expected (45.0% vs. 65.6%) while maintaining a sample of DMT-naive patients. Data from a specific incidence cohort of patients with baseline data collected within 5 years of symptom onset in addition to standard demographic, patient-perceived physical and psychosocial function, and clinical measurements also include environmental and genetic blood material, magnetic resonance imaging (MRI) markers, visual measures, and neurocognitive function at baseline and 6- and 12-month follow-up; the mean age at onset was 38.9 (10.9) years and the mean age at diagnosis was 40.3 (11.2) years. Conclusions: Longitudinal registries are important to provide real-world data on patient experience, clinical care, therapy patterns, and long-term outcomes, in contrast to the controlled environment of clinical trials.

Supported by: None
Disclosure: Barbara E. Teter: Biogen, Serono, Teva, Novartis, Genzyme (grant/research support). Katelyn S. Kavak, Karen Zakalik: Nothing to disclose. Bianca Weinstock-Guttman: Biogen, Teva Pharmaceuticals, EMD Serono, Inc., Pfizer, Novartis, Acorda (consulting fees); Biogen Idec, Teva Pharmaceuticals, EMD Serono, Inc., Pfizer, Novartis, Acorda, Cyberonics (grant/research support); Biogen Idec, Teva Pharmaceuticals, EMD Serono, Inc., Pfizer, Novartis, Acorda (speaker fees, fees for non-CME services from commercial interests or their agents).
Keywords: Disease-modifying treatments in MS, Epidemiology of MS, Prospective study

(EPO3) PREVALENCE OF THYROID DISEASE IN A MULTIPLE SCLEROSIS CLINIC COHORT
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Background: Multiple sclerosis (MS) has been associated with thyroid disease, but there are conflicting reports. Thyroid disease has been reported as a consequence of interferon beta and alemtuzumab therapies for MS. Objectives: To report the prevalence of thyroid disease in an American MS clinic cohort, most on approved MS therapies. Methods: A retrospective study of 382 patient charts from 2010 to 2011 identified the incidence and prevalence of autoimmune illnesses associated with MS. Patients had a confirmed MS diagnosis based on 2010 McDonald criteria. Findings regarding thyroid disease are reported. Results: Forty-seven patients (12.3%) had thyroid disease. Forty-six had hypothyroidism and 4 of these patients also had thyroiditis; 2 had thyroid surgery; 1 had benign thyroid nodules. One patient had thyroiditis alone. Forty-two of these patients were female and 5 male. All 5 patients with thyroiditis are female. Eighteen patients were on interferon beta, 10 on glatiramer acetate, and 7 on interferon beta and glatiramer acetate at some time in their therapy. Eleven of the remaining patients had exposure to multiple medications, including interferon beta (8), glatiramer acetate (7), natalizumab (3), fingolimod...
(2), monthly intravenous methylprednisolone (2), and several other medications. One patient with primary progressive MS was on no therapy. Confounding factors include tongue cancer surgery, chemotherapy, and radiation (1), Hodgkin lymphoma with radiation therapy and splenectomy (1), and radiation of thymus (1).

Conclusions: These data indicate that thyroid disease is commonly observed in an MS clinic cohort. While interferon beta is the most commonly associated therapeutic exposure in these MS patients with thyroid disease, glatiramer acetate is also well represented, suggesting that the underlying disease process itself is a major factor in the occurrence of thyroid disease for these patients. These data provide some further perspective regarding the occurrence of thyroid disease in the MS population, an important issue in the new era of MS therapeutics, as induction of autoimmune disease is a concern.

Supported by: None
Disclosure: Donald A. Baron; Acorda, Bayer, Biogen, EMD Serono, Genzyme, Novartis, Teva (consulting fees). Sergey Khelemsky, Decozy D.D. Hercules, Kathleen A. Baron: Nothing to disclose.

Keywords: Epidemiology of MS

(EP04) RESPONSIVENESS TO CHANGE OF AN ITEM RESPONSE THEORY SCORE OF GLOBAL DISABILITY DERIVED FROM NARCOMS PERFORMANCE SCALES  
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Background: At the 2013 CMSC annual meeting, we described the cross-sectional psychometric properties of a patient-reported outcome measure of global neurologic disability derived from the North American Research Committee on Multiple Sclerosis (NARCOMS) Performance Scales (PS) using item response theory (IRT). Objectives: To assess responsiveness and minimally important change (MIC) in PS IRT score by comparing changes on the new measure with changes on several external measures of disease activity and progression, including 1) Patient-Determined Disease Steps (PDDS), 2) self-evaluation of change in overall MS symptoms compared with 6 months ago, and 3) number of relapses in the last 6 months. Methods: Each single-item PS assesses perceived disability in 1 of 11 neurologic domains (mobility, hand, spasticity, tremor, bladder/bowel, vision, fatigue, cognition, sensory, pain, depression). Summary IRT scores of global disability were scaled to have baseline mean of 50 and standard deviation (SD) of 15 among MS patients recruited by the NARCOMS Registry in 1998–2011. Analyses of responsiveness were conducted using the biannual updates of NARCOMS participants enrolled in 2003–2008 who had at least an update immediately after enrollment and at 5 years of follow-up. We used linear mixed-effects models for longitudinal data to assess the associations between within-person changes on the anchors and 6-month changes in PS IRT score. Results: The study sample included 2788 people with MS. Median number of completed updates was 9 per subject (range, 2–12). Mean 6-month change in PS IRT score was 0.1 point (SD, 6.8). Change of one step on the PDDS was associated, on average, with a 2.3-point change in PS IRT score (95% confidence interval [CI], 2.2-2.4; P < .001). Patients’ assessment of symptoms now compared with 6 months ago was associated with a 0.7-point increase in PS IRT score (95% CI, 0.4-1.1; P < .001) when symptoms were described as worse/much worse and with a 1.0-point decrease in PS IRT score (95% CI, −1.4 to −0.7; P < .001) when symptoms were described as better/much better. PS IRT score marginally increased by 0.2 point (95% CI, −0.0 to 0.5; P = .09) when subjects experienced 1 or 2 relapses during the past 6 months, and by 0.9 point (95% CI, 0.4-1.4; P < .001) when they had 3 or more relapses. Conclusions: In this preliminary analysis, associations were in the expected directions and small changes in IRT score of global disability appeared to be meaningful to the patients.

Supported by: Novartis Pharmaceuticals; NARCOMS is supported in part by the CMSC and its Foundation.
Disclosure: Eric Chamot; Consortium of Multiple Sclerosis Centers (grant/research support). Amber R. Saller; GlaxoSmithKline (consulting fees). Ilya Kister; Biogen Inc (grant/research support). Gary Cutter; Alexion, Alnylome, Consortium of Multiple Sclerosis Centers (grant support); Dogenix, Klein-Buendel Incorporated, Genzyme, MedImmune, Novartis, Nuron Biotech, Receptors, Spinphlex Pharmaceuticals, Solabnul, Teva Pharmaceuticals, Xerox (consulting fees); Apotek, Biogen Idec, Cleveland Clinic, GlaxoSmithKline Pharmaceuticals, Gilead Pharmaceuticals, Modugenecheth/Prolor, Merck/Ono Pharmaceuticals, Merck, Neuren, PCT Bio, Revalaisio, Sanofi-Aventis, Teva, Vivos, National Heart, Lung, and Blood Institute (protocol review committee), National Institute of Neurological Disorders and Stroke, NMS (data and safety monitoring committee); Pythagoras, Inc (president of a private consulting company).

Keywords: Epidemiology of MS, MS outcome measure, Natural history of MS

(EPO5) COEXISTING MULTIPLE SCLEROSIS AND HUNTINGTON DISEASE: REFLECTIONS ON THE IMMUNE THEORY IN NEURODEGENERATIVE DISORDERS  
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Background: Variable disease associations have been described with multiple sclerosis (MS), including other immune-mediated and neurodegenerative disorders. Coexisting MS and Huntington disease (HD) has not been previously described. This association raises questions about the interactions between immune dysfunction, neurodegeneration, and genetics. Case Reports: Case 1 is a 44-year-old woman who developed diplopia and ataxia at the age of 31. Brain magnetic resonance imaging (MRI) showed supratentorial and brainstem T2 lesions with morphology typical of MS. Cerebrospinal fluid (CSF) evaluation showed elevated IgG index and positive oligoclonal bands (OCBs). Symptoms resolved spontaneously. She was started on interferon beta-1a (IFNβ-1a) 2 years later because of new enhancing MRI lesions. She subsequently developed gradual cognitive decline and abnormal movements of the face and limbs. Familiar history was positive for a paternal grandmother with HD. Her father had early dementia but was never tested for HD prior to his death at the age of 60 from heart disease. Exami-
nati on showed generalized chorea and hyperreflexia with a UH oRs of 15 and Expanded Disabi lity Status Scale (EDSS) score of 3.0. HD was confirmed by genetic testing showing 38 CAG repeats. Case 2 is a 45-year-old woman who at the age of 43 developed progressive abnormal movements of the face and limbs with gradual cognitive decline. She had no family history of HD. Initial workup showed periventricular T2 lesions and CSF positive for high IgG index and OCBs. She was diagnosed with MS and started on IFNB-1a. She kept getting worse despite treatment. At the time of her initial evaluation at our institution, she exhibited generalized chorea with a UH oRs of 56. Genetic testing came back positive for 45 CAG repeats. She was diagnosed with de novo HD and radiologically isolated syndrome. Discussion: This is the first report of coexisting MS and HD. In 2012, Haghi kia et al. described a case of coexisting HD and multifocal autoimmune myelitis. Although this association between MS and HD could be coincidental, it is interesting that several recent studies have described abnormal immunity in HD mouse models and in presymptomatic patients. Immune dysfunction is thought to be an inciting factor for neurodegeneration in HD. This immune dysfunction is genetically determined and may anticipate higher risk for developing immune-mediated disorders like MS. Interestingly, both patients were continued on disease-modifying therapy for MS without apparent benefit for the course or severity of HD, which supports the “trigger” concept of the immune dysfunction in HD as opposed to the ongoing process of immune-mediated injury seen in MS. Conclusion: MS and HD may coexist, and this should be considered when symptoms cannot be explained by either disease alone. Immune-modulating therapy in presymptomatic HD patients may be an option for future clinical trials.

Supported by: None

Keywords: Genetics and MS, Immunology and MS, Neurodegenerative disorders

(EP06) DIETARY SALT INTAKE AND RISK OF PEDIATRIC MULTIPLE SCLEROSIS: A PROSPECTIVE CASE-CONTROL STUDY

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Background: Environmental and dietary factors have become increasingly recognized in the past decades as potential risk factors for developing multiple sclerosis (MS). Pediatric MS offers a unique opportunity to study such factors, due to temporal proximity at the time of diagnosis to the exposure, thereby minimizing recall bias. High salt intake has been shown to increase disease onset and progression in recent animal studies. Whether these results are applicable to human disease is currently unknown. Objectives: To determine whether dietary salt intake is higher in a multicenter cohort of pediatric MS subjects compared with pediatric controls. Methods: A prospective case-control study was performed with pediatric-onset MS patients (first clinical attack before 18 years of age) who were seen within 2 years of onset at one of 13 pediatric MS centers. Controls, less than 20 years old, were recruited from the same centers. Participants’ responses to the validated Block Kids Food Screener questionnaire (NutritionQuest) were used to estimate daily sodium intake. Sodium intake was compared between cases and controls and adjusted for age, race, and insurance status in logistic regression models. Results: Among 122 cases and 202 controls, baseline characteristics were similar for age, mean energy intake (kcal/d), total fat (g/d), and race; however, there were significantly more female and Hispanic/Latino cases compared with controls. Unadjusted dietary sodium intake was not significantly different between cases (1984 mg/d and controls (2094 mg/d). The mean sodium intake was higher in female cases than in controls (1728 vs. 1677 mg/d, P = .89). The percentages of participants exceeding adequate intake of sodium were similar between cases and controls for both males and females. Preliminary analysis adjusting for age, race, and insurance status revealed a trend toward increased odds of MS (OR, 1.018) for each 100 mg/d increase in sodium (95% confidence interval [CI], 0.994-1.042; P = .139). Adjustment of analyses for body-mass index is pending. Data from an additional 105 subjects are currently being added to the initial analyses. Conclusions: No significant difference in dietary sodium intake was found between cases and controls in the preliminary analysis. However, the trend toward an increased likelihood of MS with higher salt intake in the adjusted model highlights the need for further investigation of salt as a potential mediator of MS risk in a larger subject pool.

Supported by: National Institutes of Health (NS071462-03)
Disclosure: Jamie McDonald: Consortium of Multiple Sclerosis Centers (CMSC Medical Research Scholarship). Jennifer Groves, Sabeeb Lulu, Amy Waldman, Anita Belman, Greg Aaen, Jan Mendell-Tillema, Janace Hart, Jayne Ness, Jennifer Rubin, Lauren Krupp, Mark Gorman, Moses Rodriguez, Tanuja Chinthis, Timothy Simmons, T. Charles Casper, John Rose, Emmanuelle Waubant: Nothing to disclose. Benjamin Greenberg: Accelerated Care Project, Amplimmune, Guthy Jackson Foundation, National Institutes of Health (grant/research support); Acorda (consulting fees); Biogen Idec (consulting fees, grant/research support); Diogenix (consulting fees, stock ownership). Bianca Weinstock-Guttman: Biogen Idec, Teva Pharmaceuticals, EMD Serono, Inc., Pfizer, Novartis, Acorda (consulting fees); Biogen Idec, Teva Pharmaceuticals, EMD Serono, Inc., Pfizer, Novartis, Acorda, Cyberonics (grant/research support); Biogen Idec, Teva Pharmaceuticals, EMD Serono, Inc., Pfizer, Novartis, Acorda (speaker fees, fees for non-CME services from commercial interests or their agents).

Keywords: Epidemiology of MS

(EP07) MARITAL STATUS AND DISEASE PROGRESSION IN MULTIPLE SCLEROSIS: A POPULATION-BASED STUDY

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International Journal of MS Care 70
Background: Married individuals tend to live longer and experience greater health-related quality of life. Previous research has indicated that being married is associated with less severe disease progression in several chronic diseases, such as dementia and rheumatoid arthritis. Whether marital status influences objective disease progression in multiple sclerosis (MS) is currently unknown. Objectives: To evaluate the relationship between marital status and disease progression in MS.

Methods: We utilized the population-based Gulf War-era MS cohort (n = 2631) to investigate whether marital status predicted disease progression on the Kurtzke Disability Status Scale (DSS). Each case was classified by the McDonald criteria as definite or possible MS. Marital status was categorized at the baseline and the most recent disability assessment according to the following categories: married–no change, single–no change, married-to-single, single-to-married. In a series of analyses of variance (ANOVAs), we analyzed these marital status changes and demographic variables in relation to time from disease onset to DSS = 6 (cane) and DSS = 7 (wheelchair).

Results: Over the mean follow-up period of 6.34 years, being married significantly predicted slower progression to a DSS 6 than remaining single (F_{3,2623} = 5.96, P < .001). On average, those remaining single progressed to cane 1.16 years more quickly than those who were married at any point. Likewise, having a married status significantly predicted time from disease onset to a DSS 7 (F_{3,2623} = 9.63, P < .001). On average, those remaining single progressed to a wheelchair 1.5 years more quickly than those married at any point. There was a significant interaction between sex and marital status predicting progression to DSS 6 (F_{3,2619} = 6.83, P < .001) and to DSS 7 (F_{3,2619} = 7.13, P < .001). For those who remained single, males progressed to both DSS endpoints significantly more quickly than females. Finally, there was a significant interaction between race and marital status predicting progression to DSS 6 (F_{2,2574} = 3.29, P = .020). For those who remained married, blacks progressed more rapidly than whites.

Conclusions: Being married at any point during the course of MS appears to confer a benefit in MS disease progression. Further research is needed to understand the mechanism by which marital status influences MS disease progression.

Supported by: Veterans Affairs Merit Review (EPID-009-06F), National Multiple Sclerosis Society Pilot Grant (PP1368), Veterans Affairs MS Centers of Excellence

Disclosure: Nothing to disclose

Keywords: Epidemiology of MS, MS and the caregiver/family, Psychological issues and MS

(EP08) STUDY OF PREVALENCE AND RISK FACTORS FOR JC VIRUS ANTIBODY SEROCONVERSION IN MULTIPLE SCLEROSIS PATIENTS FROM THE UNIVERSITY OF MASSACHUSETTS MEMORIAL MULTIPLE SCLEROSIS CENTER

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Background: Multiple sclerosis (MS) is an autoimmune inflammatory demyelinating disease of the central nervous system (CNS) that is a leading cause of disability in young adults. Treatment directed at the rapid, aggressive progressive phase of MS is typically difficult. Natalizumab is an effective drug for the treatment of relapsing-remitting multiple sclerosis (RRMS). However, in rare cases, its use is associated with the development of progressive multifocal leukoencephalopathy (PML), a potentially fatal complication caused by the JC virus (JCV). It is estimated that the majority of adults are positive for JCV antibodies. Risk factors for infection with this virus are unknown. Environmental factors may play a role.

Objectives: To identify environmental factors associated with JCV antibody status.

Methods: We identified patients who have been tested for antibodies to JCV and performed chart review to determine if there is a difference in terms of gender, age, area of residence, or marital status between patients who tested positive and those who tested negative for JCV antibodies. The R statistical programming language was used to analyze the data. We developed a questionnaire asking about environmental exposures. This questionnaire will be administered to patients with available JCV serology results to determine if there is a difference in exposures between groups. Family members will be tested for JCV antibodies to determine if there is an association between family member JCV antibody status and patient JCV antibody status.

Results: 144 patients with JCV serology results were identified. 76.4% were female and 23.6% were male, with a mean age of 46.7 years. 49.3% were positive for JCV antibodies and 50.7% were negative. 55.8% and 54.2% of the women were negative and positive, respectively. 32.4% and 67.6% of the men were negative and positive, respectively (P = .01). The mean ages in the negative and positive groups were 45.7 and 47.6 years, respectively (P < .05). Patients came from various locations in Massachusetts, Rhode Island, Connecticut, New Hampshire, Tennessee, and British Columbia. There were differences in JCV seropositivity among the different areas of residence (P < .01). 54.1% of patients were married and 45.9% were single, divorced, widowed, or other (P < .05). We expect to report results from our exposures questionnaire at the conference.

Conclusions: The 49.3% prevalence of JCV antibodies in this patient population is consistent with that of other studies. In our study, gender and area of residence were associated with JCV antibody status, whereas age and marital status were not. It is theorized that JCV infection occurs through an environmental exposure, so it stands to reason that area of residence may influence JCV antibody status. A greater number of men were positive for JCV. Occupational exposures may be a factor in this result. We hope to elucidate this further with our questionnaire.

Supported by: Teva Neuroscience

Disclosure: Juan Ramirez, Carolyn Griffin: Nothing to disclose. Carolina Ionete: Acorda Therapeutics, Biogen Idec, Genzyme Corporation, Teva Pharmaceuticals (grant/research support).

Keywords: Disease-modifying treatments in MS, JC virus

(EP09) HIGH BODY-MASS INDEX AND WEIGHT IN YOUNG ADULTHOOD IS ASSOCIATED WITH A YOUNGER AGE OF MULTIPLE SCLEROSIS SYMPTOM ONSET AND DIAGNOSIS

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Background: Recent studies have linked early-life obesity to a higher risk of developing adult-onset multiple sclerosis (MS) and pediatric MS. The rate of obesity in young adulthood is rising rapidly; therefore, it is important to investigate issues with respect to MS onset. Currently, it is unknown whether weight is related to age at MS onset. Objectives: To investigate retrospectively whether increased weight or body-mass index (BMI) in young adulthood is associated with age at MS symptom onset and diagnosis. Methods: Our sample comprises a subgroup of 237 women registered with the New York State MS Consortium (NYSMSC) who completed an extensive questionnaire about reproductive events and are treated at our MS care center. Subjects were asked to recall their weight at the time of first menstruation and at age 25. BMI was calculated accordingly for age 25 but not extended to time of first menstruation, since height measures in adolescence could not reliably be deduced. Regression analyses were carried out to investigate the association between weight or BMI as a continuous measure and age at MS onset. Additionally, overweight and nonoverweight people were compared based on a division of BMI ≥25 vs. <25. Results: Weight (in pounds) of subjects at their first menstruation was significantly related to younger age at onset (β = −2.73, P < .001) and diagnosis (β = −2.96, P < .001). These results were also found at age 25 for onset (β = −2.72, P < .001) and diagnosis (β = −3.04, P < .001). Subjects with higher BMI at age 25 were younger at onset (β = −2.21, P = .002) and diagnosis (β = −2.53, P < .001). Additional analyses between overweight and nonoverweight subjects showed that overweight subjects at age 25 had a significantly earlier age at onset (27.1 ± 10.1 vs. 31.7 ± 8.7, P = .008) and diagnosis (31.2 ± 9.9 vs. 35.5 ± 8.4, P = .009). Conclusions: Patients who reported having a higher weight and BMI in early adulthood were younger at MS symptom onset and MS diagnosis. Future research should investigate whether there is a causal link between body weight and MS, as there may be underlying genetic or environmental factors, such as vitamin D deficiency, that could influence the results.

Supported by: None


Keywords: Genetics and MS, Immunology and MS

(EPI11) A CROSS-SECTIONAL WEB-BASED SURVEY OF COMORBID ILLNESSES AND SYMPTOMS AMONG ADULTS WITH MULTIPLE SCLEROSIS

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Background: Multiple sclerosis (MS) is a chronic and debilitating neurologic disease affecting those in early adulthood. With increasing age, patients with MS face the same comorbid conditions as the general population. However, it is unknown whether adults with MS experience these conditions sooner, or to a greater extent, than people who are aging without MS. Health-care providers should be aware of the extent of comorbid conditions among their patients with MS.
to suggest potential interventions, such as exercise to improve depression, fatigue, and arthritis symptoms. More research is needed to determine the specific impact of these conditions on health-care costs and quality of life. **Objectives:** The objective of this study was to compare self-reported comorbidities and severity of symptoms in patients diagnosed with MS with age-matched, US population norms. **Methods:** Patients with MS (n = 325) completed a secure web-based survey (www.Qualtrics.com) that contained questions derived from the National Health Interview Survey. **Results:** Descriptive statistics were used to summarize and compare estimates as a sample proportion for each of the following: depression, coronary artery disease (CAD), cancer, diabetes (any type), migraine headaches, and arthritis. To determine whether the two population means (MS, US population norms) were different, the z test was performed for the total sample, as well as the following age categories: 18–34 years, 35–44 years, 45–54 years, 55–64 years, and 65–74 years. In this sample participants were mainly white (91.6%) and female (77.0%), with a mean (SD) age at MS symptom onset of 33.2 (11.1) years; 85% reported having relapsing-remitting MS (RRMS), the least progressive subtype. Patients with MS who reported the presence of comorbidities of depression, CAD, rheumatoid arthritis, cancer, and migraine headaches also reported more pain, fatigue, sleep problems, and balance problems compared with those who did not report these comorbidities. **Conclusions:** These findings suggest that adults with MS have secondary comorbid conditions and report symptoms specific to each condition. Health-care providers should be aware of the extent of comorbid conditions and symptoms among their patients with MS to suggest potential interventions, such as exercise to improve depression, fatigue, sleep, and pain symptoms. More research is needed to determine the specific impact of these conditions on health-care costs and quality of life.

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**Rehabilitation**

**RH07 Does Using a Service Dog Help Ambulation in Multiple Sclerosis Patients With Gait Dysfunction?**

Cecilie Fjeldstad, Gabriel Pardo

**Background:** Walking impairment, postural balance, and inactivity are primary concerns for individuals with multiple sclerosis (MS). In recent years, service animals have become increasingly recognized as productive aids to individuals with various kinds of disabilities. The Timed 25-Foot Walk (T25FW) has been used as an outcome for medical intervention in gait dysfunction in MS. **Objectives:** To determine whether walking speed in MS patients with ambulatory dysfunction, but without requiring a walking aid, improves with the assistance of a certified service dog. **Methods:** The study cohort included 36 individuals diagnosed with MS and identified as having a gait abnormality secondary to MS, but able to walk without using any assistive device. Mean age was 52.7 ± 1.5 years, and mean duration of MS was 14.0 ± 1.4 years. 93% of the cohort had the relapsing-remitting type of MS, 77% were on disease-modifying therapies, and 82% were female. They were asked to perform two T25FW sets, each including an unassisted walk and one with a service dog. The order was reversed for the second set, which was performed after a 15-minute rest period. A paired-sample t test was performed to examine the difference between walking with and without a service dog. **Results:** There was a significant difference in the T25FW for individuals who walked with the aid of a service dog compared with individuals walking on their own (P < .05, P = .014). **Conclusions:** Walking speed was improved when individuals received the aid of a service dog. This study is the first, to our knowledge, to investigate use of a service animal to improve ambulatory dysfunction in MS. These results should encourage additional research on the use of service animals in MS.

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**RH08 Correlation Between Retinal Nerve Fiber Layer and Timed 25-Foot Walk Over a 2-Year Period in a Cohort of Individuals With Multiple Sclerosis**

Cecilie Fjeldstad, Gabriel Pardo

**Background:** There is a need to identify anatomical biomarkers of disease progression in multiple sclerosis (MS) that are practical, inexpensive, and easy to perform. Measurement of the retinal nerve fiber layer (RNFL) by optical coherence tomography (OCT) correlates with brain volume loss as measured by magnetic resonance imaging (MRI). Correlation between anatomical and functional parameters is needed. **Objectives:** Determine whether RNFL measurement by OCT correlates with Timed 25-Foot Walk (T25FW) and serves as a surrogate anatomical marker of functional decline in individuals with MS. **Methods:** This was a longitudinal study of 51 MS patients. Each subject had OCT and T25FW measured at two time points, separated by 1 to 2 years. **Results:** There was no significant correlation between T25FW and RNFL (r = 0.01, P > .05). There was a trend toward a decrease in the RNFL over time, but not at the level of statistical significance. A paired-sample t test was performed to examine any differences for T25FW and for RNFL thickness at year 1 versus year 2. No significant changes were seen for T25FW (P = .212, P > .05) or for RNFL thickness (P = .104, P > .05) in that time period. The T25FW data were further trichotomized (<6 seconds; 6–7.99 seconds, and ≥8 seconds). None of the measurements for the subgroups had significant differences from one year to the next. **Conclusions:** This pilot study examined the relationship between RNFL and T25FW over a follow-up period of 2 years. No relationship was found between the two parameters for the group as a whole or for timed performance subgroups. Future studies with larger cohorts and duration are warranted.

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**Keywords:** Comorbid conditions, Psychological issues and MS
(RH09) BENEFITS OF FUNCTIONAL ELECTRICAL STIMULATION CYCLING IN PEOPLE WITH MOBILITY RESTRICTIONS DUE TO MULTIPLE SCLEROSIS
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Background: People with multiple sclerosis (MS) and Expanded Disability Status Scale (EDSS) scores of 6 or greater experience deconditioning resulting from the impairments caused by MS, as well as their restricted mobility. Decreased physical activity can cause progression of disability and increases the risk of secondary health conditions. Emerging evidence suggests that exercise is safe and beneficial for people with MS. However, those who are limited to a wheelchair for mobility are the most understudied in this regard, and face the most barriers to exercise. Functional electrical stimulation (FES) cycling is of interest because people with significant weakness and mobility challenges can use this intervention to activate leg muscles, which may provide enough exercise to induce changes in health measures, and decrease disability. Objectives: To evaluate safety, as well as the potential for FES cycling to improve fatigue, pain, spasticity, and perceived quality of life, in people with moderate-to-severe MS. Methods: In this institutional review board–approved pilot study, we recruited 16 people with MS and EDSS scores ≥6.0. Participants trained on the RT-300 FES cycle (Restorative Therapies, Inc., Baltimore, MD) two to three times a week for approximately 1 month. The goal was to cycle at 35 to 50 rpm for 30 minutes, either actively or with electrical stimulation for assistance. Intensity of FES was adjusted for each participant based on comfort. Data collected immediately before and after the 4-week training period included Multiple Sclerosis Quality of Life Inventory (MSQLI) subscales, Modified Ashworth Scale (MAS, spasticity), and manual muscle test (MMT, strength). Data were also collected at each training session to monitor progress on the cycle, and for any changes in status. Results: Fourteen participants (6 female, 8 male) with MS completed the training. All participants were able to either maintain or increase the amount of time they could cycle; half (7/14) were able to increase the resistance against which they cycled. Participants demonstrated a significant increase in cognitive processing speed (Paced Auditory Serial Addition Test [PASAT], P < .001) and a significant decrease in pain (Medical Outcomes Study [MOS] Pain Effects Scale, P < .02). There was no significant change in the other subscales of the MSQLI. There was neither a significant increase nor a decrease in MAS and MMT scores. The type of MS (ie, relapsing-remitting, secondary progressive, or primary progressive) and the use of antispasticity medications, disease-modifying therapies, or Ampyra or 4-aminopyridine did not appear to influence the response to training. There were no adverse events or worsening of MS symptoms. Conclusions: FES cycling may be a viable and effective exercise option for people with moderate-to-severe MS. Further study is required to examine the parameters of FES cycling that are most effective for people with different constellations of MS symptoms, and to fully explore the potential benefits for optimizing function and improving health in people with MS.

Supported by: The Eula C. and Andrew C. Carlos MS Rehabilitation and Wellness Fund
Disclosure: Nothing to disclose.
Keywords: Complementary/alternative therapies in MS, Functional electrical stimulation

(RH10) DO DEMOGRAPHIC AND CLINICAL VARIABLES PREDICT CHANGE IN PHYSICAL ACTIVITY OVER TIME IN PEOPLE WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS?
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Background: People with multiple sclerosis (MS) do not engage in sufficient amounts of physical activity; further, there is a reduction in physical activity over time in this population. To date, there is limited information on the demographic and clinical variables that predict the trajectory of change in physical activity over time. Such information is important for identifying who should be targeted for delivery of a behavioral intervention for increasing physical activity. Objectives: This study involved a secondary analysis of existing data and examined demographic and clinical variables as predictors of initial status and rate of change in physical activity over a 2.5-year period of time in people with relapsing-remitting multiple sclerosis (RRMS). Methods: On six occasions separated by 6 months over 2.5 years, 269 individuals with RRMS completed a battery of questionnaires and wore an accelerometer (ActiGraph model 7164) for 7 days. The battery of questionnaires included information on disease duration, disability, sex, age, race, body-mass index (BMI), education, and income. The data were analyzed with unconditional and conditional latent growth curve modeling (LGM) using the robust maximum likelihood estimator and the Mplus software package. Results: The unconditional LGM indicated a statistically significant linear reduction in average counts per day from the accelerometer over the 2.5-year period of time. The conditional LGM indicated that education (P < .001), disability (P < .001), and BMI (P < .005) predicted initial status for physical activity. The conditional LGM further indicated that BMI predicted the rate of change in physical activity over time (P < .005); those who were more overweight had a greater reduction in physical activity over the 2.5-year period. Conclusions: Researchers should consider designing behavioral interventions for increasing physical activity among people with MS who have higher BMI, as this demographic appears susceptible to reductions in physical activity over time. This might further explain the association between BMI and other disease outcomes in RRMS.

Supported by: National Multiple Sclerosis Society (PP 1695)
Disclosure: Dominique L. Kinnett-Hopkins, Edward McAuley, Brian M. Sandroff: Nothing to disclose. Robert W. Motl: Acorda Therapeutics, Biogen Idec, National Multiple Sclerosis Society (grant/research support); EMD Serono (fees for non-CME services from commercial interests or their agents).
Keywords: Disease-modifying treatments in MS, Epidemiology of MS
(RH11) GAIT INITIATION AND FALL RISK IN INDIVIDUALS WITH MULTIPLE SCLEROSIS

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Background: Mobility impairments and falls are common in individuals with multiple sclerosis (MS). Falls can occur at any time, but often result during transitions between positions such as the initiation of gait. Therefore, dynamic balance tasks such as gait initiation offer a unique platform for the study of fall risk in MS. Objectives: To investigate the association between gait initiation and fall risk in cognitive distracting and nondistracting conditions. Methods: Thirty individuals with MS (mean ± SD age, 62.8 ± 7.8 years; median [interquartile range] Expanded Disability Status Scale [EDSS] score, 6.0 [2.0]) participated in the investigation. Participants completed 4 (ie, 2 baseline, 2 cognitive distraction) gait initiation trials on a 6.1-m pressure-sensitive walkway. Participants stood in place and started walking at a comfortable pace in response to an auditory cue. During the cognitive distraction condition the participants recited alternating letters of the alphabet (eg, A, C, E). Gait initiation was indexed by time to take the first step following the auditory cue. Participants also underwent a separate analysis of physiological fall risk as indexed by the physiological profile assessment (PPA). The PPA analyzes performance in the areas of reaction time, leg strength, vision, proprioception, and balance. The results of these assessments are combined for the calculation of an overall fall risk z score, with larger scores representing greater fall risk. Spearman correlations were used to examine the relationship with PPA. Results: Overall, participants took between 0.68 and 1.11 seconds to initiate a step during single-task conditions and between 0.77 and 1.84 seconds during dual-task conditions. PPA fall risk scores ranged from −0.03 to 3.46. There was a significant correlation between fall risk and step initiation in both the single-task condition (r = 0.65) and cognitive distraction condition (r = 0.70). Conclusions: The findings suggest that gait initiation may represent a valuable outcome measure for understanding fall risk in MS and also highlight the association between cognitive distraction and fall risk. Ultimately, the relationship with physiological fall risk provides the possibility of gait initiation tasks being adapted as a marker of fall risk.

Supported by: National Multiple Sclerosis Society (PP 1695)
Disclosure: Douglass A. Wajda, Yaejin Moon: Nothing to disclose.
Jacob J. Sosnoff: National Multiple Sclerosis Society, National Institutes of Health, Consortium of Multiple Sclerosis Centers (grant/research support); Robert W. Motl: Acorda Therapeutics, Biogen Idec, National Multiple Sclerosis Society (grant/research support); EMD Serono (fees for non-CME services from commercial interests or their agents).

Keywords: Falls and MS

(RH12) THE DESCRIPTIVE EPIDEMIOLOGY OF DAILY SITTING TIME AS A SEDENTARY BEHAVIOR IN MULTIPLE SCLEROSIS

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Background: Sedentary behavior is pervasive among the general population, but little is known about the epidemiology of this behavior in multiple sclerosis (MS). Objectives: We compared self-reported sitting time (ST), as a measure of sedentary behavior, between individuals with MS and healthy controls, and examined ST across demographic and clinical characteristics of the MS sample. Methods: 1081 people with MS and 150 healthy controls self-reported ST based on the International Physical Activity Questionnaire (IPAQ), and completed the Godin-Leisure-Time Exercise Questionnaire (GLTEQ) and a demographic/clinical scale. Data were analyzed using analysis of variance, bivariate correlations, and stepwise regression analysis. Results: There was not a significant difference in ST between people with MS and controls (F = 0.01, P = .95), and people with MS reported 450.9 ± 220.6 minutes of ST per day. ST was weakly associated with GLTEQ scores in people with MS (r = −0.21, P < .001), but not controls. ST significantly differed as functions of marital status, physical activity level, employment status, education, and disability status among those with MS. Conclusions: ST does not differ between people with MS and healthy controls, but those with MS report a large amount of this sedentary behavior that is an independent correlate of health and disease outcomes.


Keywords: Epidemiology of MS, Sedentary behavior

(RH13) PREVALENCE OF UPPER-EXTREMITY INVOLVEMENT ACROSS ICF DOMAINS AMONG PEOPLE WITH MULTIPLE SCLEROSIS

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Background: Extensive research has shown that lower-extremity (LE) involvement in multiple sclerosis (MS) has a negative effect on quality of life. However, there is comparatively little literature available on upper-extremity (UE) involvement in MS. Objectives: To estimate prevalence of UE involvement among people with MS across the ICF domains of UE impairment, capacity, and performance. Methods: Twenty-seven subjects were recruited at a community-based comprehensive MS center. UE impairment was measured using grip strength and eight self-reported UE symptoms. Capacity was measured using the Box and Block Test (BBT), Nine-Hole Peg Test (NHPT), and UE performance test for the elderly (TEMPA). Performance was measured using the DASH. Means and SDs were calculated for each quantitative measure; the percentage of patients whose measures were >2 SD worse than age-, gender-, or age- and gender-specific norms (depending on measure) were determined. Results: Across a wide range of Expanded Disability Status Scale (EDSS) scores (2–7), 85% of people with MS in the study self-reported at least one UE symptom. Weakness was the most commonly reported symptom. Over half reported UE tingling, loss of sensation, trouble doing everyday tasks with the affected limb(s), numbness, and weakness. UE spasms (19%) and stiffness (26%) were reported less frequently. Compared with gender- and age-specific norms, 33% and 19% of sub-
jects were >2 SD below norms for right and left grip strength, respectively. For capacity measures, 70% and 59% for the NHPT and 93% and 89% for the BBT were >2 SD above gender- and age-specific norms for dominant and nondominant hands, respectively. TEMPA was developed for elderly adults, so norms are based on people aged 60+ years. Nonetheless, between 44% and 93% of subjects had times to complete each task that were >2 SD above gender-specific means for the 60- to 69-year-old norms. The DASH was the measure of performance; 30% of subjects were >2 SD above norms. Conclusions: People with MS have considerable UE involvement across ICF domains of impairment, capacity, and performance.

Supported by: None

Disclosure: Elizabeth W. Triche, Mount Sinai Rehabilitation Hospital (consulting fees); National Multiple Sclerosis Society, Acorda Therapeutics (travel reimbursement); National Multiple Sclerosis Society, Acorda Therapeutics Inc., National Institutes of Health (grant/research support); Jennifer A. Ruiz, Kayla M. Olson; National Multiple Sclerosis Society, Acorda Therapeutics Inc. (grant/research support). Albert C. Le: National Multiple Sclerosis Society, Veterans Affairs, Acorda Therapeutics, Paralyzed Veterans of America (grant/research support, travel reimbursement).

Keywords: Comprehensive care and MS, Management of activities of daily living in MS, Rehabilitation of MS

(RH14) SELECTING REHABILITATION OUTCOME MEASURES: APPLYING THE FINDINGS OF THE AMERICAN PHYSICAL THERAPY ASSOCIATION MS EDGE TASK FORCE

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Background: Despite the benefits of assessing individual and programmatic outcomes, a variety of barriers limit the use of outcome measures (OMs), and clinicians do not routinely use OMs in practice. Evidence suggests that clinicians lack the knowledge to choose the most effective or appropriate OMs. Clinicians working with people with multiple sclerosis (MS) have additional challenges in OM selection because of the heterogeneous patient population and symptom variability. In 2010, the Neurology Section of the American Physical Therapy Association (APTA) appointed the Multiple Sclerosis Outcomes Measures Task Force (MSTF) to review and make evidence-based recommendations for the use of OMs in clinical practice, education, and research specific to people with MS. Sixty-three OMs were reviewed. An Evaluation Database to Guide Effectiveness form, developed by the Research Section of APTA, modified by the MSTF to incorporate MS-related constructs, was used to record the OM properties, psychometrics, clinical utility, and recommendations. Recommendations were based on an analysis of the constructs measured, a synthesis of psychometric data, and a consensus evaluation of the appropriateness of the OM for people with MS, via a modified Delphi process. A 4-point rating scale, based on the strength of the OM’s psychometrics and clinical utility, was used to evaluate OMs for use in patients across the MS disability spectrum, and in five practice settings. Objectives: The purpose of this presentation is to illustrate use of the MSTF recommendations to select appropriate OMs for a patient with MS. Methods: The patient was a 43-year-old man with a 10-year history of relapsing-remitting MS who recently had an exacerbation leading to increased difficulty walking and increased fatigue. The patient’s goal was to return to work as a computer programmer. Based on the case history, three health-related constructs were deemed most important for this patient: upper extremity (UE) function, fatigue, and gait. Using the recommendations of the MSTF, several candidate OMs were identified for each of the three constructs (7 for UE function, 14 for fatigue, and 9 for gait). A systematic decision-making process was used to evaluate the appropriateness of each OM for each construct.

Results: The systematic decision-making process led the team to select the following OMs: Nine-Hole Peg Test for UE function, Modified Fatigue Impact Scale for fatigue, and two OMs for gait: the 12-Item MS Walking Scale (a self-report OM) and the Timed 25-Foot Walk test (a performance-based test). Conclusions: Utilizing the recommendations established by the MSTF facilitated selection of OMs that pertained to the health-related constructs of interest, were clinically feasible, and had psychometric data relevant to individuals with MS.

Supported by: None


Keywords: Comprehensive care and MS, Outcome measurement

(RH15) EFFECTS OF RHYTHMIC AUDITORY STIMULATION ON GAIT AND ON CORTICAL ACTIVATION WITH MENTAL IMAGERY OF WALKING IN PATIENTS WITH MULTIPLE SCLEROSIS

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Background: Rhythmic auditory stimulation (RAS) was shown to improve gait in patients with central nervous system disorders. Previous studies conducted by our team demonstrated improvement of gait parameters after a home walking program using RAS in individuals with multiple sclerosis (MS). Patterns of cortical activation on functional magnetic resonance imaging (fMRI) were identified in relation to walking and mental imagery of walking, in various populations. To our knowledge, there has been no published study on the immediate effects of RAS on gait and on cortical activation in relation to mental imagery of walking in patients with MS.

Objectives: To measure immediate changes in spatiotemporal (ST) gait parameters with RAS, and to assess changes in cortical activation induced by RAS in MS patients performing mental imagery of walking. Methods: In this cross-sectional study, subjects with gait disturbance from MS were instructed...
to perform two series of walks on an electronic gait analysis walkway: 5 walks without RAS (W1), and 5 walks with a fixed sequence (W2: no RAS, RAS at comfortable walking cadence, then 10% and 20% above comfortable walking cadence, then no RAS). A repeated-measures analysis of variance (ANOVA) was used to test for within-subject differences in ST gait parameters. Subjects were scanned while performing walking imagery, with (W+) and without (W−) RAS at their spontaneous walking cadence. For each subject, Student t maps were generated for the W+ and W− conditions. Student t maps were spatially normalized, and a voxelwise paired t test was performed between W+ and W−. Results: Ten subjects were enrolled: mean age 51 ± 5 years, 60% women, mean duration of symptoms 17 ± 8 years, 60% relapsing MS, mean Timed 25-Foot Walk time 7 ± 3 seconds, 50% using a cane or walker. During W1, stride length (P = .03 left side, P = .004 right side) and velocity (P = .02) improved significantly between the first and second walks. During W2, there was a significant improvement in cadence (P = .01) and a trend for improvement of velocity (P = .05) with RAS. Analysis of fMRI data showed increased activation of the right cerebellum and right insula during W−, while W+ was associated with increased activation in the supplementary motor area, left middle frontal gyrus, and left anterior cingulate, and decreased activation in the right middle temporal gyrus. The W+/W− comparison showed increased activation in the left superior temporal gyrus and left anterior cingulate, and decreased activation in the right middle temporal gyrus. The W+/W− comparison showed increased activation in the left superior temporal gyrus and left anterior cingulate in the W+ condition, and increased activation in the right middle temporal gyrus in the W− condition (P < .01, corrected for multiple comparisons). Conclusions: RAS at a tempo above the subject’s spontaneous walking cadence produced an immediate increase in walking cadence. RAS also produced changes in the pattern of cortical activation associated with mental imagery of walking. These results warrant further studies on the mechanism of action and impact of RAS on walking in individuals with MS.

Supported by: Cleveland Clinic Arts and Medicine Institute

Disclosure: François Bethoux; Acorda Therapeutics, Allergan (fee for non-CME services from commercial interests or their agents); Acorda Therapeutics, Merz Pharma, GW Pharma, Concert Pharmaceuticals, Innovative Neurotronics (consulting fees); Acorda Therapeutics, Merz Pharma, Innovative Neurotronics (grant/research support); Mark Lowe, Katherine König, Darlene K. Stough, Lisa Gallagher, Dwyer Conklyn: Nothing to disclose.

Keywords: Comprehensive care and MS, Management of activities of daily living in MS, Walking and MS

(RH16) AUTONOMY AND PARTICIPATION IN EXERCISE IN PEOPLE WITH MULTIPLE SCLEROSIS
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Background: Deconditioning of patients with multiple sclerosis (MS) has been shown before. Attitudes toward exercise are important in predicting change in behavior. Subjects were patients who sought treatment for MS, who consented to participate in a prospective study of exercise attitudes and behaviors. This abstract presents the initial results of the cohort at time of entry into the study. Objectives: This prospective cohort study was designed to assess the relationship between attitudes toward exercise and autonomy and physical measures of upper and lower body strength and exercise performed. Methods: Patients from an academic MS center completed two physical measures: grip strength dynamometry and the 2-Minute Walk Test (2MWT). They also completed the Guy’s Neurological Disability Scale (GNDS), the Impact on Participation and Autonomy Questionnaire (IPA), and the Multidimensional Outcome Expectations for Exercise Scale (MOEES) previously validated in the ambulatory MS population. A medical history relevant to MS was elicited, and in the second part of the study, the subjects completed an exercise diary for 2 weeks. Data were analyzed using IBM SPSS v21. Standard deviations and confidence intervals were reported. Results: 46 subjects (35 female) were recruited and enrolled. Mean GNDS score was 10.7 (7.1) for males and 12.1 (9.4) for females, which were not significantly different. Bivariate correlation analyses showed a significant relationship between GNDS and 2MWT (r = −0.425, P < .003); and between GNDS and presence of pain or spasticity (r = 0.452, P < .002; r = 0.541, P < .001). The IPA subscales showed significant correlations with average daily pain rating: Autonomy Indoors (AI) scale r = 0.450, Family Role (FR) scale r = 0.463, and Autonomy Outdoors (AO) scale r = 0.453, all with P values less than .01. Social Role (SR) scale and pain rating showed r = 0.365, P = .013. The MOEES scale data evaluated by principal components analysis showed excellent agreement with published 3-subscale factor model. The Self-Evaluative (SELF) subscale showed significant correlation with average daily pain rating (Kendall’s tau-b = 0.247, P = .036; Somer’s d = 0.247, P = .012). Grip dynamometry was left hand 30.9 kg (11.1) and right hand 32.1 kg (12.1). Regression model showed that right hand grip was predicted by MOEES SELF, fatigue, and gender, R = 0.731, adjusted R² = 0.463 (F = 7.46, P < .001). Conclusions: GNDS correlates well with walking distance and presence of pain or spasticity. Early analysis shows interesting relationships between MS patients’ perceived autonomy and daily pain score. MOEES questionnaire 3 subscales appear valid, and the SELF scale correlates with pain score as well as physical measure (grip). Interestingly, the use of assistive devices did not correlate with other measures. The second half of our study will evaluate the subjects’ pain diaries over time and determine any predictors of exercise quantity and frequency.

Supported by: Foundation of the CMSC

Disclosure: Nothing to disclose.

Keywords: Comprehensive care and MS, Management of activities of daily living in MS, Psychological issues and MS

(RH17) COMPARISON OF AN INTERMITTENT VERSUS CONTINUOUS WALKING PROGRAM IN PEOPLE WITH MULTIPLE SCLEROSIS USING THE 6-MINUTE WALK TEST: A RANDOMIZED CROSSOVER PILOT STUDY
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Background: Difficulty with gait is one of the most common complaints of people with multiple sclerosis (MS) and can be due to many causes, including neurogenic fatigue. Neurogenic fatigue is one of the most common MS symptoms and can prevent people with MS from walking longer dis...
tances, thus limiting their ability to improve gait endurance. Intermittent walking, a technique in which people take breaks during walking rather than walking continuously, may allow people with MS to walk longer distances due to less accrual of fatigue, and as a result allow for improvement of gait endurance. **Objectives:** The purpose of this pilot study was to examine whether a program of intermittent walking will result in a greater improvement in gait endurance in people with MS than a continuous walking program. **Methods:** A randomized crossover design was used. Subjects were randomized into intermittent (INT) and continuous (CONT) groups. All subjects performed a baseline 6-Minute Walk Test (6MWT), after which they followed a training regimen of eight 6-minute walks over a 4-week period, followed by a 6MWT posttest. Subjects in the INT group trained with 3-minute walks interspersed with 2-minute seated rests, while the CONT group trained 6 minutes continuously without taking any rests. Subjects then underwent a 4-week detraining period, followed by another 4-week walking period in which they performed whatever type of training they did not do originally, with 6MWTS again performed before and after the eight training bouts. To determine whether the subjects found one type of training more fatiguing than the other, a Visual Analogue Fatigue Scale (VAFS) was used to measure subjective perception of fatigue for both walking conditions.

**Results:** Nine subjects (6 female, 3 male, mean Expanded Disability Status Scale [EDSS] score 3.9) completed both training conditions. Intermittent training resulted in a significant \( F_{1,8} = 9.634, P < .015 \) improvement in 6MWT (mean 134.01 ± 183.7 feet) relative to continuous training, which resulted in a mean decrease of 59.2 ± 134.9 feet. Subjective perceptions of fatigue while walking were not significantly different for the two walking conditions. **Conclusions:** Despite the small sample size, intermittent gait training was clearly superior to continuous gait training in improving 6MWT performance. This suggests that gait endurance in MS may be better improved with gait training that emphasizes intermittent rests as opposed to walking continuously.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Comprehensive care and MS, Management of activities of daily living in MS, Neurorehabilitation

**RH18** WITHDRAWN

**RH19** EXERCISE TRAINING IMPROVES DEPRESSIVE SYMPTOMS IN PEOPLE WITH MULTIPLE SCLEROSIS: RESULTS OF A META-ANALYSIS

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**Background:** There is a high prevalence of depression and depressive symptoms in people with multiple sclerosis (MS), but these are untreated by conventional therapy. **Objectives:** We conducted a meta-analysis examining the effect of exercise training on depressive symptoms in MS. **Methods:** We searched PubMed for randomized controlled trials (RCTs) of exercise training and depression as an outcome in samples with MS. There were 12 RCTs that met inclusion criteria and provided enough data for effect size (ES) generation (Cohen’s d). An overall ES was calculated using a random effects model and expressed as Hedge’s g. **Results:** The weighted mean ES was small but statistically significant (Hedge’s g = 0.37; SE = 0.08; 95% confidence interval [CI], 0.20–0.53; z = 4.38; P < .001), indicating that the exercise training resulted in an improvement in depressive symptoms compared with control. The overall effect was not heterogeneous \( Q = 12.66, df = 11, P = .316, F = 13.07 \). **Conclusions:** The cumulative evidence indicates that exercise training can yield a small yet statistically significant and reliable reduction in depressive symptoms in people with MS.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Physical activity, Psychological issues and MS

**RH20** COMPARING EFFECTS OF DIFFERENT INTENSITIES OF ACUTE EXERCISE ON STATE ANXIETY IN MULTIPLE SCLEROSIS: A RANDOMIZED CONTROLLED STUDY

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**Background:** Previous research suggests a beneficial change in mood from before to after a single bout of exercise in multiple sclerosis (MS). However, there are limited data comparing the effects of different intensities of acute exercise with a true control condition (ie, sitting on the ergometer without cycling) on mood states in individuals with relapsing-remitting multiple sclerosis (RRMS). **Objectives:** The present study investigated the effect of acute exercise on state anxiety immediately and 1 hour after 10-minute bouts of moderate- and high-intensity cycling compared with a true control. **Methods:** The study used a complete within-subjects design. All participants (N = 16, mean age 51.58 years) had RRMS (Expanded Disability Status Scale [EDSS] score 1.5–4.5) and completed three conditions delivered in a randomized order with 1 week between conditions. The three conditions included 10 minutes of moderate (40% peak oxygen consumption) or high- (60% peak oxygen consumption) intensity cycle ergometry as well as a true control of sitting on the ergometer for 10 minutes. This was followed by 1 hour of seated rest in a comfortable chair located in the laboratory for documenting prolonged change in anxiety. Participants completed the abbreviated 6-item State Anxiety Inventory (SAI) immediately before and 1 hour after each condition. **Results:** Multivariate analysis of SAI scores indicated a statistically significant condition by time interaction \( (P < .05) \) on SAI scores. There was an immediate reduction in SAI scores after the two exercise conditions, but not the control condition. The reduction was sustained at 1 hour after completion of the high-intensity, but not the moderate-intensity, exercise condition. **Conclusions:** These findings suggest that acute bouts of exercise may be associated with reductions in state anxiety in people with RRMS, and the duration of these effects may depend on the intensity of exercise.

Supported by: NMMS (RG 4333A2/2)
Disclosure: Nothing to disclose
Keywords: Physical activity, Psychological issues and MS
(RH21) FALL RISK REDUCTION IN INDIVIDUALS WITH MULTIPLE SCLEROSIS: PILOT EXAMINATION OF EXERCISE AND EDUCATION

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Background: Falls are common in individuals with multiple sclerosis (MS) and are associated with adverse physical and psychological outcomes. The effectiveness of various fall risk reduction strategies for people with MS, however, is not clear. Objectives: To determine the effectiveness of three distinct, 12-week fall risk reduction programs specifically designed for individuals with MS: 1) a home-based exercise program targeting physiological risk factors; 2) an educational program targeting behavioral risk factors; and 3) a combined exercise and education program targeting both physiological and behavioral risk factors. Methods: 37 individuals with MS who had fallen in the last year participated in the study. Following baseline testing, participants were randomly assigned into one of four groups: wait-list control (CON; n = 9), home-based exercise (EX; n = 11), education (ED; n = 9), or combined exercise and education (EX + ED; n = 8). Participants underwent fall risk (Physiological Profile Assessment; PPA), balance (Berg Balance Scale; BBS), and walking (Timed 25-Foot Walk; T25FW) testing prior to and immediately following the 12-week intervention. They also self-reported information on the frequency of fall prevention behaviors (Falls Prevention Strategy Survey) and balance confidence (Activities-specific Balance Confidence scale). Each outcome measure was placed in an independent repeated-measures analysis of variance with group as the between-subject factor and time as the within-subject factor. Results: 34 participants (n = 8 CON; n = 10 EX; n = 8 ED; n = 8 EX + ED) completed postintervention testing. Overall, fall risk was found to decrease in both the EX and ED groups following the intervention (1.8 ± 1.1 vs. 1.3 ± 1.3; d = 0.4), while there was a small increase in fall risk in the other groups (1.2 ± 0.8 vs. 1.7 ± 1.1; d = 0.1). There was an overall increase in the utilization of fall prevention behaviors in all four groups following the intervention (11.7 ± 4.1 vs. 13.0 ± 4.3; d = 0.3), but no significant differences across groups. Following the intervention there was a significant decrease in balance confidence only in the education-only group (62.5 ± 11.3 vs. 34.9 ± 19.1; d = 1.65). There was no significant change in balance or walking following the intervention in any of the groups. Conclusions: The findings add to the knowledge base concerning the benefit of exercise and fall prevention education on fall risk among people with MS. Given their positive influence on physiological fall risk, the home-based exercise program in isolation and in combination with an education component warrant further investigation. Future studies involving larger sample sizes and a longer follow-up period investigating the relative benefits of exercise-only and exercise combined with education are indicated.

Supported by: National Multiple Sclerosis Society

Keywords: Management of activities of daily living in MS

(RH22) SENSORIMOTOR DELAYS ARE RELATED TO GAIT KINETICS IN PEOPLE WITH MULTIPLE SCLEROSIS

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Background: Gait and balance, critical elements in independent living and quality of life, are severely impaired in people with multiple sclerosis (MS). Gait analyses of people with MS reveal abnormalities in speed, stride length, cadence, double-support time, and swing time, as well as significantly altered joint kinetics. The causes of gait dysfunction in people with MS are complex and incompletely understood, but contributing factors may include slowed spinal somatosensory conduction and abnormal sensorimotor control. Objectives: The purpose of this study was to examine the relationship between neural control of muscle activation, as represented by sensorimotor delays, and gait mechanics in people with MS. Methods: Thirteen individuals with MS (mean age 45.8 ± 8.5 years, mean Expanded Disability Status Scale [EDSS] score 2.3 ± 1.3) participated. Gait kinematics and kinetics were measured bilaterally during overground walking at a self-selected pace. Next, sensorimotor delays were measured bilaterally with electromyography as subjects stood on a translating surface (6 cm at 15 cm/s). The sensorimotor delay was defined as the time, in milliseconds (ms), between the onset of the surface translation and the first detectable firing of either the tibialis anterior (response to forward translation) or the gastrocnemius (response to backward translation). Subjects performed three trials each of forward and backward translation. To examine the relationship between sensorimotor delays and joint kinetics (ankle plantarflexion moment and dorsiflexion moment during the stance phase), Spearman correlations were used. Results: Mean sensorimotor delay of the gastrocnemius was 143.6 ± 30.7 ms and of the tibialis anterior was 127.1 ± 27.4 ms. There was a significant relationship between the sensorimotor delay of the tibialis anterior and both the dorsiflexor (ρ = .29) or plantarflexor (ρ = .34) joint torque (p = .003) and the plantarflexor joint (ρ = .041, P = .031) during the stance phase. The sensorimotor delay of the gastrocnemius did not correlate with dorsiflexor (ρ = .0225, P = .29) or plantarflexor (ρ = .90, P = .65) torque. Conclusions: These results indicate that in people with MS, sensorimotor delays are strongly related to deficits in dorsiflexor and plantarflexor torque at the ankle during stance. These findings indicate that it is likely not only strength deficits of the muscles of the lower limbs that contribute to changes in gait kinetics in people with MS. Rather, delays in somatosensory feedback and motor responses in people with MS directly contribute to changes in gait kinetics.

Supported by: Frontiers grant UL1TR000001
Disclosure: Nothing to disclose
Keywords: Gait and balance
(RH23) PHYSICAL FITNESS ASSESSMENT ACROSS THE DISABILITY SPECTRUM IN MULTIPLE SCLEROSIS
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Background: Appropriate assessment of physical fitness (ie, aerobic capacity and muscular strength) is necessary to the design and evaluation of exercise training for those with multiple sclerosis (MS). One of the primary limitations in evaluating fitness across the disability spectrum is physical inaccessibility of traditional testing modes (eg, walking on a treadmill). Further, traditional tests lack sensitivity and accuracy in determining maximal physical capacity. This restricts the capacity for well-designed clinical trials of exercise training across the MS disability spectrum. Objectives: This study compared different methods of measuring cardiorespiratory (arm ergometer vs. recumbent stepper) and muscular (manual muscle testing [MMT] vs. seated dynamometry) fitness across the MS disability spectrum. Further, it examined the associations between fitness indices, measured by different testing modes, and clinical, functional, symptomatic, and participation measures. Methods: Participants completed two testing sessions separated by 1 week. At each session, participants completed one cardiorespiratory and one muscular fitness test. A clinically administered Expanded Disability Status Scale (EDSS) was conducted at the first session. Participants also completed measures of walking speed and endurance, cognition, fatigue, quality of life (QOL), activities of daily living (ADL), and physical activity. Results: 64 participants completed testing and were grouped as mild (EDSS 1–3.5; n = 21), moderate (EDSS 4–6; n = 22), and severe (EDSS 6.5–8; n = 21). Peak aerobic capacity assessed by recumbent stepping was higher when compared with arm ergometry (P < .001). Peak torque assessed by seated dynamometry was higher when compared with MMT (P < .001). Peak aerobic capacity and peak torque decreased as a function of increasing disability (P < .001). Significant, moderate-to-strong correlations were observed between physical fitness and EDSS score, walking speed and endurance, cognition, fatigue, QOL, and ADL for all aerobic and strength testing modes. Conclusions: Overall, maximal physical capacity was higher when assessed by recumbent stepping and seated dynamometry and decreased as a function of increasing disability. This suggests that the prescription of exercise training in MS should be based on more sophisticated testing modes to provide the most appropriate stimulus for training adaptations. There continues to be an important association between physical fitness and other outcomes in MS, regardless of assessment modality.

Supported by: National Multiple Sclerosis Society, National Institute of Neurological Disorders and Stroke (NS054050)

Keywords: Fitness assessment in MS

(RH24) PHYSICAL ACTIVITY INTERVENTION IMPROVES BODY COMPOSITION IN MULTIPLE SCLEROSIS: PRELIMINARY EVIDENCE FROM A RANDOMIZED CONTROLLED TRIAL
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Background: There is increasing interest in body composition in people with multiple sclerosis (MS), and there is evidence that those with MS have an unhealthy body composition profile. This can increase the risk of secondary disease consequences, such as bone fractures and comorbid health conditions. Physical inactivity is a modifiable risk factor for an unhealthy body composition profile. Consequently, increasing physical activity might favorably affect bone health and body composition in people with MS. Objectives: To examine the efficacy of a physical activity behavioral intervention for improving outcomes of body composition in people with MS. Methods: We conducted a 6-month randomized controlled trial (RCT) that examined the efficacy of an Internet-delivered physical activity behavioral intervention for improving outcomes of body composition, including whole body bone mineral content (BMC), bone mineral density (BMD), and soft-tissue composition, in 82 ambulatory individuals with MS. Participants were randomly assigned to the intervention (n = 41) or wait-list control (n = 41) condition using a computer-generated random numbers sequence. Results: 35 intervention and 37 control participants completed the study. There was a significant effect of the intervention on whole body BMC (P = .04, partial-η² = 0.06) and BMD (P = .01, partial-η² = 0.09). The effect of the intervention on fat mass (P = .05, partial-η² = 0.06) and percent body fat (P = .09, partial-η² = 0.04) approached significance. There was not a significant effect on whole body lean soft tissue (P = .28, partial-η² = 0.02) or body-mass index (BMI; P = .86, partial-η² < 0.001). Conclusions: Our results provide preliminary evidence that an Internet-delivered lifestyle physical activity intervention improves bone health, and to some extent body composition, in people with MS. Such findings are important considering the status of physical activity as a modifiable behavior and the potential long-term benefits in the prevention and management of fracture risk and comorbidities among those with MS.

Supported by: National Multiple Sclerosis Society

Keywords: Body composition in MS

(RH25) THE ROLE OF THE REGISTERED DIETITIAN AND OCCUPATIONAL THERAPIST IN IMPROVING QUALITY OF LIFE IN THOSE WITH MULTIPLE SCLEROSIS
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The Central Alberta Multiple Sclerosis Clinic offers an inte-
grated interdisciplinary approach to multiple sclerosis (MS) care in an outpatient setting. It aims to provide the necessary services in order to empower people affected by MS to achieve optimal levels of quality of life. The team of neurologists, nurses, registered dietitian, occupational therapist, and social worker serves approximately 700 clients in Central Alberta living with MS, their family members, caregivers, and other health-care professionals. The registered dietitian (RD) and occupational therapist (OT) provide specialized services for the Central Alberta MS Clinic. Along with guidance regarding general healthy eating, the RD in the MS clinic setting provides education on fatigue management, appetite changes, weight control, supplementation and complementary medicine, bowel and bladder management, safe swallowing, and bone health. The OT provides suggestions and recommends devices in order to improve the clients’ functioning in activities of daily living. On an annual basis, the Central Alberta MS Clinic mails a client questionnaire to collect data on the current health concerns and severity of symptoms of its clients. These data provide insight into the unique needs and symptom presentation of individuals with MS and enable the interdisciplinary team to implement appropriate therapeutic strategies in symptom management. As per a random selection of 100 clients in the Central Alberta MS Clinic, approximately 67% report fatigue as a concern. Together, the RD and OT focus on improving dietary patterns and energy conservation, with a goal to improve fatigue. The RD provides information on menu planning, easy meal preparation, and efficient grocery shopping techniques, along with aiding the client in meeting goals for proper blood sugar management, hydration, and weight control. Through the combined effort of the RD in helping the client consume a well-balanced diet and OT in providing guidance on healthy sleep techniques, assistive equipment, and technological strategies, this interdisciplinary team aims to improve the quality of life of MS clients with fatigue. The goal of this retrospective review was to determine whether the needs of the clients were met by collaborating with the RD and OT. MS clients seen by the RD and OT together for fatigue management indicated that their fatigue level improved through implementation of the combined strategies suggested by these health-care providers. Other areas of review were weight control, bowel management, supplementation and complementary medicine, swallowing, and general healthy eating. Random chart reviews were completed in each of these areas, and results showed that quality of life of MS clients improved with RD intervention. This review demonstrates that RDs in clinics similar to the Central Alberta MS Clinic can improve quality of life in MS clients and that the combined efforts of the RD and OT can improve fatigue in MS clients.

Supported by: Lori Boothby, RN, MA, Manager, Medical Specialty Clinic, Red Deer, Alberta, Canada

Disclosure: Nothing to disclose

Keywords: Comprehensive care and MS, Management of activities of daily living in MS, Registered dietitian

(RH26) EFFECTS OF COOLING DURING EXERCISE ON BALANCE PERFORMANCE IN PEOPLE WITH MULTIPLE SCLEROSIS

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Background: Thermosensitivity limits physical performance in multiple sclerosis (MS), preventing patients from engaging in rehabilitation programs of sufficient intensity to result in meaningful improvements. If MS thermosensitivity could be decreased, patients could engage in more vigorous rehabilitation programs, and potentially achieve greater improvements in mobility. Objectives: The purpose of this study was to examine the effects of cooling on exercise-induced thermosensitivity in people with MS by measuring post-exercise balance performance in cooled and uncooled conditions. We hypothesized that cooling during exercise would improve post-exercise balance. If our hypothesis was correct, it would suggest that cooling may lead to improved balance training and performance in people with MS. Methods: A randomized crossover design was used. Fourteen subjects were randomized into either cooled (C) or uncooled (UC) groups. Balance was assessed for all subjects using the Berg Balance Scale (BBS). All subjects then received a thermal lode via performance of 10 minutes of cycling ergometry in either a C or UC condition. Cooling was achieved via use of a cooling vest. One week later, subjects crossed over, performing the cycling in whatever condition they did not perform previously, with the BBS again done before and after. BBS scores were then compared for the two conditions. Results: Mean BBS scores showed nonsignificant increases in the cooled condition (50.0–50.7) and nonsignificant decreases in the uncooled condition (50.6–49.7) (P > .2568), suggesting that balance improved slightly following the cooled condition and worsened slightly following the uncooled condition. The small trend toward improvement that was seen in post-exercise balance performance with use of the cooling vest during moderate exercise may point to a functionally important mitigation of fatigue-related balance deficits in people with MS. It is possible that more significant results could have been obtained with an outcome measure of greater sensitivity. Conclusions: Cooling may result in improved balance performance in MS by limiting the effects of thermosensitivity. However, more sensitive tests may be required to clearly demonstrate this effect.

Supported by: None


Keywords: Management of activities of daily living in MS, Mobility

(RH27) THE SAFETY OF EXERCISE TRAINING IN MULTIPLE SCLEROSIS: A SYSTEMATIC REVIEW

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Background: There are many reviews documenting the benefits of exercise training in people with multiple sclerosis (MS). We are unaware of any review that summarizes risks of relapse and adverse events (AEs) associated with exercise training, yet this is critical for informing decisions and recommendations regarding the safety of this behavior. Objectives: We conducted a systematic review of relapse and AEs
reported in randomized controlled trials (RCTs) of exercise training in MS. **Methods:** We searched electronic databases for RCTs of exercise training in MS. We calculated the rate of relapse and AEs, and the relative risk of relapse and AEs for exercise training versus control. **Results:** 27 studies with 1330 participants were included. We determined that the rate of relapse was 6.0% and 4.5% for control and exercise, respectively. The rate of AEs was 1.1% and 1.9% for control and exercise, respectively. The relative risk of relapse was 0.75, whereas the relative risk of AEs for exercise training was 1.73. **Conclusions:** Exercise training was not associated with an increased risk of relapse, and risk of AEs was not higher than in healthy populations. This evidence should alleviate uncertainty regarding the safety of exercise training in MS.

**Supported by:** None

**Disclosure:** Matthew E. Platta, Lara A. Pilutti, Amy E. Latimer-Chelfeng; Nothing to disclose. Robert W. Mall: Biogen Idec, Acorda Therapeutics, National Multiple Sclerosis Society, National Institutes of Health, Consortium of Multiple Sclerosis Centers (multiple sources).  

**Keywords:** Exercise safety

**RH28** PHYSICAL TELEREHABILITATION IN MULTIPLE SCLEROSIS: A QUALITATIVE INQUIRY

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**Background:** Physical telerehabilitation can potentially facilitate home-based exercise and patient self-care. However, successful implementation of such systems depends on integrating patient needs, values, and preferences into the system design. **Objectives:** The goal of this study was to identify telerehabilitation acceptance, attitudes, and preferences in patients with multiple sclerosis (MS) who used a physical telerehabilitation system for 6 weeks. **Methods:** At the baseline visit information was collected that included sociodemographics, disease history, and psychological and behavioral profiles. A Home Automated Telerehabilitation (HAT) system was used by patients at home for 6 weeks. HAT included pre-exercise symptom diary, individualized tailored exercise plan prescribed by a licensed physical therapist after a full clinical evaluation, daily exercise progress log, exercise videos with instructions on how to properly perform each exercise, structured education, and two-way communication with the study team. At the 6-week follow-up, patients completed an attitudinal survey measuring their attitudes and acceptance of the telerehabilitation system, which was followed by a semistructured qualitative interview aimed at identifying patient values, needs, and preferences. **Results:** Despite varying levels of previous exercise and computer experience, nearly all participants expressed high interest in and dedication to continued use of the program. Patients felt safer knowing that they were monitored by the system at home: “The major benefit of using this system is that it monitors me and my symptoms daily.” Patients also reported that using the system helped with remembering to exercise correctly and on time: “The system also helps with my memory because you have to remember to log in and do the exercises because you are being held accountable, it becomes part of your routine.” Major additions to the system requested by the patients included adding voiceover to the pre-exercise diary questions, adding a question about level of motivation to exercise daily, and making the program more challenging. **Conclusions:** All patients were comfortable with the intensity and frequency of exercises prescribed, as well as using a computer at home to exercise at their own pace throughout the day. Addressing needs, values, and preferences of MS patients can facilitate their use and further acceptance of physical telerehabilitation systems for exercise and self-care.

**Supported by:** VA RR&D Merit Review grant, MS Center of Excellence-East.

**Disclosure:** Nothing to disclose.

**Keywords:** Telerehabilitation

**RH29** VALIDATING A COMMUNITY-BASED MEASURE OF LEG USE FOR MULTIPLE SCLEROSIS

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**Background:** Impaired mobility is a cardinal disability for multiple sclerosis (MS). Of particular significance is how well patients with MS actually engage in walking and other uses of the lower extremities in life situations. Although existing community-based assessments of lower-extremity use reflect walking capacity or spontaneous walking for people with MS, many other common lower-extremity activities are excluded (eg, exiting a car or shower, standing from a toilet). An alternate structured interview developed by our laboratory may more comprehensively assess lower-extremity use as well as complement the other community-based assessments, and thus may improve assessment of the extent of lower-extremity disability in MS. The Lower Extremity Motor Activity Log (LE-MAL) consists of three subscales. The Functional Performance subscale asks respondents to rate the quality of their lower-extremity use on 14 different activities on a scale of 0 to 10. The other two subscales evaluate confidence and orthotics/assistance in the same manner. The final score is the average from the three subscales. **Objectives:** 1) Assess the convergent validity of the LE-MAL with the MS Walking Scale–12 (MSWS-12) among people with disabled walking as a result of MS. 2) Assess the test-retest reliability of the LE-MAL among the same individuals. **Methods:** 16 adults aged 36 to 71 years with recently stable relapsing-remitting or progressive MS and self-reported walking disability (PDSS range 1–6, mean 4.3) were administered the LE-MAL and the MSWS-12 by telephone. Within 2 to 4 weeks, the LE-MAL was readministered. **Results:** The LE-MAL was highly correlated with the MSWS-12 (r = 0.83, P < .001) and demonstrated excellent test-retest reliability (r = 0.99, P < .001). **Conclusions:** The LE-MAL has convergent validity with the MSWS-12 over a wide range of walking abilities and is reliable. It is sensitive to real-world lower-extremity use for a wider range of activities important to people with MS than other scales. The LE-MAL may add value to clinical and research programs concerning lower-extremity disability in people with MS.
(RH30) THE MODIFIED TRIATHLON FOR PEOPLE WITH MULTIPLE SCLEROSIS
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Background: For people living with multiple sclerosis (MS), opportunities to participate in exercise and fitness activities are limited. Some of the limitation comes from the disease itself. Much of the limitation comes from the fact that most exercise and fitness programs and events are not modified for people with mobility limitations. Therefore, even if someone with MS had the motivation to participate or compete, the uncertainty of being able to perform and keep up with people without mobility limitations would be daunting. While there are thousands of triathlons for people without mobility limitations to choose from, there have not been any triathlons specific to and modified for people with MS. This abstract will address one way to modify a triathlon for people with MS, with the goals being to provide a safe setting for people with MS to be active and to generate motivation to become and/or stay active. Teaching Points: People living with MS can participate in a triathlon with the right modifications. The modifications made for the “MS Modified Triathlon” in Minnesota on November 17, 2013, are outlined:

Swim: The swim portion of the event was held at a local fitness center. The swim consisted of a 30-minute swim with continuous running time. Participants were able to rest as needed. Participants were able to use life preservers, floating devices, fins, kickboards, or any other assistance needed to complete the event. The pool did not have a deep end, which was an advantage for those with a fear of swimming/ floating. These participants did a combination of swimming and pool walking. There were volunteers to help in the locker rooms both before and after the swim portion in order to assist with changing as well as save the participant’s energy for the actual event.

Bike: The bike portion of the event was held at the clinic where the author treats patients. It consisted of a 30-minute bike with continuous running time. Participants were able to rest as needed. Stationary recumbent bikes were used. The bike event was done indoors. Upper-extremity bikes (UEBs) were also available for participants with extreme leg weakness or spasticity.

Run/Walk: The run (modified to be run or walk) portion of the event was held at the clinic where the author treats patients. The run/walk consisted of a 30-minute run/walk with continuous running time. Participants were able to rest as needed. The run/walk was done indoors on treadmills. Three of the treadmills had the ability to provide body weight support for participants with balance/LE concerns.

Summary: A modified triathlon is an innovative way to help people with MS stay motivated and active in a safe setting. It is also an effective way to support and empower people with MS to stay healthy and active.

Supported by: MS Research Council
Disclosure: Acorda (fees for non-CME services from commercial interests or their agents), STEP Physical Therapy (ownership interest)
Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS, MS and the caregiver/family

(RH31) THE ROLE OF VISUAL FEEDBACK IN MOVEMENT CONTROL IN INDIVIDUALS WITH MULTIPLE SCLEROSIS
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Background: In individuals with multiple sclerosis (MS), upper-extremity motor impairments, including intention tremor, can arise around the endpoint of a movement; when endpoint accuracy is not emphasized, tremor is reduced. We previously examined tremor using a series of continuous, compensatory tracking tasks. Our results suggest that individuals with MS exhibit significant changes in sensory feedback (lengthened visual delay) and prediction mechanisms (inaccurate estimation of visual delay and limb dynamics) when stabilizing the hand about an endpoint. Objectives: Use a continuous pursuit tracking task to examine whether previous results can be extended to a task where trajectory, and not endpoint accuracy, is emphasized. Methods: Seven subjects with MS (aged 25–68 years, 5 women, 6 right-handed) and seven control subjects (aged 25–61 years, 5 women, 7 right-handed) completed several continuous compensatory and pursuit tracking tasks (0–10 Hz, band-limited white noise). During the tasks, subjects used a 1-D robotic manipulandum controlled by flexion/extension of the right elbow to control a cursor on a computer monitor. Subjects were asked to visually track a target by placing the cursor on the target as quickly and accurately as possible. Subjects’ performance was fit to a dual-feedback model of sensorimotor control to characterize differences in control between tasks. Results: During pursuit tracking, MS subjects exhibited a frequency response that was consistent with that of control subjects. However, visual gains for MS subjects were significantly lower during pursuit (vs. compensatory) tracking, and lower than the visual gains of control subjects for both tasks (controls: 0.45 ± 0.20 vs. 0.67 ± 0.24 [t6 = 1.95, P = .071]; MS: 0.11 ± 0.15 vs. 0.40 ± 0.24 [t6 = −2.70, P = .036]). In MS subjects who exhibited tremor on the day of testing (N = 4), mismatches between actual and internal estimates of inertia (t6 = −4.90, P = .0163) and viscosity (t6 = −4.73, P = .0178) were also significantly lower during pursuit tracking. Mismatches in stiffness did not decrease in pursuit tracking (t6 = −1.23, P = .31); however, the correlation with tremor severity observed during compensatory tracking was not present. Control subjects had no significant mismatches (P > .05). Conclusions: Results suggest that subjects with MS take advantage of the reduced need for visual feedback during pursuit tracking and reduce tremor by significantly down-weighting visual gain. The task dependence of the mismatch between actual and predicted limb inertia, viscosity, and stiffness argues against a central impairment. This is consistent with simulations suggesting that mismatches in limb dynamics can be compensatory in the presence of a delay mismatch. Together, these results support the interpretation that an inability to compensate for increased visual feedback delays may be the primary cause of intention tremor in people with MS.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Tremor

International Journal of MS Care
(RH32) FALL RATES AMONG PEOPLE WITH MULTIPLE SCLEROSIS AND HEALTHY CONTROLS: A COMPARATIVE STUDY
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Background: Falls are common among people with multiple sclerosis (MS), but healthy people also fall. It is not known if the rate of falls among people with MS is different from that among healthy individuals of similar age and gender.
Objectives: To compare the rates of falls over 6 months between people with MS and age-matched healthy controls.
Methods: 58 people with MS and 58 age-matched healthy controls prospectively counted their falls for 6 months using fall calendars. Time to first fall and time to recurrent falls (second fall) were ascertained from the fall calendars. Time to these events was operationalized as the number of days enrolled in the study prior to the event. A Cox proportional hazards model was used to test whether time to first fall and time to recurrent falls were significantly different between people with MS and healthy controls after adjusting for age.
Results: 52 people with MS and 49 controls completed all assessments and were included in this analysis. Their mean age was 39.7 (MS) and 38.7 (controls) years, and the median Expanded Disability Status Scale (EDSS) score for those with MS was 3 (range, 0–6). 71% of people with MS and 41% of healthy controls reported at least one fall, and 48.1% of people with MS and 18.4% of healthy controls reported recurrent falls. The hazard rate for the time to first fall (HR, 1.87; P = .027) and time to recurrent falls (HR, 3.00; P = .0042) were significantly different between people with MS and healthy controls, after controlling for age.
Conclusions: People with MS are at higher risk for falling sooner, and having recurrent falls sooner, than healthy people of the same age. Further study is required to compare the underlying physiological and environmental risk factors that predispose people with MS to fall more than people without MS.
Supported by: Department of Veterans Affairs
Disclosure: Michelle H. Cameron: Acorda Therapeutics (consulting fees, grant research support); Rajarshi Mazumder, Charles Murchison: Nothing to disclose.
Keywords: Accidental falls, Comprehensive care and MS, Management of activities of daily living in MS

(RH33) IDENTIFYING THE NATURE AND EXTENT OF POST-RELAPSE REHABILITATION SERVICES UTILIZATION IN MULTIPLE SCLEROSIS
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Background: Approximately 90% of people with multiple sclerosis (MS) experience periodic and unpredictable relapses as part of their disease course. A relapse is typically accompanied by new or worsening symptoms that can have a significant effect on individuals’ health and quality of life. Relapses are commonly treated by steroids. Steroids may reduce the acute inflammation, but they do not address the challenges of managing symptoms and disabilities accompanied by relapses. Up to 58% of individuals report a measurable and sustained effect of relapses on disability. Studies suggest that rehabilitation can play a significant role in managing health and quality of life of people with MS. Yet, current evidence does not paint a clear picture as to what types of rehabilitation services are used or if rehabilitation services are being utilized post-relapse to enhance recovery.
Objectives: To evaluate the feasibility of supervised multidirectional reactive stepping training to improve mobility in individuals with MS.
Methods: Cross-sectional study using convenience sampling that engages individuals with MS in a telephone survey. We are surveying a total of 138 adults in North America (50% in the United States and 50% in Canada) who experienced at least one relapse 6 months prior to their interview. Multiple recruitment methods are being used: 1) direct invitations mailed to selected individuals from the North American Research Committee on Multiple Sclerosis and the participating MS clinics in Canada; 2) study advertisements posted on the National Multiple Sclerosis Society’s and MS Society of Canada’s websites. Interested individuals are asked to call the research office in Canada using a toll-free number. Participants are asked to answer a series of questions about their most recent relapse, recovery process, and post-relapse rehabilitation services that they used or attempted to use to manage the relapse. The survey development was informed by the findings from our recent qualitative study on post-relapse management.
Conclusions: The newly gathered data will help us better understand the types of rehabilitation services that people with MS use or consider for managing relapses. The information may be useful for improving future MS care to help individuals with MS recover from relapses.
Supported by: CMSC
Disclosure: Nothing to disclose
Keywords: Rehabilitation, Relapse, Residual disability

(RH34) A NOVEL APPROACH TO IMPROVE MOBILITY MEASURES BY USING MULTIDIRECTIONAL REACTIVE STEPPING IN INDIVIDUALS WITH MULTIPLE SCLEROSIS—A PILOT STUDY
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Background: Individuals with multiple sclerosis (MS) commonly experience mobility limitations that pose a serious challenge to achieving independent living. Rehabilitation approaches to improve mobility in individuals with MS are limited. Objectives: To evaluate the feasibility of supervised multidirectional reactive stepping training to improve mobility in individuals with MS.
Methods: Three individuals with relapsing-remitting MS (mean age, 54.6 ± 4 years; mean Expanded Disability Status Scale score, 3 ± 0.5) participated in training (30 minutes/session on 3 days/week for 4 weeks) focused on multidirectional reactive stepping. Each session consisted of three 10-minute training sets separated by 2 minutes of rest. The subjects stood in a central position and were asked to step as quickly as...
Subjects pedaled on a cycle ergometer at 60% of their individual maximal workload for as long as possible while core temperature (Tc, CorTemp ingestible pills), skin temperature (Ts, thermocouples), electrocardiography (ECG), blood pressure, and heart rate were measured continuously. Before and after the cycling in the environmental chamber, the subjects were monitored in a 70°F room for approximately 1 hour. Perceived physical and cognitive fatigue were assessed during exercise and recovery using a 10-cm visual analogue scale. **Results:** Exercise duration increased for all conditions compared to No Cooling (NC) (PC: 30.3 ± 12.6 min, 23%; ALC: 29.2 ± 12.9 min, 19%; CDE: 29.1 ± 13.7 min, 18%). Perceived physical and cognitive fatigue significantly increased from before to after exercise for all conditions, with ALC having the least change. Tc increased the least amount during exercise for PC (0.58°C) and most for CDE (0.76°C) \( (P < .05) \). Tc continued to increase after the end of exercise for all conditions, ranging from 10 min (PC) to 4 min (CDE) \( (P < .05) \). After 1 hour of recovery, 56% of CDE subjects had returned to baseline Tc, while only 25% of ALC had \( (P < .05) \). Total Ts was the lowest for CDE after exercise \( (30.1 \pm 0.9 \, ^\circ C) \), while ALC was the highest \( (31.6 \pm 0.8 \, ^\circ C) \). After 1 hour of recovery, 80% of the CDE had returned to baseline Ts, while only 14% to 17% had for the other conditions. For all conditions except CDE, subjects had their highest Ts during recovery. **Conclusions:** MS patients exercised longest after PC; however, the most beneficial cooling condition was CDE. During CDE, the subjects exercised longer than NC, and Ts and Ts recovered more rapidly than for any other condition. This result may assist in guiding health-care professionals when making recommendations to their MS patients about exercising in hot environments.

**Supported by:** National Institute on Disability and Rehabilitation Research (grant H133G050198)

**Disclosure:** Nothing to disclose

**Keywords:** Exercise, Care and skin temperatures, Fatigue

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(RH35) **COOLING STRATEGIES FOR IMPROVING PERFORMANCE AND RECOVERY FROM EXERCISE AND REDUCING FATIGUE IN INDIVIDUALS WITH MULTIPLE SCLEROSIS**

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**Background:** The incidence of heat sensitivity is 60% to 80% in multiple sclerosis (MS). A common complaint associated with increased heat stress (core and skin temperatures) is the early onset of fatigue. Also, the sweat response may be reduced in MS. Therefore, strategies to reduce heat production and improve heat dissipation, and consequently reduce fatigue during activity, are needed. **Objectives:** The objective of this study was to examine the effects of Pre-Cooling (PC), Ad Lib Cooling (ALC), and Cooling During Exercise (CDE) on core and skin temperatures, and subsequent exercise performance and fatigue, as compared to No Cooling (NC) in MS patients. **Methods:** Forty-five MS patients (79% female, 91% relapsing-remitting, mean age 50.1 ± 8.3 years, mean Expanded Disability Status Scale [EDSS] score 1.4 ± 1.2, mean years since diagnosis 11.5 ± 8.1) participated. All subjects were tested under four conditions (PC, ALC, CDE, and NC) in an environmental chamber set at 80°F and 50% humidity. The order of conditions was randomly assigned and tests were conducted once a week for 4 weeks to ensure complete recovery from fatigue between conditions. Subjects pedaled on a cycle ergometer at 60% of their individual maximal workload for as long as possible while core temperature (Tc, CorTemp ingestible pills), skin temperature (Ts, thermocouples), electrocardiography (ECG), blood pressure, and heart rate were measured continuously. Before and after the cycling in the environmental chamber, the subjects were monitored in a 70°F room for approximately 1 hour. Perceived physical and cognitive fatigue were assessed during exercise and recovery using a 10-cm visual analogue scale. **Results:** Exercise duration increased for all conditions compared to No Cooling (NC) (PC: 30.3 ± 12.6 min, 23%; ALC: 29.2 ± 12.9 min, 19%; CDE: 29.1 ± 13.7 min, 18%). Perceived physical and cognitive fatigue significantly increased from before to after exercise for all conditions, with ALC having the least change. Tc increased the least amount during exercise for PC (0.58°C) and most for CDE (0.76°C) \( (P < .05) \). Tc continued to increase after the end of exercise for all conditions, ranging from 10 min (PC) to 4 min (CDE) \( (P < .05) \). After 1 hour of recovery, 56% of CDE subjects had returned to baseline Tc, while only 25% of ALC had \( (P < .05) \). Total Ts was the lowest for CDE after exercise \( (30.1 \pm 0.9 \, ^\circ C) \), while ALC was the highest \( (31.6 \pm 0.8 \, ^\circ C) \). After 1 hour of recovery, 80% of the CDE had returned to baseline Ts, while only 14% to 17% had for the other conditions. For all conditions except CDE, subjects had their highest Ts during recovery. **Conclusions:** MS patients exercised longest after PC; however, the most beneficial cooling condition was CDE. During CDE, the subjects exercised longer than NC, and Ts and Ts recovered more rapidly than for any other condition. This result may assist in guiding health-care professionals when making recommendations to their MS patients about exercising in hot environments.

**Supported by:** National Institute on Disability and Rehabilitation Research (grant H133G050198)

**Disclosure:** Nothing to disclose

**Keywords:** Exercise, Care and skin temperatures, Fatigue

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(RH36) **TWELVE WEEKS OF ANTIFATIGUING AEROBIC EXERCISE LEADS TO INCREASED EXERCISE DURATION IN INDIVIDUALS WITH MULTIPLE SCLEROSIS**

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**Background:** Aerobic exercise is typically recommended for multiple sclerosis (MS) patients. However, the amount of heat generated during this type of activity can be significant and result in the early onset of fatigue. **Objectives:** The objective of this study was to determine the effects of 12 weeks of antifatiguing aerobic exercise during exercise performance with cooling versus no cooling in MS patients. **Methods:** Forty-five MS patients (79% female, 91% relapsing-remitting, mean age 50.1 ± 8.3 years, mean Expanded Disability Status Scale [EDSS] score 1.4 ± 1.2, mean years since diagnosis 11.5 ± 8.1) participated. Subjects were randomly assigned to one of three groups: exercise + cooling \( (E + C, n = 12) \), exercise with no cooling \( (E + C, n = 12) \), exercise with no cooling \( (E + C, n = 12) \), exercise with no cooling (ENC, n = 13), or control \( (C, n = 19) \). Before and after the 12-week intervention, all subjects performed a maximal graded exercise test (GXT) in a 70°F room and then, on another day, cycled at 60% of their individual maximal workload for as long as possible in an environmental chamber set at 80°F with 50%
humidity. Core (Tc) and skin (Ts) temperatures, blood pressure, and heart rate were measured continuously. During these tests, the subjects were not cooled. For those randomized to the 12 weeks of antifatiguing aerobic cycling, E + C subjects wore a passive cooling vest during each training session, while ENC subjects did not. C subjects did not do any training. The intermittent cycling program (cycles of 2, 4, or 6 min of pedaling followed by 2 min of rest for 1 hour, 3 times/week) used progressive intensities of 40%, 60%, 80%, and 100% of each person’s maximal workload over the 12 weeks. Perceived physical and cognitive fatigue were assessed during exercise and recovery using a 10-cm visual analogue scale. Results: Overall, the maximal exercise duration significantly increased by 41% for the exercisers (23.7 ± 8.7 to 33.4 ± 9.8 min) (P < .05) and decreased by 6% in controls (23.5 ± 12.0 to 22.1 ± 15.0 min). Each exercise group had significant increases in duration, with the ENC group increasing by 57% (22.3 ± 10.8 to 35.0 ± 8.7 min) and the E + C group increasing by 29% (24.8 ± 7.0 to 32.0 ± 11.0 min) (P < .05). VO2max increased by 10% for ENC and 2% for E + C, but decreased by 3% for C. Maximal workload increased by 32% for ENC and 28% for E + C, but decreased by 5% for C. There was no change in perceived fatigue. Tc for the exercisers, on the posttest, did not increase proportionally to the increase in their work capacity. Conclusions: Both exercise groups (ENC and E + C) achieved a higher work capacity, while Tc and perceived fatigue were the same after 12 weeks of antifatiguing aerobic exercise. ENC had better improvements than E + C, while C either stayed the same or declined. These data indicate an adaptation to exercise training and exercise in the heat.

Supported by: National Institute on Disability and Rehabilitation Research (grant H133G050198)

Disclosure: Nothing to disclose

Keywords: Aerobic exercise, Cooling, Fatigue

(RH37) THE SIX SPOT STEP TEST: EVALUATING THE BENEFITS OF AN UNDERSTUDIED AMBULATION TEST IN MULTIPLE SCLEROSIS

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Background: The Six Spot Step Test (SSST) is a quantitative test of ambulation with components of coordination, dynamic balance, and lower-limb function in individuals with multiple sclerosis (MS). The SSST has unique characteristics that are not replicated in other tests; it requires individuals to stop and start while ambulating, shift weight, and kick weighted objects from six “spot” targets. The SSST is clinically feasible because it is easy to systematically administer and requires only a small amount of space to perform. The SSST was initially validated with the Timed 25-Foot Walk (T25FW) and found to have less of a floor effect than the T25FW, but its relationship to clinical walking measures that include turning and longer distances has not been examined. Objectives: To explore the relationship and potential concurrent validity of the SSST with the Timed Up and Go (TUG) and the 2-Minute Walk Test (2MWT) in MS. Methods: Sixteen individuals with relapsing-remitting MS (average age, 51.2 ± 9.5 years; symptom duration, 14 ± 9.7 years; Expanded Disability Status Scale [EDSS] score, 3.9 ± 1.4; 9 females, 7 males) participated in the study. In a single session, individuals performed the TUG, T25FW, 2MWT, and ZenoMat gait assessment. Pearson correlation coefficients were used to assess statistical significance. Results: The SSST is strongly related to both the TUG (r = 0.7518) and 2MWT (r = 0.8051) and less so to the T25FW (r = 0.6991). The TUG includes a functional transfer (sit-to-stand) and turning, while the 2MWT includes turning and walking endurance. Both of these tests require more challenging and real-world elements than walking alone, as on the T25FW. Conclusions: The SSST demonstrates concurrent validity with both the TUG and the 2MWT in our cohort of individuals with MS. The SSST captures an important element of MS disability by examining walking in a more comprehensive manner than the other three walking tests. Furthermore, the SSST requires minimal training to administer and may be a time-efficient measure of real-life functional activities that would be useful in large clinical trials. The SSST may be a relevant alternative to the TUG and 2MWT in outcome measure assessment for individuals with MS. These data are part of a larger study, and data collection is ongoing; future analyses will examine the relationship of the SSST to falls and spatiotemporal measures of walking.

Supported by: National Multiple Sclerosis Society


Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS, Rehabilitation outcome measures

(RH38) FOUR-YEAR EVALUATION OF A MULTIPLE SCLEROSIS EDUCATIONAL TRACK FOR PHYSICAL THERAPY STUDENTS

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Background: The Multiple Sclerosis Standardized Training and Education Program with University Partners (MS STEP UP) is a collaboration between the University of North Carolina (UNC) Doctorate of Physical Therapy (DPT) program and the Greater Carolinas Chapter of the National Multiple Sclerosis Society, with the goal to educate and mentor DPT students to become MS-Certified Specialists (MSCS). Objectives: The purpose of this study was to evaluate the outcomes of the first four cohorts of students to complete MS STEP UP. Methods: Students applied for selection to MS STEP UP in their first year of the DPT program at UNC. The 2-year educational track, conducted concurrently with the second and third year of the DPT curriculum, included didactic instruction, clinical experiences, service, and involvement with MS organizations. Scholars were encouraged to tailor class assignments and capstone projects to focus on MS-related topics. Volunteer clinical experiences allowed the students to observe MS-specialized physical therapists and neurologists. Scholars regularly participated in community opportunities including National Multiple Sclerosis Society events, board meetings, fundraisers, and self-help groups. The primary outcome used...
to evaluate the educational track was the MS Competencies Rating Scale (MSCRS), which was completed by each scholar before they started MS STEP UP and at the end of the first and second years. The activities of the scholars were also recorded in an Activity Tracking Form throughout the program. **Results:** Since 2008, eight DPT students have completed MS STEP UP; four of the first six have obtained theMSCS certification. On average, MSCRS ratings changed from a pre-program Likert scale rating of “below average” to an end-program rating of “above average” in most domains, indicating improved student competencies in MS-specific knowledge and skills at the completion of the 2-year program. **Conclusions:** MS STEP UP improves the clinical skills and knowledge of DPT students and adequately prepares graduates to become certified specialists in MS. MS patient care will most likely benefit from the national expansion of MS STEP UP among DPT programs. Future research should evaluate the effects of specialized training for therapists and students on patient outcomes.

**Supported by:** None

**Disclosure:** Nothing to disclose

**Keywords:** Physical therapy, Rehabilitation, Multiple sclerosis

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**(RH40) DALFAMPRIDINE UTILIZATION AND EFFICACY ASSESSMENT IN CLINICAL PRACTICE**

Sylvia Klineova, Rebecca G. Farber, Joshua Friedman, Colleen Farrell, Christine Hannigan, Fred D. Lublin, Stephen Krieger

**Background:** A comprehensive physical therapy evaluation was performed on each individual. Intervention was chosen based on the patient’s impairments in addition to gait deficits. The gait interventions included lower-extremity orthoses, assistive devices, and neuromuscular electrical stimulation. All patients also received an individualized home-based exercise and walking program. **Results:** Spatiotemporal gait measurement (GAITRite), 6-Minute Walk Test, and video observational gait analysis were used to assess the impact of the interventions. Each of the case examples described exhibited improvements in the above measures. **Conclusions:** Through the application of the described combination of interventions, the patients discussed had excellent outcomes related to their gait. Thus, these patients were able to continue with safe community mobility, engage in their life roles, and have improved quality of life.

**Supported by:** None

**Disclosure:** Sylvia Klineova, Rebecca G. Farber, Joshua Friedman, Colleen Farrell, Christine Hannigan: Nothing to disclose. Fred D. Lublin: Teva (consulting fees).

**Keywords:** Comprehensive care and MS, Gait training, Management of activities of daily living in MS

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**(RH39) A MULTIFACETED, TASK-SPECIFIC APPROACH FOR SUCCESSFUL GAIT INTERVENTION IN MULTIPLE SCLEROSIS**

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**Background:** Gait dysfunction has been referred to as the most visible feature of multiple sclerosis (MS). It appears that individuals with MS who also have gait impairments initially present with weakness primarily affecting distal muscles. This primary weakness may lead to faulty biomechanics over time, thus causing secondary impairments and further gait dysfunction. Mobility is vital to patients’ quality of life, overall health, and life roles. There is no consensus on the best gait intervention for this population. The interventions chosen in these cases were based on evidence-based principles of task-specific training stressing maximal repetitions, appropriate gait mechanics, and functional skills both in the clinic and at home. We selected three patients from the University of Texas Southwestern Gait Disorders Clinic to represent the various innovative strategies that are typically utilized to achieve meaningful functional outcomes for this patient population. **Objectives:** To highlight three innovative strategies for optimizing gait outcomes in people with MS. **Methods:** A comprehensive physical therapy evaluation was performed on each individual. Intervention was chosen based on the patient’s impairments in addition to gait deficits. The gait interventions included lower-extremity orthoses, assistive devices, and neuromuscular electrical stimulation. All patients also received an individualized home-based exercise and walking program. **Results:** Through the application of the described combination of interventions, the patients discussed had excellent outcomes related to their gait. Thus, these patients were able to continue with safe community mobility, engage in their life roles, and have improved quality of life.

**Supported by:** None

**Disclosure:** Melanie F. Farrar, Staci Shearin: Nothing to disclose. Diana W. Logan: Teva (consulting fees).

**Keywords:** Comprehensive care and MS, Gait training, Management of activities of daily living in MS
Acorda Therapeutics, Inc., Biogen Idec, Novartis Pharmaceuticals Corp, Teva Neuroscience, Inc., Genzyme, Sanofi, Celgene, National Institutes of Health, National Multiple Sclerosis Society (grant/research support); Bayer HealthCare Pharmaceuticals, Biogen Idec, EMD Serono, Inc., Novartis, Teva Neuroscience, Actelion, Sanofi-Aventis, Acorda, Questcor, Roche, Genentech, Celgene, Johnson & Johnson, Resalio, Coronado Bioscience, Genzyme, MedImmune, Bristol-Myers Squibb, Xenoport, ReceptoRx, Forward Pharma (consulting fees); Cognition Pharmaceuticals, Inc. (current financial interests/stock ownership); Multiple Sclerosis and Related Diseases (co-chief editor). Stephen Krieger: Acorda Therapeutics, Bayer HealthCare, Biogen Idec, Genzyme, Questcor, Teva Neuroscience (consulting fees); Bayer HealthCare (grant/research support); Teva Neurosciences (fees for non-CME services from commercial interests or their agents).

Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS, Management of activities of daily living in MS

(RH41) TURNING TIME AND VELOCITY ARE ASSOCIATED WITH BALANCE CONFIDENCE AND SELF-PERCEIVED WALKING LIMITATION IN MULTIPLE SCLEROSIS
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Background: People with multiple sclerosis (MS) frequently report difficulty turning and transitioning between seated and standing positions. Rehabilitation strategies can target these impairments to improve mobility and independence, and prevent falls and injury. Objectives: People with MS with greater self-perceived impairments of balance and walking demonstrate more impairment in postural transitions that incorporate turning. Methods: 50 individuals with MS (mean age 47.3 ± 10.3, 40 female, 10 male) and mild-to-moderate clinical disability (Expanded Disability Status Scale [EDSS] score 0–4, median 2.5) completed three trials of a 7-m Timed Up and Go (TUG) test while wearing opaque body-worn motion sensors (APDM®, Portland, OR). The TUG is a standardized clinical scale of functional mobility that includes turning and postural transitions. Mobility Lab software (APDM®, Portland, OR) measured TUG total duration and postural transition parameters during sit-to-stand, turning, and turn-to-sit. The Activities-specific Balance Confidence Scale (ABC) and 12-item Multiple Sclerosis Walking Scale (MSWS-12) assessed balance confidence and self-perceived limitations in walking. Spearman rho correlations assessed associations between postural transition parameters to the ABC and MSWS-12.

Results: Balance confidence on the ABC decreased with longer turning duration, turn-to-sit duration (r = −0.49, r = −0.51; both P < .001), and lower peak turning velocity and peak turn-to-sit velocity (r = 0.49, r = 0.58; both P < .001). Greater self-perceived walking limitation on the MSWS-12 was associated with longer turning duration (r = 0.36, P = .01), longer turn-to-sit duration (r = 0.53, P < .001), lower turning velocity (r = −0.38, P < .01), and lower turn-to-sit velocity (r = −0.59, P < .001). Stand-to-sit duration and peak sit-to-stand velocity were not significantly associated with the balance confidence [ABC: 1 r < 0.19] or self-perceived walking limitation (MSWS-12: 1 r < 0.19). People with MS with moderate disability took longer to complete the TUG (18.4 ± 4.1 seconds vs. 15.9 ± 2.3 seconds; P = .02). Turning duration (2.73 ± 0.49 seconds vs. 3.20 ± 0.79 seconds; P = .01), peak turning velocity (144.3 ± 30.0 °/s vs. 129.8 ± 27.4 °/s; P = .05), and turn-to-sit duration (3.53 ± 0.38 seconds vs. 4.18 ± 0.91 seconds; P = .02) differed between mild and moderate disability groups.

Conclusions: People with MS with more impaired turning duration and velocity described more difficulties with balance and walking. Transitioning from seated to standing was not associated with balance and walking problems. Patients with EDSS scores of 2.5 to 4.0 demonstrated greater turning impairments compared to the 0 to 2.0 group. Further studies should determine whether a rehabilitation approach targeting turning in MS could result in improved balance confidence, decreased walking limitations, fewer falls, and increased independence.

Supported by: National Multiple Sclerosis Society

Keywords: Gait and balance

(RH42) EFFECTS OF AQUATIC EXERCISES ON MOBILITY FUNCTION AND QUALITY OF LIFE IN INDIVIDUALS WITH MULTIPLE SCLEROSIS: A RANDOMIZED CONTROLLED TRIAL
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Background: Aquatic exercises have been recommended for individuals with multiple sclerosis (MS). Despite the growing practice of aquatic exercise and trend toward evidence-based practice, limited research has been conducted on the effects of aquatic exercises in individuals with MS. Objectives: The purpose of this study was to examine the effects of a 10-week aquatic training program on mobility function, strength, fatigue, and quality of life in individuals with MS. Methods: This study was a single-blind, randomized controlled trial. The participants were 20 subjects with chronic MS recruited through a community-based support group. Participants were randomly assigned to an exercise group (n = 10) or a control group (n = 10). The training program for the exercise group consisted of a 10-week group aquatic exercise regimen including strength, balance, walking, and aerobic training. Participants were assessed 1 week before and after participation in the study by a blind investigator. The outcome measures were self-paced Ten-Meter Walk Test (10MWTT), Timed Up and Go test (TUG), Berg Balance Scale (BBS), grip strength measured by a handheld dynamometer, Modified Fatigue Impact Scale (MFIS), quality of life using the 36-item Short Form Health Status Survey (SF-36), and a satisfaction survey. An intention-to-treat analysis was used.

Results: All subjects completed the study with no MS-related exacerbations reported. Baseline characteristics between the groups were similar for all variables (P > .05). Participants in the exercise program exhibited better overall scores on walking speed, balance, grip strength, fatigue, and qual-
ity of life than participants in the control group. The exercise group significantly improved (P < .05) compared to the control group on TUG, BBS, grip strength, MFIS, and SF-36. A majority of participants expressed excellent satisfaction with the program. Conclusions: The results of this study suggest that an aquatic training program may be an effective intervention strategy for improving mobility function and quality of life in individuals with MS. To our knowledge, this is the first randomized controlled trial that examined the effects of aquatic exercises for individuals with MS. Our results suggest that a 10-week aquatic training program can improve balance, strength, fatigue, and quality of life in people with MS. Aquatic training holds promise as an effective treatment strategy to minimize detrimental effects and maximize function in people with MS.

Disclosure: Nothing to disclose

Keywords: Rehabilitation

(RH43) SYSTEMATIC REVIEW AND EVIDENCE-BASED CLINICAL RECOMMENDATION FOR AQUATIC EXERCISES FOR INDIVIDUALS WITH MULTIPLE SCLEROSIS

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Background: The use of aquatic training for individuals with multiple sclerosis (MS) has received attention in recent years. Although there is a limited number of studies examining the effects of aquatic exercises for individuals with MS, those that have been conducted consistently demonstrate positive outcomes. However, no review has been performed synthesizing research findings for individuals with MS.

Objectives: The purpose of this review was to examine the evidence concerning the effectiveness of aquatic exercises in individuals with MS. Safety concerns, potential benefits, and practical application are discussed.

Methods: In this systematic review, we identified 11 studies that met the selection criteria, which included a total of 141 participants with MS. Electronic databases and hand searches were undertaken to locate studies published in English. The databases searched included PubMed, PsychINFO, CINAHL, OVID, PEDro, and ProQuest. The keywords searched were multiple sclerosis, aquatic, and hydrotherapy. The initial search resulted in retrieval of a total of 83 potential articles. We screened those articles for duplication and selection criteria.

Results: A total of 11 studies examining the effectiveness of aquatic exercises for individuals with MS were identified. Of the 11 studies, 3 were randomized controlled trials, 5 had a single-subject design, and 3 were case studies. Across all studies, a total of 141 individuals with MS were investigated. The sample size for each published report ranged from 1 to 22 participants. All of the identified studies (100%) reported that aquatic training resulted in positive outcomes. Research on the effects of aquatic training for individuals with MS suggests that aquatic training is effective for improving flexibility and range of motion, cardiovascular endurance, fatigue level, muscle strength, mobility function (including gait and balance), quality of life, and psychological well-being. None of the studies identified any exacerbation or reported adverse change in neurologic status.

Conclusions: To our knowledge, this is the first systematic review to examine the effects of aquatic exercise for individuals with MS. There is a limited number of studies examining the effectiveness of aquatic exercises in MS. The results from all the studies indicate that individuals with MS benefit from aquatic training to improve physical function and enhance quality of life. Although the number of studies evaluating the effectiveness of aquatic exercise for individuals with MS is limited, those studies consistently demonstrate positive outcomes. There is a need for more studies with longer-term follow-up to determine whether any gains are retained over the long term.

Disclosure: Nothing to disclose

(RH44) PERSPECTIVES OF PHYSICAL ACTIVITY IN PEOPLE WITH MULTIPLE SCLEROSIS WHO ARE WHEELCHAIR USERS: INFORMING THE DESIGN OF FUTURE INTERVENTIONS

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Background: It has been established that physical activity and exercise offer many benefits to those with multiple sclerosis (MS) who have minimal disability. However, limited research has been conducted to examine the impact on individuals with advanced MS who use a wheelchair. To inform the design and delivery of physical activity and exercise interventions in this segment of the MS population, qualitative inquiry is needed.

Objectives: To explore the meanings, motivations, and barriers related to physical activity and exercise in wheelchair users with MS.

Methods: Fifteen wheelchair users with MS were evaluated. Clinical status (MS type and years since diagnosis) and demographic variables (age, sex, and ethnicity) were established using surveys. Individual semistructured interviews lasted approximately 45 minutes and concentrated on the meanings, motivations, and barriers related to physical activity and exercise. Interviews were audiorecorded and transcribed verbatim, and thematic analysis was performed on the data by two researchers.

Results: Participants represented a typical sample of people with advanced MS. Three interrelated subthemes emerged: 1) meanings of physical activity and exercise, 2) benefits of physical activity and exercise, and 3) barriers and facilitators to exercise. Many participants acknowledged differences between physical activity and exercise, and further acknowledged physical and psychological benefits from both, including improvement in fatigue, strength, mobility, and everyday function alongside improved self-control and mood. Common barriers to physical activity and exercise were symptoms, internal motivations, the environment, and professional input. Results suggest that participants would be more likely to increase their physical activity and exercise levels if interventional facilitators were incorporated, including symptom-appropriate physical activity and exercise, behavioral management strategies, use of appropriate environments, and good professional guidance.

Conclusions: Clinicians and researchers designing physical activity and exercise interventions for those with advanced MS must develop interventions that are symptom-appropriate, inclusive of behavioral change strategies, undertaken in appropriate environments, and delivered through appropriate professional interaction.
**Background:** Few case reports have highlighted neuromyelitis optica (NMO) involving the entire spinal cord. Moreover, NMO has been described as a central nervous system (CNS) disease, without evidence to date of peripheral nervous system (PNS) involvement. The effect of immunosuppression on NMO severity has not been well studied.**Methods:** We report a renal transplant patient who developed severe, rapidly progressive aquaporin 4 antibody (AQP4 Ab)–negative, clinically definite NMO resulting in quadriparesis and blindness. Subsequent peripheral involvement was suggested by nerve conduction studies (NCS).**Results:** A 51-year-old Hispanic woman who had undergone renal transplant 1 year previously and was on a tapering dose of tacrolimus, with a history of optic neuritis, presented with sudden-onset lower-extremity numbness. Symptoms progressed to complete paraplegia and sensory loss over 24 hours. The following day, she developed weakness and numbness in both upper extremities, at the T3–T4 sensory level, and complete vision loss. Cerebrospinal fluid analysis revealed elevated protein with neutrophilic pleocytosis. Magnetic resonance imaging (MRI) showed T2 hypointensity involving the entire spine and pre-chiasmatic optic nerves. Serum AQP4 Ab was negative. High-dose methylprednisolone and plasmapheresis were initiated. Subsequently, four weekly cycles of rituximab therapy were administered. At discharge, the patient had significant improvement in muscle strength and sensation in the upper extremities. However, she had persistent paraplegia despite repeat MRI showing near-complete resolution of lesions. NCS revealed severe reduction in compound motor action potential amplitudes with denervation bilaterally on needle examination, most obvious in the lower extremities. Discharge AQP4 Ab was again negative.**Conclusions:** The clinical spectrum of NMO may be wider than previously thought. Further studies are needed to assess PNS involvement in fulminant presentations of NMO and the effect of immunocompromised state on disease severity.

**Disclosure:** Nothing to disclose

**Keywords:** Disease-modifying treatments in MS, Glial biology, Neuromyelitis optica

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**Background:** Internuclear ophthalmoplegia results in the slowing, limitation, or loss of ability to adduct one eye associated with nystagmus in the abducting eye and is caused by a lesion in the medial longitudinal fasciculus. While history is crucial (age, acuteness of onset, comorbidities), brain magnetic resonance imaging (MRI) is the diagnostic test of choice for determining the underlying cause. An increasing number of patients who present with neurologic problems and can benefit from the diagnostic power of MRI have implanted cardiac pacemakers.**Objectives:** To demonstrate the possibility of performing MRI in selected patients with implanted cardiac pacemakers.**Methods:** A 39-year-old woman who had been diagnosed with intracranial dural arteriovenous fistula and neurocysticercosis presented with sudden-onset vertigo, diplopia, and bilateral internuclear ophthalmoplegia. A vascular etiology was suspected because of the acuteness of onset and her prior history, but MRI could not be initially performed to assess this because she had a cardiac pacemaker. After collaboration with colleagues from the cardiology and radiology departments, brain MRI revealed the correct diagnosis.**Results:** Brain MRI showed a pattern characteristic of inflammatory demyelination.**Conclusions:** Many neurologists assume that having a cardiac pacemaker is an absolute contraindication to performing MRI. Here, we demonstrate that MRI can be performed in a selected group of patients with cardiac pacemakers when the information obtained from MRI would change the clinical management.

**Disclosure:** Nothing to disclose

**Keywords:** Magnetic resonance imaging

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**Background:** Vitamin D levels are associated with multiple sclerosis (MS) disease risk and severity clinically and radiographically. Retinal nerve fiber layer (RNFL) thickness, as measured by optical coherence tomography (OCT), also correlates with MS disease severity. It is not clear whether vitamin D might influence retinal and optic nerve changes in MS patients.**Objectives:** We sought to determine whether vitamin D levels are associated with retinal structure in MS patients, hypothesizing a neuroprotective role for higher levels.**Methods:** We conducted a retrospective review of spectral-domain OCT findings from our MS population in 53 patients (104 eyes) at various stages of disease (mean duration, 9.7 years; 79% relapsing-remitting MS). 15% of eyes had a history of optic neuritis; none had alternative ocular pathology. Serum vitamin 25(OH)-D levels and spectral-domain OCT testing were conducted within 6 months of each other. OCT measures included total macular and ganglion cell layer volume and peripapillary RNFL thickness.**Results:** None of the OCT measures correlated with vitamin D levels. There were nonsignificant trends toward lower tissue volumes with higher vitamin D levels, in contrast to our hypothesis. These findings were similar in the larger subgroup without a history of optic neuritis.**Conclusions:** We did not iden-
tify an association between measures of retinal ganglion cell axonal or somatic integrity and random vitamin D levels in an unselected cohort of MS patients. However, vitamin D values may vary significantly over short intervals, especially with supplementation. Given the evidence of vitamin D’s role in MS, a prospective study of changes in retinal structure over time with frequent monitoring of levels would be optimal.

Supported by: None

Disclosure: Bijal Mehta: Biogen (consulting fees), Fawzi Abukhalil, Thong D. Pham, Farah Villanueva, Celina Hayashi, Mark J. Morrow: Nothing to disclose.

Keywords: Epidemiology of MS, Imaging and MS, Optical coherence tomography

(SC04) VITAMIN A (RETINOIC ACID) IN MULTIPLE SCLEROSIS: AVOIDING THE MISTAKES MADE WITH VITAMIN D

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Background: This study will determine whether higher vitamin A levels and normal vitamin D levels in conjunction with interferon beta or glatiramer acetate disease-modifying therapy treatments are associated with decreased multiple sclerosis (MS) severity at 3 years. As the normal range for vitamin A levels is between 30 and 95 μg/dL, it is not clear whether lower levels are just as good as the higher range. Previous studies in other diseases separated patients based on their vitamin A levels into 3 to 5 categories (less than 29, 30–50, 51–70, 71–95, greater than 95). It is expected that patients’ levels do not fluctuate significantly from year to year and tend to remain within one group. Methods: We will measure the vitamin A levels every 3 months to determine whether there was a change in the levels such that the patient has moved from their previous quintile group. We will also measure retinol binding protein and serum beta-carotene levels, as these influence the vitamin A level and prior studies utilized these measures. By measuring all three of these, we will be able to better determine which marker of vitamin A status is best for future studies. Annually, we will take an average of the vitamin A levels and assign to a quintile group. Inclusion criteria will include relapsing-remitting (RRMS) disease type with variable severity (we can further divide these into Expanded Disability Status Scale [EDSS] score groups of 1–3, 3.5–5.5, 6–7.5, and ≥8). A previous study demonstrated that EDSS changes in more severe RRMS (EDSS ≥4) patients had a greater change in rank in a 5-year period but also greater than 2 years. Because our patient population has an average EDSS score in the slightly higher ranges (EDSS 4–6), it is ideal for a study of 3 years’ duration. Additionally, these patients must have a normal vitamin D level at the start of the study; if their level is low, they will be treated with vitamin D. Demographic data will be collected for patients with RRMS who are taking or have started on either glatiramer acetate or an interferon beta. Qualifying patients will be followed for a total of 3 years (with annual review of the data). In addition to following severity (EDSS score), we will record annualized relapse rate, magnetic resonance imaging (MRI) data, and results of an MRI study known as magnetization transfer (MTR), which has been used to determine remyelination in MS patients. This will provide data regarding the rate of remyelination in the MS patients in the various quintile groups of vitamin A. Vitamin A has been shown to improve myelination in the experimental autoimmune encephalomyelitis (EAE) model. Results: We expect to present preliminary results. Conclusions: It is not known whether remyelination is greater and progression is slower in the higher vitamin A level groups.

Supported by: None

Disclosure: Biogen (consulting fees)

Keywords: CNS repair, Imaging and MS, Immunology and MS

(SC05) AUTOIMMUNE LIMBIC ENCEPHALITIS AND ADULT-ONSET TYPE 1 DIABETES CAUSED BY ANTI-GAD65 ANTIBODIES

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Background: The glutamic acid decarboxylase enzyme is present in high concentrations in both the brain and pancreatic islet beta cells. Antibodies to GAD65 have been implicated in the pathogenesis of type 1 diabetes and limbic encephalitis with temporal lobe epilepsy; however, these diseases rarely present concurrently. Objectives: We intend to present a rare case of anti-glutamic acid decarboxylase (GAD65) antibody-mediated autoimmune limbic encephalitis with temporal lobe epilepsy in which the patient later developed type 1 diabetes. Methods: We performed a thorough chart review of a 49-year-old man with hypothyroidism who presented with new-onset complex partial seizures and subsequently developed adult-onset type 1 diabetes. Results: The patient’s complex partial seizures were described as a arising “adrenaline rush” followed by a stereotyped memory of song lyrics. Intercital neurologic examination was nonfocal, whereas the ictal examination revealed acalculia despite his profession as a mathematics teacher. Post-ictal examination revealed amnesia of ictal events. Electroencephalography (EEG) revealed interictal bitemporal slowing within the theta range and ictal rhythmic theta originating from the left anterior temporal lobe. Brain magnetic resonance imaging (MRI) revealed gadolinium enhancement of the left mesiotemporal lobe with corresponding hypometabolism on interictal FDG positron emission tomography. Computed tomography with contrast of the chest, abdomen, and pelvis did not reveal an underlying malignancy. Serologic work-up including rheumatologic markers and a paraneoplastic panel were unremarkable; however, anti-GAD65 antibody titers were elevated at a level of 1:4800. Complex partial seizures were refractory to levetiracetam, carbamazepine, phenytoin, and valproic acid. The patient’s seizure frequency improved only while receiving high-dose intravenous methylprednisolone but later increased to more than ten daily after the course was completed. Concurrently, the patient’s random blood glucose levels were noted to be greater than 500 mg/dL and he required insulin for glycemic control. Hyperglycemic episodes occurred prior to steroid administration and were attributed to the onset of type 1 diabetes. Conclusions: In rare situations, anti-GAD65 antibodies can cause adult-onset temporal lobe epilepsy secondary to an autoimmune, non-paraneoplastic limbic encephalitis as well as adult-onset type 1 diabetes. Anti-GAD65 antibody titers should be evaluated in patients presenting with adult-onset temporal lobe epilepsy or type 1 diabetes.

Supported by: None

Disclosure: Nothing to disclose

Keywords: Autoimmune encephalitis, Immunology and MS
(SC06) THE EFFECTS OF ANTIOXIDANT SUPPLEMENTS ON PROGRESSION OF MULTIPLE SCLEROSIS: A SYSTEMATIC REVIEW OF HUMAN AND ANIMAL STUDIES FOR CLINICIANS AND PATIENTS

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Background: Naturally occurring compounds that have antioxidant and anti-inflammatory effects, found in over-the-counter supplements and certain plants and foods, are becoming of interest to researchers, clinicians, and patients as a treatment for multiple sclerosis (MS). We undertook this study as part of the MS Society of Canada endMS Research and Training Network to review potentially important findings in studies involving patients and animal models of MS in order to develop evidence-based clinician and patient information. Objectives: To develop an easy-to-read evidence-based informational pamphlet describing antioxidant dietary interventions in the treatment of MS disease progression for patients and clinicians. Methods: With the assistance of a librarian with experience in systematic reviews, and using predefined search criteria, we searched PubMed, CINAHL, PsycINFO, the Cochrane Library, and the Central Register of Controlled Clinical Trials, including all years up to October 30, 2013 (English language only). Reference lists of included articles were hand-searched and all titles were scrutinized by two authors against inclusion/exclusion criteria. Clinical studies were included if the participants had MS or the biological products tested were from people with MS. Animal studies were included if a disease similar to MS was induced in animals and included behavioral or relevant histological findings, such as remyelination. In order to synthesize findings, we required a minimum of three studies testing a specific compound of interest. Findings were assessed for risk-of-bias using published tools; data were synthesized, written in plain language format, and pretested among people with MS. Results: 3507 titles were retrieved examining the effects of naturally occurring compounds in MS patients and in models of MS. 965 abstracts were reviewed, and the findings of 145 manuscripts analyzed. Final compounds for which data were synthesized included α-lipoic acid, antioxidant vitamins, gingko biloba, quercetin, resveratrol, and epigallocatechin-3-gallate. Specific results and final clinician/patient information for each compound will be discussed. Conclusions: Although researchers stress the need for knowledge translation (especially to patients), most systematic reviews are designed for other scientists. We used the systematic review methodology to successfully develop easy-to-understand yet scientifically sound information for patients and clinicians in the popular field of antioxidant supplements.

Supported by: endMS Research and Training Network, MS Society of Canada
Disclosure: Nothing to disclose
Keywords: Antioxidants, Complementary/alternative therapies in MS

(SC07) CLINICAL CHARACTERISTICS AND IMAGING FEATURES OF LATE-ONSET MULTIPLE SCLEROSIS
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Background: Multiple sclerosis (MS) is an inflammatory, demyelinating disorder of the central nervous system (CNS) mostly affecting young adults between 18 and 45 years of age. The onset of MS in patients older than 50 years of age, so-called late-onset multiple sclerosis (LOMS), is no longer unheard of, occurring in 2.7% to 12% of patients, but the literature describing this entity is limited. Objectives: To describe the clinical characteristics and imaging features of LOMS. Methods: We retrospectively reviewed our MS database and selected patients with new-onset MS at age 50 or older. Clinical presentation, magnetic resonance imaging (MRI) features, treatment, and clinical evolution were evaluated. Results: We had 50 patients who were diagnosed as developing definitive MS after age 50, representing 7% of the MS patients seen in our clinic. We identified two distinct groups based on the clinical picture: G1, characterized by a relapsing-remitting course, and G2, characterized by a progressive illness. Forty-one patients were included in G1: 30 women and 11 men, with a mean age of 55. G2 had 9 patients: 7 women and 2 men, with a mean age of 53.6. Gait difficulties were common in both groups and present in 80% of patients in G1 and all patients in G2. Motor deficits and a higher Expanded Disability Status Scale (EDSS) score on initial examination were significantly more frequent in G2 (P = .003, P < .0001). Even though the findings were not statistically significant, G2 patients had higher odds of cognitive impairment [OR, 6.33; 95% confidence interval (CI), 1.03-38.96] and more difficulties with coordination [OR, 3.61; 95% CI, 0.51-25.76] than G1 patients, while G1 patients had 2.2 times the odds of having sensory abnormalities (95% CI, 0.49-9.63). No statistically significant difference was found for MRI measures between the two groups, including the presence of supra and infratentorial lesions, spinal cord involvement, contrast enhancement, and cerebral atrophy. However, the odds of infratentorial [OR, 1.93; 95% CI, 0.44-8.46] and spinal cord involvement [cervical spine: OR, 2.93; 95% CI, 0.33-26.23; thoracic spine: OR, 2.10; 95% CI, 0.46-9.64] were higher in G1 and G2, respectively. Ninety percent of patients in G1 were treated with a disease-modifying agent, as compared with 78% in G2 (OR, 2.64; 95% CI, 0.40-17.31). The average follow-up was 4.5 years for G1 and 3.6 years for G2, with a nonsignificant mean change in EDSS between the two groups (P = .65). Conclusions: In our MS center, 7% of patients presented with LOMS. Contrary to the literature, 82% of our patients had a relapsing-remitting course, and the remaining 18% had a progressive illness. Gait difficulties were common in both groups, with motor deficits and higher EDSS score significantly more common in patients with progressive disease. The MRI findings and clinical evolution were not significantly different between the two groups over the time period studied.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Natural history of MS
(SC08) MIGHT MISDIAGNOSIS OF MULTIPLE SCLEROSIS COMPROMISE OUTCOMES OF CLINICAL TRIALS?
Collin F. Mulcahy,1 Jerry S. Wolinsky,1 on behalf of the CombiRx investigators1,2
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Background: Multiple sclerosis (MS) is a neurologic disorder characterized by inflammatory demyelination and abnormal neurologic function. Magnetic resonance imaging (MRI) is the imaging technique of choice and provides an essential component of modern diagnosis of MS (the McDonald criteria). These guidelines have been periodically revised. Objectives: This study was designed to categorize and quantify lesion patterns in patients enrolled in a phase 3 clinical drug trial for MS. We suspected that patients with atypical lesion patterns upon entry into the trial might have different on-study outcomes than those with more typical MRI findings. Methods: MRI scans from 1008 randomized patients were reviewed and processed in the UT MRI Analysis Center. Lesions were categorized and counted, and any “special features” were noted. “Typical” versus “atypical” lesion patterns were identified. Scans were categorized by 2005 and 2010 McDonald criteria. Multiple on-study MRI and behavior comparisons were considered, including binary gadolinium (Gd) enhancement, burden of disease (BOD), clinical activity–free status (CAFS), combined unique activity (CUA), disease activity–free status (DAFS), protocol-defined exacerbations (PDE), and clinical progression (PROG). Results: Significant differences were found when comparing 2005 and 2010 McDonald criteria patients with binary Gd enhancement, BOD, and CUA. 2005 criteria patients also had a significant difference in DAFS. Significant differences appeared when comparing typical versus atypical pattern presentation with 2005 and 2010 McDonald criteria, binary Gd enhancement, BOD, CUA, and DAFS. Differences were not found when PDE and PROG were considered. Conclusions: Having Gd enhancements and a higher BOD at baseline corresponded with meeting both 2005 and 2010 McDonald criteria more often. Thus, more stringent entry criteria may ensure more on-study events, a finding consistent with analysis of an earlier independent trial [Barkhof F, et al. Ann Neurol. 2003;53:718]. This was also evident when evaluating comparisons between the 2005 and 2010 McDonald criteria. However, having more MRI features at study entry did not correspond with differences in on-study clinical events. In addition, having more MRI features considered as typical of MS at study entry corresponded with more on-study activity in the face of partially effective treatments. It did not correspond with differences in on-study clinically defined events. The presence of typical MRI lesion patterns met both 2005 and 2010 McDonald criteria more often, had Gd enhancements, and had a higher BOD at baseline. These results suggest that although patients with atypical lesion patterns sometimes showed baseline or on-study MRI activity, they did not show any difference in clinical disease progression.

Supported by: Foundation of the CMSC, Teva (Neuroscience Research Scholar)
Disclosure: Collin F. Mulcahy: Foundation of the Consortium of Multiple Sclerosis Centers, Teva (grant/research support). Jerry S. Wolinsky, on behalf of the CombiRx investigators: Nothing to disclose.

Keywords: Imaging and MS, Lesion patterns in MS

(Sc09) TRANSFER OF KV1.3 DEFICIENT T CELLS WITH STABLE REGULATORY PROPERTIES AMELIORATES EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS IN A MANNER THAT IS PARTIALLY DEPENDENT ON INTERLEUKIN-2
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Background: Kv1.3 is a voltage gated potassium channel known to be expressed on myelin-reactive T cells of patients with multiple sclerosis (MS). Deletion of Kv1.3 in T cells protects mice from experimental autoimmune encephalomyelitis (EAE), a murine model of MS. Characterization of T cells from Kv1.3−/− mice identified a unique population of Th cells with regulatory properties that were not dependent on the expression of Foxp3. Antigenic stimulation of Kv1.3−/− CD4+ T cells results in upregulation of CD25 and CTLA4, and increased pSTAT5, FoxO1, and GATA1 expression. Objectives: To determine the stability of the Kv1.3−/− cell phenotype and to evaluate therapeutic potential of these cells in EAE. Methods: To address the stability of this phenotype, we polarized Kv1.3−/− and WT T cells to Th1, Th2, Th17, and Treg subsets and measured IFNy, GATA3, IL17, Foxp3, FoxO1, and GATA1 expression using flow cytometry or western blotting. To test whether Kv1.3−/− T cells could ameliorate EAE, they were stimulated in vitro and transferred into WT mice that were immunized to induce EAE. Behavioral scores and Foxp3 expression in host T cells were evaluated. Interleukin-2 (IL-2) was evaluated by ELISA to determine its importance for Kv1.3−/− cell mediated suppression. IL-2 was inhibited by anti-IL-2 in vitro, and CD25, pSTAT5, FoxO1, and cytokine expression were evaluated by flow cytometry, ELISA, and western blotting. T cells treated with anti-IL-2 were also transferred into WT mice that were immunized for EAE and monitored daily. Results: Kv1.3−/− T cells that were polarized to various subsets secreted less IFNy and IL-17, whereas GATA3 and Foxp3 were unchanged compared to WT cells. Th1, Th2, and Treg subsets of Kv1.3−/− T cells maintained increased expression of GATA1 and FoxO1. Mice that received Kv1.3−/− T cells were protected from EAE compared to mice that received WT T cells, and this suppression was not due to increased endogenous Foxp3+ Tregs. Kv1.3−/− T cells produced more IL-2 than WT T cells. Blockade of IL-2 resulted in decreased CD25 and pSTAT5 expression in Kv1.3−/− T cells while FoxO1 expression was not decreased. IL-4 and IL-10 production was decreased when IL-2 was inhibited, but IFNy and IL-17 production remained low in Kv1.3−/− T cells. Mice receiving cells cultured with anti-IL-2 were partially protected against EAE. Conclusions: Herein we demonstrate that Kv1.3 KO CD4+ T cells maintain a stable phenotype in the face of strong inflammatory signals and suppress EAE in WT animals, and this effect is partially dependent on increased IL-2 signaling, highlighting the therapeutic potential for this novel subset of regulatory T cells.

Supported by: Foundation of the CMSC, Teva (Neuroscience Research Scholar)
Disclosure: Collin F. Mulcahy: Foundation of the Consortium of Multiple Sclerosis Centers, Teva (grant/research support). Jerry S. Wolinsky, on behalf of the CombiRx investigators: Nothing to disclose.

Keywords: Imaging and MS, Lesion patterns in MS
**SC10** EVALUATING THE OUTCOMES OF FAT GRAFTING FOR LIPOTROPHY DEFECTS IN MULTIPLE SCLEROSIS PATIENTS TREATED WITH SUBCUTANEOUS DISEASE-MODIFYING THERAPIES
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**Background:** Patients with multiple sclerosis (MS) are commonly stabilized on disease-modifying therapies (DMTs), including glatiramer acetate (Copaxone) or interferon beta (Betaseron, Rebif, Extavia, Avonex). One of the potential side effects is lipoatrophy at the injection site. This results in the loss of that site for injections and a cosmetically displeasing appearance. We have recruited patients to undergo a fat grafting procedure for lipoatrophy at their injection sites. The procedure is well validated and widely used under local anesthetic to correct contour and soft-tissue defects. It involves harvesting fat from an area with ample deposits, a purification process, and injecting the fat for volume augmentation in any subcutaneous plane. Volume outcomes using 3D camera imaging have been used successfully in many areas of plastic surgery. However, there is no report of fat grafting in MS patients who have lipoatrophy secondary to treatment with DMTs. This study enrolls MS patients prescribed the procedure as part of their clinical care for lipoatrophy. The study involves imaging the injection site using a 3D scanner before the procedure and at 3, 6, and 12 months after the procedure. The study also collects demographic information, and subjects will complete self-esteem and body image satisfaction questionnaires before the procedure and at 3, 6, and 12 months postoperatively. **Objectives:** The primary objective of this study is to evaluate the short-and long-term changes in subcutaneous tissue volume following fat grafting for lipoatrophy at DMT injection sites in MS patients. Secondary objectives of this study are to evaluate impact of fat grafting for lipoatrophy on patient-reported self-esteem and body image satisfaction, to correlate self-esteem and body image satisfaction with subcutaneous tissue volume, and to have the grafted sites available for potential reuse as injection sites. **Methods:** Enrollment consists of 20 MS patients on DMTs who will undergo a fat grafting procedure for lipoatrophy at injection sites. Upon enrollment, subjects will complete a paper-based demographic questionnaire. A 3D scanner (Go!Scan™ manufactured by Creaform) is used to measure subcutaneous volumetric data. The scanner captures images and gives 3D volume measurements in the area of interest. The amount of fat injected in each patient will be recorded and analyzed over time to determine the volume that remains at the measured time points. We also utilize questionnaires to evaluate self-esteem and body image satisfaction. The study will provide cross-sectional and longitudinal data at multiple time points: before the procedure and at 3, 6, and 12 months postoperatively. **Results:** Pending. The first 6 patients have had the fat grafting procedure and initial imaging done. Awaiting 3-month follow-up data.
Background: Risk factors for neuromyelitis optica (NMO) are largely unknown. **Objectives:** To determine whether environmental factors known to modify multiple sclerosis (MS) risk are associated with the risk of NMO in children. **Methods:** This is a case-control study of prospectively enrolled pediatric NMO, MS, and healthy subjects. Early life exposures were obtained by standardized questionnaire. Serum 25(OH) vitamin D levels were measured by chemoluminescence assay. EBV, CMV, HSV-1, and HSV-2 antibody responses were determined by ELISA. Multivariate logistic regression models were used to determine risk factor associations with NMO, including adjustments for age at sampling, sex, race, and ethnicity. **Results:** Early life exposures were obtained from 36 pediatric subjects with NMO, 491 with MS, and 224 healthy controls. Daycare (OR, 0.33; 95% confidence interval [CI], 0.14-0.80; P = .01) and breastfeeding (OR, 0.41; 95% CI, 0.18-0.96; P = .04) were associated with lower odds of having NMO compared with healthy subjects. C-section tended to be associated with 2-fold higher odds of NMO. Parental smoking was not meaningfully associated with NMO risk. A subgroup of the subjects had serotyping (34 NMO, 189 MS, 94 controls). Compared with MS patients, EBV exposure tended to be associated with lower odds of having NMO (EBNA1: OR, 0.156; 95% CI, 0.022-1.089; P = .06), HSV-1 exposure (OR, 1.47; 95% CI, 0.25-0.862; P = .034) and being DRB1*15 positive (OR, 0.18; 95% CI, 0.035-0.93; P = .040) were also associated with lower odds of having NMO. **Conclusions:** Early exposure to other young children may be a protective factor against the development of NMO, as previously reported for MS, suggesting that viral infections may contribute to disease risk modification. Unlike MS, pediatric NMO does not appear to be associated with exposures to common herpes viruses.

Supported by: Genzyme, a Sanofi company; National Multiple Sclerosis Society, Guthy Jackson Foundation; Foundation of the CMSC.


Keywords: Epidemiology of MS, Etiology of MS, Neuromyelitis optica

**Posters: Basic Science**

**SC13** DEATH CAUSED BY DISSEMINATED PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY IN A NATALIZUMAB-TREATED MULTIPLE SCLEROSIS PATIENT WHOSE IMMUNE COMPETENCE COULD NOT BE RESTORED

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**Background:** Progressive multifocal leukoencephalopathy (PML) occurs in multiple sclerosis (MS) patients treated with natalizumab. Medication cessation and treatment with plasmapheresis often provoke a brisk inflammatory reaction, the immune reconstitution inflammatory syndrome (IRIS). **Objectives:** We present a case of natalizumab-induced PML in an MS patient whose immune competence was not restored, resulting in widespread infection and ultimately death. **Methods:** Case report. **Results:** The patient was a 70-year-old right-handed woman with a 37-year history of MS. She had multiple mild exacerbations from 1999 to 2007 while treated with glatiramer acetate. Natalizumab was initiated in 2007 and produced radiologic and clinical stability. In 2010, after 36 infusions, she was found to be JC antibody positive, and natalizumab was discontinued. She worsened, and natalizumab was resumed after missing 3 doses. In January 2013, after an additional 31 doses, she complained of subtle word-finding difficulty. Magnetic resonance imaging (MRI) was reported to be unchanged, consistent with MS. Cerebrospinal fluid (CSF) PCR was positive for the JC virus. There was no history of prior immunosuppressive treatment. Five weeks after the last natalizumab treatment, she was admitted to Winthrop University Hospital and had 5 plasmapheresis treatments, followed by a 5-day course of IV Solu-Medrol 1 g daily. There was no change in her MRI results, which were interpreted as consistent with MS and not indicative of PML; no enhancement was present. 10 days later, her condition deteriorated, with 4/5 right hemiparesis and difficulty following complex commands. A 3-day course of IV Solu-Medrol 1 g daily was administered without benefit. Follow-up MRI showed an expanding left hemisphere lesion that reached a size of 5 × 5.9 × 2.8 cm. It crossed the corpus callosum and involved the right hemisphere. There was no mass effect or enhancement. Mefloquine HCL and mirtazapine were initiated. Over the next 5 weeks, she became globally aphasic with scant movement of her right hemibody. The family elected supportive care; she died 2 months after discharge. MRI performed 3 weeks prior to death showed no evidence of IRIS. **Conclusions:** This case is notable because of the inability to restore immune competence and the difficulty of diagnosing early PML by MRI. Three good-quality MRI scans were interpreted by four neuroradiologists as consistent with MS; there was no radiologic suspicion of PML despite its being present at an early stage. The initial PML presentation, subtle cognitive dysfunction without focal findings, made diagnosis difficult in an older patient with chronic psychiatric difficulties. We speculate that initiating steroids before enhancement, as noted on the MRI, and the patient’s older age may have prevented the restoration of immune competence and allowed the virus to disseminate widely, ultimately causing death. On the basis of this case, we suggest that steroids not be initiated in older PML patients until there is radiologic evidence of early IRIS.

Supported by: None

Disclosures: Malcolm H. Gottesman: Biogen, Teva, Genzyme (consulting fees). Stephen M. Newman: Biogen, Genzyme, Teva, Novartis, Acorda, Pfizer, Questcor (consulting fees); Novartis (grant/research support). Tiffany M. Harding: Nothing to disclose.

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

**SC14** IT’S NOT AS SIMPLE AS PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

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**Background:** This is a case study of a young woman with significant treatment anxiety/resistance around deciding to go on natalizumab [Tysabri], which was interesting because
she was well informed, JC virus negative, and willing to go on anything else, even wanting to try intravenous cladribine before natalizumab (which she has researched despite its being not indicated). She has been on Rebif, Copaxone, Movectro, and Gilenya. This report explores some of the strategies and nursing interventions used to help her with her anxiety about her treatment decision. Previously, a lot of treatment anxiety we have dealt with as multiple sclerosis specialist nurses has been injection/needle phobia, so it was interesting to deal with this patient and the treatment anxiety that she experienced. Objectives: Share this case and strategies for helping with the concerns that are present with our more effective treatments.

Supported by: None
Disclosure: Biogen Idec, Genzyme, Novartis (consulting fee)
Keywords: Disease-modifying treatments in MS, Nursing management in MS, Psychosocial issues and MS

(SC15) DIFFUSION-RESTRICTED LESIONS IN MULTIPLE SCLEROSIS
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Background: Magnetic resonance imaging (MRI) is valuable in the diagnosis of multiple sclerosis (MS). Demyelinating lesions are typically visualized on T1- and T2-weighted and FLAIR sequences. Hyperintense diffusion-weighted imaging (DWI) lesions with corresponding hypointensity on apparent diffusion coefficient (ADC) reflect diffusion restriction due to regional cytotoxic edema. Cavitation or gliosis in the area of previous ischemia or demyelination results in elevation of ADC values (T2 shine-through). Objectives: Report a case of relapsing-remitting multiple sclerosis (RRMS) and coexistent acute ischemic lesions with an emphasis on neuroimaging findings and diagnostic clues. Methods: A 43-year-old man presented with optic neuritis, dizziness, and numbness. Brain MRI showed multiple white matter lesions and Dawson fingers consistent with MS. The patient was readmitted 4 months later with difficulty walking and blurred vision. Repeat brain MRI showed new enhancing lesions, some with diffusion restriction. The patient’s symptoms improved with intravenous steroids. MRI 3 weeks after treatment showed improvement of enhancing lesions with increased ADC levels. The patient’s clinical presentation, neuroimaging results, and responsiveness to steroids were consistent with RRMS. One month after his last relapse, the patient developed acute-onset left-sided hemiparesis. Repeat MRI revealed diffusion-restricted lesions in the right ACA territory (MRI and more clinical information will be presented).

Results: Recent studies have shown that MS patients tend to have increased risk of cerebrovascular events. Contrast enhancement is a neuroimaging biomarker that identifies active MS lesions. Rarely, active lesions may show diffusion restriction (pseudostrokes). The differentiation of infarcts and demyelinating lesions is critical because the management options differ significantly. Histologically, acute demyelinating MS plaques show vasogenic edema that accounts for the high ADC values. ADC sequence appears to play a key role in differentiating these two distinct histological variations. Conclusions: This case illustrates a patient with both acute demyelinating and ischemic lesions on MRI. The presence of diffusion restriction in patients with acute neurologic symptoms, distribution of the lesion in a distinct vascular territory, and appearance of diffusion-restricted lesions in the cortex strongly suggest ischemia. Demyelinating lesions typically involve white matter and likely show T2 shine-through, although diffusion restriction can be seen and it can vary remarkably, mimicking an ischemic infarct. Perfusion MRI scans can offer superior demarcation in complicated cases of MS with coexistent ischemic infarcts.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Imaging and MS

(SC16) A STUDY OF INSULIN RESISTANCE IN MULTIPLE SCLEROSIS SUBJECTS AND HEALTHY CONTROLS
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Background: Diabetes and cardiovascular comorbidities are associated with accelerated multiple sclerosis (MS) disease progression. Reduced mobility, sedentary lifestyle, and repeat steroid exposure are insulin resistance risk factors common in MS. Objectives: Determine the incidence of insulin resistance in MS subjects compared with healthy controls using the oral glucose tolerance test (OGTT). Methods: Recruitment is ongoing for 50 subjects (25 each): age 18 to 64 years, nonobese, fasting blood glucose (BG) <126 mg/dL, and without diabetes mellitus. The OGTT was completed with BG measured at 30, 60, and 120 minutes. The Multiple Sclerosis Functional Composite (MSFC), 6-Minute (6MW) and 2-Minute Walks (2MW), and health and quality of life surveys were administered. Community ambulation was measured with a 7-day accelerometer. Results: Preliminary analysis of the first 28 subjects (14 MS/14 controls) showed they were similar in age, gender, and body-mass index (BMI). At all OGTT time points, MS subjects demonstrated significantly higher mean BG levels than controls: at 120 minutes, mean (25th, 75th), 114 (99, 132) vs. 93 (92, 103); P = .037. Within the MS cohort, time from MS symptom onset was significantly correlated with 2-hour BG (rho = 0.464, P = .01). There were statistically significant differences in total daily accelerometer counts and 6MW and 2MW distances between MS subjects and controls; however, there was no significant correlation between these measures and 120-min BG levels. Further analyses are ongoing. Conclusions: Preliminary analyses demonstrate that compared with controls, MS subjects have higher BG levels with OGTT at 30, 60, and 120 minutes. While MS subjects have reduced measured distance on timed walk tests and in the community, this is not correlated to OGTT results. One interpretation is that the subject’s fitness level is not the explanation for the OGTT findings, but rather may be MS disease specific. Notably, OGTT results did significantly correlate to time since MS symptom onset. This work is in progress. Complete enrollment and data analysis will be ready for meeting presentation.

Supported by: National Institutes of Health, National Institute of Neurological Disorders and Stroke (grant K23NS062898); ziMS Foundation
Disclosure: Nothing to disclose
Neuromyelitis optica (NMO) is a severe demyelinating disorder of the central nervous system that predominantly affects the optic nerves and the spinal cord. NMO spectrum disorders (NMOSD) include other clinical syndromes associated with white matter lesions restricted to areas of high aquaporin-4 (AQP4) expression. Anti-AQP4 antibodies are 73% sensitive and 91% specific for the diagnosis of NMO. A review of the literature identifies only 3 out of 26 NMO patients with NMO-IgG positivity restricted to cerebrospinal fluid (CSF).

**Objectives:** We present a case of NMOSD in a patient who presented with somnolence and autonomic dysfunction consistent with disturbance of the hypothalamic-pituitary axis and magnetic resonance imaging (MRI) lesions restricted to the hypothalamic pathways. Serum NMO-IgG was negative, but CSF NMO-IgG was positive.

**Methods:** Case report. Results: We report a case of a 22-year-old, previously healthy woman with a 3-week history of progressive somnolence, hypothermia, bradycardia, hypotension, and hypernatremia. Neurologic examination was significant only for inability to maintain wakefulness. The patient did not have clinical signs of optic neuritis (ON) or myelitis. The patient’s wakefulness, hypothermia, and hypernatremia improved after a 5-day course of intravenous methylprednisolone 1 g daily. Hypotension and bradycardia persisted for several weeks. She was able to return to work and school but required modafinil to maintain wakefulness as an outpatient. She did not have exacerbation on 3-month follow-up. MRI of the brain revealed T2 hyperintensities involving the hypothalamus, thalami, and anterior head of the caudate with patchy contrast enhancement in the hypothalamus. MRI of the spine and orbits were normal. Antinuclear antibody (ANA) was weakly positive at 1:40 and serum NMO-IgG was negative; however, CSF NMO-IgG was positive. Other CSF studies revealed WBC of 14, no RBC, normal glucose and protein, a mildly elevated IgG index at 0.8, 3 OCBs, and MBP of 28.1.

**Conclusions:** Hypothalamic-pituitary axis dysfunctions can be the presenting features of NMO in the absence of signs of ON or myelitis. Negative serum NMO-IgG does not exclude the diagnosis of NMO. If clinical suspicion persists, CSF NMO-IgG should be pursued.

**Supported by:** None

**Disclosure:** Parul Jindal, Evgeny Sidorov, Jaclyn R. Duvall; Nothing to disclose. Tania Reyna: Biogen Idec, Teva Pharmaceuticals (fees for non-CME services from commercial interests or their agents); Novartis (grant/research support).

**Keywords:** NMOSD

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**SC18** THE PREVALENCE OF THYROID AUTOANTIBODIES IN MULTIPLE SCLEROSIS

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**Background:** Multiple sclerosis (MS) is a chronic autoimmune demyelinating disease of the central nervous system, which mainly affects young adults. Some autoimmune disorders such as Hashimoto’s thyroiditis are associated with MS and can mimic some symptoms of MS such as fatigue, cognitive difficulties, muscle weakness, generalized tingling, and so on. The identification of thyroid peroxidase (TPO) as the main antigen of the thyroid microsomal fraction is commonly used to diagnose Hashimoto’s thyroiditis and Graves’ disease. Ten to fifteen percent of normal individuals can have mildly elevated anti-TPO antibody titers. **Objectives:** The aim of the study was to determine the prevalence of Hashimoto’s thyroiditis and prevalence of anti-thyroid antibodies in patients from a community-based MS clinic. **Methods:** We performed a retrospective chart review of 2425 MS patients. Only 210 patients (8.6%) were tested for thyroid dysfunction by measuring anti-thyroid peroxidase (anti-TPO) antibodies. Anti-TPO was considered positive at titers >36 IU/mL. Our results were compared with data from healthy controls reported in the literature. **Results:** Anti-TPO was positive in 32 (15%) MS patients, all females with an average age of 42 years. Twelve patients (6%) had high titers above 200 IU/mL and were assessed and treated by an endocrinologist. All patients with high anti-TPO titers had Expanded Disability Status Scale (EDSS) scores between 2 and 3. Additional clinical information and results of the treatment will be presented in the poster. **Conclusions:** Our results indicate that the frequency of mildly elevated anti-TPO in our MS population is similar to that of the healthy population, but the incidence of autoimmune thyroid disorders is higher in MS patients (6%) than in healthy subjects from a literature search (1%). This study brings attention to the importance of testing thyroid function in patients with MS to improve symptom management of fatigue and rule out comorbidities. It also may be helpful to monitor thyroid dysfunction in patients who are at risk of developing secondary autoimmune conditions.

**Supported by:** None

**Disclosure:** Sinead McGowan, Jacob (Jake) Reznik; Nothing to disclose. Galina Vorobeychik: Biogen Idec, EMD Serono, Genzyme Canada, Novartis, Teva Neuroscience (consulting fees).

**Keywords:** Comprehensive care and MS, Epidemiology of MS
nosed with NMO based on positive NMO IgG cerebrospinal fluid (CSF) and biopsy-proven loss of aquaporin-4 (AQP-4) in a pattern of demyelination consistent with NMO. **Methods:** Single case report. **Results:** The patient is a 67-year-old woman who presented with headache, confusion, right hemiparesis, and dysarthria. Her initial MRI of the brain was suggestive of primary central nervous system lymphoma (PCNSL). Her MRI revealed superficial nonspecific T2 hyperintensities that were atypical for demyelination without a viable lesion abutting on the ventricular surface, with a large white matter signal anomaly with heterogeneous ring enhancement. There was involvement of the corpus callosum and also pericallosal lesions that could suggest demyelination. Given the MRI findings, biopsies were performed on two separate occasions and were negative. She was negative for vascular, infectious, autoimmune, and paraneoplastic etiologies, and MS was unlikely based on CSF and imaging studies. She then returned with deteriorating function including bitemporal hemianopia. A repeat MRI of the brain revealed marked chiasmal enhancement as well as subependymal enhancement of the frontal horns of the lateral ventricles and floor of the third ventricle along with some involvement of the pituitary stalk. She underwent a repeat lumbar puncture, and CSF analysis was positive for the AQP-4 antibody on the cell-based assay. Remaining previous biopsy tissues were sent as well, confirming loss of AQP-4 within the region of active demyelination in which the pattern was consistent with NMO. **Conclusions:** This case demonstrates that NMO may present with a brain mass lesion and hydrocephalus. We describe initial findings of large enhancing brain lesions, hydrocephalus, and lack of myelitis or optic neuritis. It was only after optic chiasmal inflammation was detected that NMO was considered in the differential diagnosis.

**Disclosure:** Nothing to disclose

**Keywords:** Imaging and MS, Immunology and MS, NMO

**SYMPTOM MANAGEMENT**

**(SX07) FEASIBILITY OF COMBINING GROUP ACUPUNCTURE WITH A WELLNESS INTERVENTION FOR WOMEN WITH MULTIPLE SCLEROSIS**

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**Background:** Acupuncture is widely used for neurologic disorders; however, very few clinical trials have been published in English on acupuncture and multiple sclerosis (MS). Of particular interest is how acupuncture might enhance other interventions designed to improve physical and mental health in people with MS. **Objectives:** This study evaluated the feasibility of combining a previously validated 8-week wellness intervention for women with MS with weekly group acupuncture treatments. The class sessions provided the information and skills to promote a healthy lifestyle, and the acupuncture treatments were provided in a small group setting either immediately before or after the wellness classes. The acupuncture treatments focused on using needling points below the knee and elbow, on the head, and on the ear so that patients could remain fully clothed. **Methods:** Feasibility related to recruitment, enrollment, and intervention delivery were assessed using process evaluation methods and focus groups. After completing an initial acupuncture evaluation,
all participants received standardized treatment using high-impact points to address their general clinical presentation: St 36, Sp 6, Kd 3 (bilateral); P6, Ht 7, Lv 3 counterlateral to LI 4; Yintang Du 20 on the head and Shenmen, Point Zero, and Sympathetic on the ear; switching sides every week. Points were needled with even stimulation until obtaining “de qi.” Electrostimulation with continuous wave, 4 Hz, was applied to St 36 and Sp 6. Needles were retained for 30 minutes.

**Results:** Fourteen of the 20 women who responded to recruitment materials enrolled and completed the study. The women, aged 32 to 66 years, had been diagnosed with MS from 1 to 24 years previously; most were married (57%) and had completed some college (78%). All attended at least 75% of the intervention sessions. In postintervention focus groups, participants generally agreed that the acupuncture was relaxing and that they valued the comprehensive approach (classes and acupuncture) to lifestyle management. They reported sleeping better and feeling less fatigued. There were several reports of transient side effects (itching in legs, leg cramps, transient blurry vision, pain on moving). Only one woman expressed that the acupuncture had been a negative experience for her.

**Conclusions:** A wellness intervention with acupuncture may be more effective in reducing stress, pain, and depression, thus facilitating attempts to make lifestyle modifications and enhance overall health.

**Supported by:** St Davids Center for Health Promotion, University of Texas at Austin

**Disclosure:** Nothing to disclose

**Keywords:** Complementary/alternative therapies in MS

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**(SX08) SEVERITY AND CHARACTERISTICS OF OVERACTIVE BLADDER CONDITION IN MULTIPLE SCLEROSIS: AN ANCILLARY ANALYSIS OF THE NARCOMS REGISTRY DATA**

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**Background:** Bladder dysfunction is a common problem in multiple sclerosis (MS); it has been associated with a reduced quality of life and may interfere with daily activities. Dysfunction can range from minor to severe, and specialist care may often be required. **Objectives:** To establish the prevalence of self-report bladder dysfunction in a large MS population and assess factors associated with the severity of dysfunction, such as MS disability level and urology-related care. **Methods:** Participants included respondents to the Fall 2005 North American Research Committee on Multiple Sclerosis (NARCOMS) update survey bladder function questions, who were US residents with no surgical alteration to the bladder. Urology-related care measures and health-care utilization were also assessed. Participants were classified as follows: No overactive bladder (No-OAB), Dry-OAB (urgency without leakage), or Wet-OAB (urgency with leakage). Statistical comparisons were made with chi-square tests. **Results:** Of the 8380 respondents, 61.6% had Wet-OAB, 14.7% Dry-OAB, and 23.7% No-OAB. Those with Wet-OAB had a longer median disease duration (12 years) compared with Dry-OAB (9 years) and No-OAB (8 years; P < .0001). Some leakage related to activity, coughing, or sneezing was reported by 65.0% in the Wet-OAB group, and to a lesser extent in the otherwise Dry-OAB (23.5%) and No-OAB (26.5%; P < .0001) groups. A higher proportion of participants with Wet-OAB reported moderate or worse disability on the Patient-Determined Disease Steps (PDDS) (80.7%) compared with Dry-OAB (65.4%) and No-OAB (48.4%; P < .0001). Participants with Wet-OAB were most likely to report ever having a urinary tract infection (UTI) (63.4%) compared with Dry-OAB (61.9%) and No-OAB (56.2%; P < .0001) and most likely to report taking prophylactic antibiotics (Wet-OAB, 9.7%; Dry-OAB, 4.8%; No-OAB, 5.3%; P < .0001). Specialty care in the prior 6 months by a urologist was reported by 22.5% of participants with Wet-OAB, compared with 15.2% with Dry-OAB and 12.0% with No-OAB (P < .0001), with more participants in the Wet-OAB group reporting ever having seen a urologist (51.1%) compared with Dry-OAB (40.9%) and No-OAB (28.6%; P < .0001). **Conclusions:** Wet-OAB is associated with a longer duration of MS disease and overall MS disability, as well as a higher prevalence of UTI occurrence and prophylactic antibiotic use. Those with Wet-OAB reported a higher rate of urologist care than those without Wet-OAB, although the overall rate of urology care for any OAB was low.

**Supported by:** Allergan, Inc; NARCOMS is supported in part by the CMSC and its Foundation.


**Keywords:** Complementary care and MS, Epidemiology of MS, Overactive bladder

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**(SX09) CASE REPORT ON PERSON AFFECTED BY MARBURG DISEASE**

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**Background:** Marburg disease is a rare demyelinating encephalomyelitis with brain lesions in the brainstem and cervical spinal cord similar to multiple sclerosis (MS). It is characterized by acute onset and rapid, aggressive progression and can lead to severe motor disabilities and ultimately death. **Objectives:** To present a case study of Marburg disease. **Methods:** A 35-year-old man, married with one daughter and a high school education, was admitted to a hospital in October 2012 with sudden weakness and paralysis of the lower and upper limbs. He remained in the hospital for diagnosis for 3 months. He had limited motor skills with cognitive and mental changes. He was totally dependent for care, and gastrostomy was performed. He left the hospital in January 2013, with gastrostomy remaining until March 2013. Data were collected through the family, physician and hospital reports, and laboratory tests. Upon his arrival at the neurorehabilitation institute in March 2013, neurologic,
speech therapy, physical therapy, and psychological assessments were made. The patient had an Expanded Disability Status Scale (EDSS) score of 8.5 (wheelchair) and exhibited cognitive impairment, confusion, muscle atrophy, and abnormal speech. He received speech therapy, physical therapy, and psychological care, and psychological care was also extended to his wife. Because of the severity of the illness, psychological support of the patient and family was essential.

Results: After 5 months of treatment, the patient showed significant clinical improvement. He exhibited development of motor skills of the upper and lower limbs and speech organs and had increasing independence in performing small tasks, had clear verbal communication, and was lucid and expressed affection. Conclusions: Given the seriousness of this case, provision of comprehensive care to the patient and family by a multidisciplinary team was especially important.

Supported by: ABEM–Associação Brasileira de Escola de Multipla Disclosure: Nothing to disclose

Keywords: Management of activities of daily living in MS, MS and the caregiver/family, Psychological issues and MS

(SX10) THE INFLUENCE OF BOWEL DYSFUNCTION AND DEPRESSION ON ILLNESS INTRUSIVENESS IN MULTIPLE SCLEROSIS USING A MODERATOR MODEL

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Background: Multiple sclerosis (MS) is an autoimmune disorder affecting the central nervous system. Bowel dysfunction can occur, with constipation and fecal incontinence as the two most frequently reported issues (prevalence rates of 35–54% and 29–51%, respectively). Both gastrointestinal issues can cause physical and social problems, thus potentially affecting MS patients’ quality of life (QOL). One way of measuring QOL in MS is with the Illness Intrusiveness Ratings Scale (IIRS), a 13-item questionnaire that measures several different domains, including relationships and instrumental tasks of daily living. Objectives: We hypothesize that by using depression as measured by the Beck Depression Inventory (BDI) as a moderator, bowel dysfunction as measured by the Incapacity Status Scale (ISS) will be related to perceived illness intrusiveness. Methods: Data are analyzed with a moderator model, using Hayes’ PROCESS Conceptual Model 1. Results: Participants’ (N = 213) bowel dysfunction ranges from severe to none, with the majority having mild to none. The model is significant (P < .0005), as is the relationship between illness intrusiveness and depression (P < .0005). The relationship between bowel dysfunction and illness intrusiveness is not significant (P = .1237), and the relationship between bowel intrusiveness and the interaction of bowel dysfunction and depression is nearly significant (P = .0514), suggesting a trend. Conclusions: As our participants have milder bowel dysfunction, we hypothesize that MS patients with more severe bowel dysfunction may report higher levels of illness intrusiveness.

Supported by: CMSC
Disclosure: Andrew S. Castiglione, Elizabeth S. Gromisch, Stacey Snyder, Vance Zemon, Laura C. Schairer, Mary Ann Picone, Eileen Farrell, Meghan Beier, Sonya Kim: Nothing to disclose. Frederick W. Foley: Bayer Therapeutics (consulting fees, grant/research support); Biogen Idec, Novartis (consulting fees).

(SX11) INFLUENCE OF SURGICAL OR NATURAL MENOPAUSE ON DISEASE SYMPTOMS IN WOMEN WITH MULTIPLE SCLEROSIS

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Background: Menopause is an important milestone and typically occurs during peak years of productivity for mature women relative to social, family, and professional responsibilities. Limited data are available on this topic in relation to patients with multiple sclerosis (MS). Objectives: To evaluate the effect of natural or surgical menopause on MS disease status using patient-reported outcomes. Methods: This study is a targeted analysis from a reproductive events study that included 237 women enrolled at the Jacobs MS Center and registered with the New York State MS Consortium (NYMSC) who completed an extensive questionnaire about reproductive events. Independent-samples t tests and chi-square tests were conducted to investigate differences between women who had a natural or surgical menopause. Logistic regression modeling was used adjusting for covariates. Results: Eighty-three women reported natural menopause and 39 reported surgical menopause. Of women with a natural menopause, 78.2% reported an improvement in, or stabilization of, MS symptoms after menopause versus 75% of women with a surgical menopause. We observed that women who bore a child before the onset of MS were slightly less likely to have a natural menopause compared with those who had a child after onset of MS (OR, 0.47; P = .071). Women with a natural menopause were significantly older at MS symptom onset (mean age 34.7 [SD 9.1] years) compared with women who underwent a surgical menopause (mean age 30.6 [SD 8.3] years, P = .037). In logistic regression modeling, only age at onset of MS was significantly related (OR, 0.93; 95% confidence interval [CI], 0.88-0.99). Age at menses and birth before or after onset of MS were not significantly associated with natural or surgical menopause. Type of MS at registration (relapsing or progressive) and Expanded Disability Status Scale (EDSS) score at registration or age of using an assistive device did not differ. Conclusions: A majority of women reported feeling better or the same following menopause regardless of menopause being natural or surgical in nature. Our results suggest that women with younger age at onset of MS were more likely to have surgical menopause. We plan to investigate associations of birth control, hormone replacement therapy, and use of disease-modifying therapies.

Supported by: None
Disclosure: Barbara E. Teter: Biogen, Serono, Teva, Novartis, Genzyme (grant/research support); Katelyn S. Kavak, Karen Zakalik, Mitchell Kopacz: Nothing to disclose. Channa Kolb-Sobieraj: Biogen Idec,
Delayed-release dimethyl fumarate (DMF) has been shown to be effective in managing symptoms in multiple sclerosis (MS) patients. Patients reported their general health as “fair,” and 16% were unable to bathe and dress themselves without aid. Conclusions: Irritative and obstructive LUTS were common among patients with MS but did not fall clearly into either category; rather, a spectrum with varying degrees of each was found.

Supported by: National Institutes of Health/National Institute of Diabetes and Digestive and Kidney Diseases (grant P20-DK097819)

Disclosure: Nothing to disclose

Keywords: Bladder, Comprehensive care and MS, Natural history of MS

(SX12) SELF-REPORTED BLADDER AND BOWEL SYMPTOMS IN MULTIPLE SCLEROSIS PATIENTS

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Background: Nearly 75% of patients with multiple sclerosis (MS) experience lower urinary tract symptoms (LUTS) (Fowler, 1997). Demyelination and inflammation, the hallmark features of MS, can affect the neural pathways between the central nervous system and bladder that control bladder function (McCombe, 2009). LUTS in patients with MS vary widely in type and severity; symptoms may be present early in the disease course and may even predate the diagnosis of MS (Nortvedt, 2007). Some patients are spared early symptoms; however, as MS progresses, bladder dysfunction affects the majority of patients (de Seze, 2007). Objectives: To phenotype MS patients with LUTS and correlate a specific constellation of symptoms, as well as symptom severity, with functional status. We tested the hypothesis that irritative LUTS occur across all ranges of age, durations of disease, and disability scores with moderate correlation and obstructive symptoms occur in patients with longer duration of disease and those with higher disability scores with strong correlation. Methods: Patients with MS and LUTS, recruited from the urology and neurology clinics at the University of Pennsylvania, were queried regarding the most bothersome urinary and bowel symptoms as well as the presence of irritative LUTS (urgency, frequency, incontinence), obstructive LUTS (eg, incomplete bladder emptying, straining to void, hesitancy), or both. Correlation between the bladder subscore on multiple questionnaires (Functional Symptom Score [FSS] and the Medical, Epidemiological, and Social Aspects of Aging [MESA], Urogenital Distress Inventory [UDI], and International Consultation on Incontinence-Bowel [ICI-Q]) was performed to assess the reliability of the FSS bladder/bowel subscore in assessing bladder symptoms. Health-related quality of life was also assessed using the 36-item Short Form Health Status Survey (SF-36) and compared with measures of voiding symptoms.

Results: A total of 171 patients were prescreened, and 32 were enrolled (6 males, 26 females; 75% white, 25% African American); the average age was 45 years, and the average duration since MS diagnosis was 13.7 years. The average duration of LUTS was 8.5 years. Bladder symptoms were irritative in 58.7% (69% experienced urinary frequency, urgency, and urgency UI, and 59% nocturia) and obstructive in 42.3% (47% reported difficulty voiding and incomplete emptying). Bowel function was reported as difficult, requiring straining (56%) and digital manipulation (15%). Despite reporting bothersome bladder and bowel symptoms, most patients reported their general health as “fair,” “good,” “very good,” or “excellent” (very good/excellent, 28% [n = 9]; good/fair, 50% [n = 16]). Regarding functional ability, 38% reported difficulty (a little/a lot) participating in moderate activity, 38% reported inability to climb one flight of stairs, and 16% were unable to bathe and dress themselves without aid.

Supported by: Biogen Idec

Disclosure: Vanessa Zimmerman, Biogen Idec, Teva Pharmaceuticals, EMD Serono, Inc., Pfizer, Novartis, Acorda (consulting fees, speaker fees, fees for non-CME services from commercial interests or their agents); Biogen Idec, Teva Pharmaceuticals, EMD Serono, Inc., Pfizer, Novartis, Acorda, Cyberonics (grant/research support).

Keywords: Epidemiology of MS, Menopause

(SX13) GASTROINTESTINAL TOLERABILITY OF DELAYED-RELEASE DIMETHYL FUMARATE IN RELAPSING MULTIPLE SCLEROSIS: A MULTICENTER, OPEN-LABEL STUDY

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Background: Delayed-release dimethyl fumarate (DMF) demonstrated efficacy and safety in relapsing-remitting multiple sclerosis (RRMS) in the 2-year, phase 3 DEFINE and CONFIRM studies. Common adverse events associated with delayed-release DMF included flushing and gastrointestinal (GI)–related events such as nausea, diarrhea, and abdominal pain. Objectives: To evaluate the effect of symptomatic therapies on GI-related events in adult patients with relapsing forms of MS initiating delayed-release DMF therapy in clinical practice in the United States in the 12-week, multicenter, open-label MANAGE study. Methods: Patients were treated with delayed-release DMF, taken with or without 1 hour after a meal, at 120 mg twice daily for 7 days and 240 mg twice daily thereafter. The primary endpoint is the frequency, severity, and duration of GI-related events. Secondary endpoints include the cumulative proportion of patients requiring symptomatic therapy; the type, frequency, and duration of symptomatic therapies; and discontinuation rates due to events requiring symptomatic therapy. Results: MANAGE enrolled 237 patients with a mean age of 47 years (range, 18.0–74.0) and mean duration of MS of 9.5 years (range, 0.0–42.0). Among them, 184 (77.6%) were female and 219 (92.4%) were white. Patients’ mean baseline Expanded Disability Status Scale (EDSS) score was 2.6 (range, 0.0–7.5) and mean numbers of relapses within the previous 1, 2, and 3 years were 0.7 (range, 0–16), 1.1 (0–31), and 1.6 (0–47), respectively. MANAGE is ongoing; results will be reported. Conclusions: MANAGE is a 12-week, multicenter, open-label study evaluating the effect of symptomatic therapies on GI-related events in relapsing MS patients initiating delayed-release DMF therapy.

Supported by: Biogen Idec

Disclosure: Edward J. Fox: Acorda, Bayer, Biogen Idec, EMD Serono, Genzyme, Novartis, Sanofi, Teva (fees for non-CME services from commercial interests or their agents); Bayer, Biogen Idec, EMD Serono, Genzyme, Novartis, Sanofi, Teva (consulting fees); Biogen Idec, EMD Serono, Genzyme, GlaxoSmithKline, Novartis, Opera, Roche, Sanofi,
(SX14) TO PEE OR NOT TO PEE? THE UTILIZATION OF BLADDER SCANS IN MULTIPLE SCLEROSIS
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Background: Bladder dysfunction is common in multiple sclerosis (MS) and can be asymptomatic. Detrusor overactivity and dysuria share a lead to urinary frequency, urgency, incontinence, and incomplete bladder emptying, which increase the risk of recurrent urinary tract infections (UTIs), hydronephrosis, and renal dysfunction. With early detection, bladder dysfunction can be treated medically, reducing morbidity and improving quality of life. Measurement of postvoid residual (PVR) can be a valuable tool in optimizing the treatment plan in both symptomatic and asymptomatic patients. Objectives: We studied the correlation between PVR, frequency of UTI, use of anticholinergic medications, and the presence of spinal cord involvement in MS patients with and without urinary symptoms. Methods: We prospectively studied 101 consecutive patients in an MS clinic during their routine neurologic visit for a 3-month period. Each patient was given the Urogenital Distress Inventory (UDI), Incontinence Impact Questionnaire (IIQ), and additional questions regarding UTI history and management. A patient was considered asymptomatic if they scored a 0 or 1 on the UDI and IIQ. PVR was obtained using a Bladder Scan BVI3000. PVR below 49 mL was considered normal, and PVR of 50 mL or more was abnormal. A urine analysis and culture was performed on all patients, and those with abnormal PVR were further screened with a renal ultrasound and serum urea nitrogen/creatinine levels. Results: We studied 101 patients, 70 with relapsing-remitting multiple sclerosis (RRMS) and 31 with secondary progressive multiple sclerosis (SPMS). 90% were female and 10% were male, and the mean age was 51 years. 20% had PVR, and 50% of those had UTIs. In those without PVR, only 26% had UTIs. In the RRMS group, 20 patients were asymptomatic, 3 of whom had PVR. Of those, 2 had a history of UTI during the past year. In the SPMS group only one patient was asymptomatic, and she had a history of both PVR and UTI. Of the 30 symptomatic SPMS patients, 11 (37%) had PVR and 4 (36%) had UTI. In the 19 patients without PVR, 6 (32%) had UTI. Conclusions: Measurement of PVR is a valuable tool for detection of urinary retention, especially in asymptomatic patients, as occult retention may occur in a small but meaningful percentage of patients with RRMS. We found a high correlation between urinary symptoms, UTI, and PVR in our SPMS population. In RRMS, there was little correlation between the presence of symptoms and PVR.

Supported by: None
Disclosure: Nothing to disclose
Keywords: Comprehensive care and MS

(SX15) HIGH FATIGUE LEVELS AFFECT FUNCTIONAL MOBILITY, QUALITY OF LIFE, AND DEPRESSION IN PEOPLE WITH MULTIPLE SCLEROSIS
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Background: Fatigue is a commonly presenting symptom in people with multiple sclerosis (MS). The associations between fatigue and neurologic disability, functional mobility, depression, and quality of life (QOL) are unclear in MS, demanding further investigation. Objectives: This study aimed to determine the effect of different levels of fatigue on disability, performance-based and self-reported functional mobility, depression, and physical and mental QOL in people with MS. Methods: Ninety-one individuals (30 male, 61 female; mean [SD] age, 54.3 [11.9] years; diagnosis duration, 13.6 [9.8] years; Expanded Disability Status Scale (EDSS) score, 5.3 [1.5]; height, 169 [10.2] cm; weight, 79 [21.5] kg) with clinically definite MS and no concurrent relapses were included and retrospectively analyzed. Subjects were divided into two groups based on a Modified Fatigue Impact Scale–5 (MFIS-5) cutoff score: Group LF (n = 34, MFIS-5 ≤ 10, representing low levels of fatigue) and Group HF (n = 57, MFIS-5 > 10, representing high levels of fatigue). Functional mobility measures included the 8-feet Timed Up and Go (TUG), Activities-specific Balance Confidence (ABC), and 12-item Multiple Sclerosis Walking Scale (MSWS-12). Depression was assessed by Beck Depression Inventory–Fast Screen (BDI-FS), and QOL was determined by physical and mental composites of the Multiple Sclerosis Quality of Life–54 (MSQOL-54) questionnaire. Mann-Whitney tests for independent samples were used for nonparametric statistical analysis. Results: High fatigue levels (MFIS-5 > 10) were noted in 62.6% of the people with MS. As compared with Group LF, Group HF demonstrated significantly impaired TUG (median seconds: Group HF, 9.18 vs. Group LF, 7.50; U = 706.00; z = −1.96; P < .05; r = −0.21), ABC (median [SD%]: Group HF, 50.62 vs. Group LF, 72.80; U = 658; z = −2.55; P < .01; r = −0.27), MSWS-12 (median [SD%]: Group HF, 58.33 vs. Group LF, 31.67; U = 336; z = −3.79; P < .001; r = −0.43), BDIF-S (median: Group HF, 3 vs. Group LF, 1; U = 310.5; z = −2.81; P < .01; r = −0.34), physical QOL (median: Group HF, 39.56 vs. Group LF, 59.4; U = 374; z = −4.88; P < .001; r = −0.51), and mental QOL (median: Group HF, 68.29 vs. Group LF, 83.01; U = 490; z = −3.26; P < .001; r = −0.35). EDSS score was similar across both the groups (median: Group HF, 5.25 vs. Group LF, 6.0; U = 794.00; z = −1.33; P > .05). Conclusions: Fatigue is a predominant symptom in people with MS. Individuals with high fatigue levels exhibit significant and clinically meaningful impairments in performance-based as well as self-reported functional mobility, depression, and physical and mental QOL. Therefore, effective interventions targeting fatigue may result in improvements in functional performance, depression, and QOL in people with MS. Neurologic disability was not found to be related to the level of fatigue experienced by people with MS.

Supported by: None
Keywords: Comprehensive care and MS, Management of activities of daily living in MS, MS-related fatigue

International Journal of MS Care
(SX16) MEDICAL TOURISM FOR CHRONIC CEREBROSPINAL VENOUS INSUFFICIENCY (CCSVI) TREATMENT IN MULTIPLE SCLEROSIS

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Background: Medical tourism involves patient travel across international borders to obtain medical care. Because procedures for chronic cerebrospinal venous insufficiency (CCSVI) are not approved in Canada, many people with multiple sclerosis (MS) have traveled out of the country and paid out-of-pocket to have these interventions.

Objectives: Among people with MS who obtained venous angioplasty with or without stenting for CCSVI, we aimed to describe the factors that influenced the choice of the treating facility and to examine differences in clinical practices and outcomes by the country in which treatment was performed.

Methods: The Alberta Multiple Sclerosis Initiative (TAMSII) is a longitudinal observational study that uses online questionnaires to collect patient-reported information about the safety, experiences, and outcomes following CCSVI treatment. In total, 866 subjects enrolled between July 2011 and June 2013, of whom 124 traveled abroad to obtain CCSVI treatment, with one patient going twice.

Results: Patients traveled to the United States (44.0%), Mexico (20.8%), Costa Rica (11.2%), and Poland (10.4%). A few patients also traveled to Bulgaria, Germany, India, Jordan, and the United Kingdom (13.6%). Most patients learned about the treating facility on the Internet (56.0%) or from a friend or relative (50.4%) and chose the facility based on their impression of the reputation of the physicians (66.4%), recommendations from an acquaintance (44.8%), or travel distance (41.6%). The specialty of the physician who performed the treatment, placement of venous stents in addition to angioplasty, the costs of treatment and travel, and any follow-up treatments or tests were each strongly associated with the country of the treating facility (P < .0001). There was also a moderate relationship with the number of veins treated (P = .04). Regardless of the country in which treatment was performed, most patients felt that the treatment was successful (79.1%) and that it was as easy to tolerate as expected (90.4%).

Conclusions: Because CCSVI treatment is an unproven experimental therapy, there is currently no standardized protocol for these procedures. As expected, there was considerable variability in the clinical practices of facilities treating MS patients who traveled abroad for CCSVI interventions.

Supported by: Alberta Health

Disclosure: Jamie Greenfield, Winona Wall, Mayank Goyal, Nathalie Jette, James Newsome, Scott Patten: Nothing to disclose. Ruth Ann Marrie: Sanofi-Aventis (grant/research support). Luanne Metz: EMD Serono (grant/research support); Novartis, Biogen Idec, Teva Neurosciences (consulting fees). Oksana Suchowersky: Abbvie, Allergan (consulting fees); Abbvie, Merck, National Institutes of Health, CIHR (grant/research support); UpToDate (royalty).

Keywords: CCSVI, Complementary/alternative therapies in MS

(SX17) FACTORS PREDICTING FATIGUE IMPACT IN PEOPLE WITH LONG-STANDING MULTIPLE SCLEROSIS

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Background: Fatigue is a complex phenomenon experienced by most people with multiple sclerosis (MS). Fatigue negatively influences quality of life, activities of daily living, and employment. Understanding factors that are predictive of MS-related fatigue is vital to promoting optimal health and well-being.

Objectives: Little is known about factors that predict fatigue impact in people with long-standing MS (duration of MS greater than 17 years). The purpose of this study was to examine the relationships among fatigue impact, demographic characteristics (ie, age and duration of MS), functional limitations, depressive symptoms, barriers to health-promoting activities, personal resources, and health-promoting behaviors in people with long-standing MS.

Methods: A sample of 330 individuals with MS (86% female, mean age 62.9 ± 9.3 years, mean length of diagnosis 26.5 ± 6.5 years) in an ongoing longitudinal study of health promotion and quality of life completed the Modified Fatigue Impact Scale (MFIS), MS Incapacity Status Scale, Center for Epidemiologic Studies Depression Scale (CES-D), Barriers to Health Promoting Activities for Disabled Persons Scale, Personal Resource Questionnaire, and Health Promoting Lifestyle Profile II. The MFIS assesses how fatigue symptoms affect the lives of people with MS over the previous 4 weeks in terms of physical, cognitive, and psychosocial functioning. Descriptive statistics, Pearson correlations, and hierarchical linear regression were used to analyze the data.

Results: Significant (P < .01) positive relationships were found among fatigue impact and MS functional incapacity, depressive symptoms, and barriers. Significant (P < .01) negative relationships were found among fatigue impact and personal resources and health-promoting behaviors. The model containing functional incapacity, depressive symptoms, and barriers to health-promoting activities contributed significantly (P < .001) to the overall variance accounted for in total (54.2%), physical (51.2%), cognitive (40.9%), and psychosocial (50.9%) fatigue impact. MS functional limitation was found to be the strongest predictor of physical and psychosocial fatigue impact, while depressive symptoms was the strongest predictor of total and cognitive fatigue impact.

Conclusions: Additional research is needed to explore whether interventions designed to promote functional capacity, decrease depressive symptoms, and reduce barriers to health-promoting activities may have beneficial influences on fatigue impact in MS.

Supported by: National Institute of Nursing Research, National Institutes of Health (grant R01NR003195); St Davids Center for Health Promotion, University of Texas at Austin

Disclosure: Nothing to disclose

Keywords: Management of activities of daily living in MS

(SX18) FATIGUE AND QUALITY OF LIFE IN MULTIPLE SCLEROSIS PATIENTS

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Background: Fatigue is a common symptom of comorbidities and treatment-related side effects in MS patients. Fatigue affects the quality of life of MS patients and is associated with a higher incidence of depression, disability, and chronification. Patients report a negative impact of fatigue on their activities of daily living (ADL). However, little is known about the predictive factors of fatigue in MS patients in terms of fatigue and ADL impact.

Objectives: The purpose of our study was to examine the relationship between fatigue and quality of life in MS patients.

Methods: A cross-sectional study was conducted on 150 patients with MS. Fatigue was assessed with the Modified Fatigue Impact Scale (MFIS). The impact of fatigue on quality of life was assessed with the 36-Item Short Form Health Survey (SF-36). The analysis of the data was performed using Pearson correlations, multiple linear regression analysis, and the best subset method. The significance level was set at P < .05.

Results: The average age of the patients was 53.5 ± 10.3 years, the mean disease duration was 14.7 ± 8.6 years, and the median disease duration was 20.0 years. The average fatigue impact was 56.5 ± 21.2, and the mean quality of life was 72.3 ± 22.2. The results of the study showed that fatigue impact was significantly correlated with the impact of fatigue on physical (r = .49), role physical (r = .38), bodily pain (r = .44), social functioning (r = .39), vitality (r = .45), general health perception (r = .38), and mental health (r = .43). The best predictor of fatigue impact was the impact of fatigue on physical (β = .49), role physical (β = .38), mental health (β = .43), and vitality (β = .45). The impact of fatigue on quality of life was significantly correlated with fatigue impact (r = .65). The best predictor of fatigue and quality of life was fatigue impact (β = .65).

Conclusions: Fatigue and quality of life are significantly related. Fatigue impact is the best predictor of fatigue and quality of life in MS patients.

Disclosure: Nothing to disclose

Keywords: Fatigue, quality of life, multiple sclerosis, predictive factors, fatigueimpact, quality of life, activity of daily living, cross-sectional study.
Background: Fatigue in patients with multiple sclerosis (MS) can be associated with lower health-related quality of life (HRQOL). Objectives: The aim of this study was to explore the association of fatigue with physical and mental components of HRQOL in MS patients, controlling for sociodemographic and clinical data. Methods: The study comprised 152 patients (75.7% women, mean age 40.0 ± 10 years, mean Expanded Disability Status Score [EDSS] score 3.2 ± 1.4). Fatigue was measured by the Multidimensional Fatigue Inventory (MFI-20); two subscales of fatigue were used: physical and mental. Anxiety and depression were assessed by the Hospital Anxiety and Depression Scale (HADS) and HRQOL by the 36-item Short Form Health Status Survey (SF-36). Functional disability was assessed using the EDSS. Multiple linear regression analyses were performed. Results: Physical fatigue was present in 61% and mental fatigue in 44% of patients. Physical consisting of physical fatigue (P < .001), EDSS (P < .001), age (P = .591), and mental fatigue (P = .552) explained 68% of the variance in the Physical Component Summary (PCS). The model consisting of mental fatigue (P < .001), anxiety (P < .001), and depression (P = .001) explained 60% of the variance in the Mental Component Summary (MCS). Conclusions: Both physical and mental fatigue are highly prevalent in MS. Higher physical fatigue, more severe disability, older age, and higher mental fatigue were associated with worse score on the PCS. Higher mental fatigue and more severe anxiety and depression were associated with worse score on the MCS. Fatigue has an important impact on quality of life in patients with MS. Thus, effective treatment of the fatigue could improve a patient’s HRQOL.

Disclosure: Nothing to disclose

Keywords: Management of activities of daily living in MS

(SX19) OLFACTORY DYSFUNCTION IN NEUROMYELITIS OPTICA VERSUS MULTIPLE SCLEROSIS
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Background: While optic nerves and spinal cord are preferentially affected in neuromyelitis optica (NMO), it is widely recognized that NMO pathology is not restricted to these areas. Emerging evidence suggests that olfactory dysfunction may be a feature of NMO. In this study, we provide independent confirmation that olfactory dysfunction not only occurs in NMO, but is more frequent and severe than in MS. Additionally, we provide evidence, for the first time, that olfactory deficits correlate significantly with measures of disability in NMO. Objectives: To evaluate the presence and extent of olfactory dysfunction in aquaporin-4 (AQP-4)–positive NMO compared to multiple sclerosis (MS) and to relate these findings to clinical factors, including measures of disability. Methods: A prospective study at a tertiary NMO and MS center evaluating olfactory function using the Sniffin’ Sticks Identification Test in a cohort of clinically definite NMO (n = 19) and MS (n = 27) patients in whom demographic and clinical measures of disability (European Database for Multiple Sclerosis [EDMUS]) were available. Results: NMO patients were slightly older and had a shorter duration of disease compared to the MS group, with no significant differences in disability being observed between groups. Olfactory dysfunction was not only more frequent in NMO compared to MS (NMO: 10/19 [52.6%] vs. MS: 6/27 [22.2%]; P < .05) but also more severe when adjusted for age, sex, and duration of disease. No patients from either disease group reported subjective olfactory disturbance. Olfactory dysfunction in NMO and MS correlated significantly with age (r = −0.454, P = .002) and EDMUS score (r = −0.381, P = .009), with these relationships being driven mostly by the NMO group. Conclusions: Olfactory dysfunction occurs frequently in NMO, is more severe than the olfactory loss seen in MS, and correlates with measures of clinical disability. These findings expand the widening clinical spectrum of NMO.

Disclosure: Nothing to disclose

Keywords: Etiology of MS, Immunology and MS, NMO

(SX20) SELF-PERCEIVED REASONS FOR DECREASES IN LIBIDO IN A COHORT OF WOMEN WITH MULTIPLE SCLEROSIS
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Background: Research has shown that people with multiple sclerosis (MS) report sexual dysfunctions at a greater rate than age-matched healthy controls. Some have reported a decrease in quality of life due to sexual dysfunctions. One of the most commonly reported sexual dysfunctions is a decrease in libido. It is therefore important to investigate this in greater detail, as it may lead to increased awareness by health-care professionals and suitable treatments increasing the quality of life of MS patients. Objectives: To investigate whether women with MS experience a change in libido due to their MS and self-perceived reasons for this. Methods: Our sample comprises a subgroup of 237 women registered with the New York State MS Consortium (NYSMSC) who completed an extensive questionnaire about reproductive events and are treated at our MS care center. Independent-samples t tests and chi-square tests were conducted to investigate whether age and MS type differ between subjects whose libido decreased and those whose did not. Results: The response rate to “Has your sex drive been influenced by MS?” was over 94%. A total of 121 (54.3%) women with MS indicated that MS had influenced their sex drive. Of those, 90 subjects answered the subsequent question to specify their perceived reason for the change in libido. The most common reason was fatigue (n = 30, 33.3%), followed by a lack of sensation (n = 13, 14.4%) and a combination thereof (n = 5, 5.6%). Some indicated that they thought antidepressants influenced their sex drive (n = 5, 5.6%), while others...
expressed that they did not have enough strength or had too much pain to have sex (n = 5, 5.6%), or that their partners worried about hurting them while having sex (n = 4, 4.4%). The rest either reported another reason (n = 9, 10.0%) or indicated that the reason was unknown (n = 19, 21.1%). Those with a decrease in libido were slightly older (mean [SD] age, 53.7 [8.6] vs. 50.5 [12.8]; P < .05), but there were no differences regarding MS type. **Conclusions:** Our results indicate that among women with MS, most have experienced a decrease in libido, typically attributed to fatigue. Considering that only a small subset of patients openly discusses sexual dysfunctions with their physician, health-care professionals should be aware that this sensitive subject is a meaningful issue for a majority of female MS patients.

**Supported by:** None

**Disclosure:** Katelyn S. Kavak, Karen Zakalik, Mitchell Kopacz: Nothing to disclose. Barbara E. Trier: Biogen, Serono, Teva, Novartis, Genzyme (grant/research support). Channa Kohli-Sohieraj: Biogen Idec, Teva Neurosciences, EMD Serono, Novartis (consulting fees). Bianca Weinstock-Gutmann: Biogen Idec, Teva Pharmaceuticals, EMD Serono, Inc., Pfzer, Novartis, Acorda (consulting fees, speaker fees, fees for non-CME services from commercial interests or their agents); Biogen Idec, Teva Pharmaceuticals, EMD Serono, Inc., Pfzer, Novartis, Acorda, Cyberonics (grant/research support).

**Keywords:** Management of activities of daily living in MS, Sexual dysfunction

**(SX22) BLADDER DYSFUNCTION AND DISABILITY IN PEOPLE NEWLY DIAGNOSED WITH MULTIPLE SCLEROSIS**

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**Background:** Neurogenic bladder occurs in 80% of people diagnosed with multiple sclerosis (MS), causing repeated urinary tract infections (UTIs) and possibly leading to progressive neurologic impairments. Urinary urgency, incontinence, nocturia, and urinary hesitancy are some issues associated with incoordination of the sphincter and urethra as well as disrupted transmission of electrical impulses that involve emptying the bladder. UTIs have been associated with increase in cytokines and interferon production, causing inflammation and leading to increase in disability from relapse, thus causing concern for the newly diagnosed individual. **Objectives:** To determine the incidence of bladder dysfunction in people diagnosed with MS within 1 year, and to assess the correlation between disability and bladder dysfunction. To affirm the necessity of frequent bladder evaluation, even in the newly diagnosed, to avoid UTIs and provide management in the early stages of dysfunction. **Methods:** People with MS diagnosed within 1 year underwent measurement of walking speed with the Timed 25-Foot Walk (T25FW) and postvoid residual (PVR) measured through a bladder ultrasound (BVI 3000). T25FW values were considered normal at 2.2 seconds and PVR values were considered normal at 1 to 49 mL. **Results:** Thirty-four newly diagnosed individuals were studied. Thirteen people (38%) presented with abnormal PVR, and all 13 subjects presented with slowed walking speeds compared with the norm. On the T25FW, 4 of 13 subjects required more than 5 seconds, indicating significant ambulatory impairment, while 9 subjects required less than 5 seconds, indicating minimal impairment. PVR ranged from 67 to 300 mL, and T25FW scores ranged from 3.6 to 6.8 seconds. **Conclusions:** 38% of those newly diagnosed presented with neurogenic bladder with high risk of UTI. Abnormal PVR correlated with decreased walking speed in all (100%) of these newly diagnosed individuals, with significant impairment in four (30%). These findings indicate the need for early detection and intervention of bladder dysfunction to lessen occurrence of further disability.

**Supported by:** None

**Disclosure:** Nothing to disclose.

**Keywords:** Bladder dysfunction and MS, Management of activities of daily living in MS, Nursing management in MS
WHITAKER RESEARCH TRACK

The late Dr. John N. Whitaker was a world-famous researcher in multiple sclerosis. His work inspired many scientists to enter the field of MS and develop their skills and talents. Each year, the Consortium of Multiple Sclerosis Centers (CMSC) honors Dr. Whitaker’s memory by presenting one award for innovative research by a young investigator. This year the CMSC and the Foundation of the CMSC will present a prize to a scholar whose work exemplifies the mission of this visionary leader in multiple sclerosis.

IN VIVO DETECTION OF DEEP RETINAL NEURONAL LAYER CHANGES FOLLOWING ACUTE OPTIC NEURITIS UTILIZING OPTICAL COHERENCE TOMOGRAPHY–DERIVED SEGMENTATION

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Background: Following acute optic neuritis (AON), retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) thinning are well described. Inner (INL) and outer nuclear layer (ONL) abnormalities have recently been detected in multiple sclerosis (MS) and may be associated with increased accumulation of disability, underpinning their clinical importance. However, comprehensive assessment of INL and ONL changes following AON remains largely unexplored. Objectives: To determine whether objective changes in INL and ONL thicknesses occur following AON, and how these may be temporally related to thickness changes of the RNFL and ganglion cell layer (GCIP) (composite thickness of GCL + inner plexiform layer) following AON. Methods: 34 patients (29 with relapsing-remitting MS and 5 with clinically isolated syndrome) underwent Cirrus-HD optical coherence tomography (OCT) imaging, including automated intra-retinal layer segmentation, as well as visual function testing within 4 weeks of AON onset and serially thereafter (median, 25 months; range, 7–55 months). The paired t-test was used to compare retinal layer thickness changes, relative to baseline, for each eye.

Results: At the 4 ± 1-month visit after AON, the mean decrease in GCIP thickness was 12.1% relative to baseline (n = 29, P < .001). During the same time period, there were concomitant increases in the average thicknesses of both the INL (mean, 2.0%; P = .003; 95% confidence interval [CI], 0.7-3.3) and the ONL (mean, 3.8%; P < .001; 95% CI, 2.6-5.1). The percentage increase in ONL thickness of the affected eyes at the 4 ± 1-month visit was strongly correlated with the percentage decrease in GCIP thickness from baseline at the same visit (r = 0.58, P = .001). In patients with more than 2 years of follow-up (n = 16), INL and ONL thicknesses were significantly increased, relative to baseline, at 4 ± 1 months (mean change, 2.6% and 2.9%; P = .021 and .0008, respectively) but not after 24 months (mean change, 0.4% and −0.2%; P = .64 and .67, respectively), despite persistent GCIP thinning (mean change, −13%; P < .001). Conclusions: OCT segmentation demonstrates increases in INL and ONL thicknesses following AON in the absence of microcystic macular edema (MME). These increases may be proportional to the degree of GCIP loss in affected eyes, which is a novel finding, raising the possibility that biological changes may occur in the deep retinal neuronal layers following AON. Exploring these changes could help further our understanding of the pathobiology of MS.

Supported by: National Multiple Sclerosis Society grants FP-1787-A1 (PB), R0-1 NS082347 (PAC), R0-1 NS082347


Keywords: CNS repair, Glial biology, Imaging and MS

THE ROLE OF VITAMIN D AND GENDER IN OPTIC NEURITIS

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Background: Optic neuritis (ON) is a common manifestation of demyelinating disease. The optic nerve can serve as a model of the central nervous system, allowing for evaluation of inflammation and degeneration using optical coherence tomography (OCT) to measure retinal nerve fiber layer (RNFL) thickness and other afferent pathway markers. Vitamin D insufficiency is a risk factor for multiple sclerosis (MS) and vitamin D is known to ameliorate inflammation. Assessment of vitamin D status in ON may support a neuroprotective role. Objectives: We hypothesize that vitamin D sufficiency (25[OH]D > 80 nmol/L) is associated with better OCT outcomes and axonal preservation/recovery after ON. Outcomes include RNFL ganglion cell layer (GCL) thickness, and inter-eye difference (IED) in both at 6 months and baseline between vitamin D sufficient and insufficient groups.

Methods: In this prospective cohort study, patients with acute ON for ≤30 days undergo OCT to assess RNFL GCL, macular volume (MV), and serum 25(OH)D testing at baseline and month 6. Additional vision metrics and Expanded Disability Status Scale (EDSS) testing are also performed at these times.

Results: Currently, 49 patients have been enrolled (36 female, 13 male) and 42 have completed the study. At baseline, 68% of patients were vitamin D insufficient, which was associated with greater mean baseline edema in RNFL (131 vs. 106 µm, P = .14) and MV (10.2 vs. 9.8 mm³, P = .036). At month 6, while RNFL edema persisted, mean GCL IED was greater in vitamin D insufficient patients (14 vs. 7 µm, P = .094). Regardless of baseline RNFL or vitamin D, men had significantly lower 6-month mean RNFL (70 vs. 81 µm, P = .025) and greater IED in both mean RNFL and GCL (both 21 vs. 8 µm, P = .005 and P = .004, respectively) versus women.

Conclusions: OCT demonstrates that in acute ON, vitamin D insufficiency is associated with greater edema, in keeping with the known anti-inflammatory actions of vitamin D. At month 6, vitamin D insufficiency and male gender are both risk factors for poorer OCT outcomes (such as GCL thinning), suggesting that both vitamin D status and female gender, possibly acting together, may confer neuroprotection and/or improved repair in the optic nerve after an ON event.
MAGNETIZATION TRANSFER IMAGING IN BRAIN CORTICOSPINAL TRACT IS ASSOCIATED WITH CLINICAL WALKING PERFORMANCE IN MULTIPLE SCLEROSIS

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Background: Walking is a common measure of physical function in individuals with multiple sclerosis (MS). Previous studies have shown an association between spinal cord magnetic resonance imaging (MRI) measures (eg, magnetization transfer ratio [MTR]) and strength or walking ability, and brain corticospinal tract (CST) MTR with strength measures. However, the relationship between brain CST MTR measures and walking performance has not been explored in MS. Objectives: The objective of this study was to examine the relationship between clinical measures of walking and CST-specific measures of myelin (MD, MTR) and axonal integrity (FA).

Methods: Seventeen individuals with relapsing-remitting MS (mean age, 50.3 ± 9.9 years; 9 females; mean Expanded Disability Status Scale [EDSS] score, 4.1 ± 1.5) and 12 age- and gender-matched healthy controls (mean age, 51.7 ± 10.4 years; 8 females) participated in clinical tests of strength (handheld dynamometer), sensation (Vibratron II), and walking (Timed Up and Go [TUG], Timed 25-Foot Walk [T25FW], 2-Minute Walk Test [2MWT]), as well as 3T imaging (DTI, MT). T tests and Pearson correlation coefficients were used to assess statistical significance. Results: Individuals with MS had weaker hip flexion strength (P = .0024), had poorer vibration sensation (P = .0001), walked more slowly (TUG: P = .0013; T25FW: P = .0112; velocity: P = .0033), and had reduced endurance demonstrated by shorter distance walked on the 2MWT (P = .0055) than controls. Subjects with MS also had a lower MTR in the CST (P < .0001). There is a strong relationship between CST MTR and TUG (r = −.50), T25FW (r = −.58), and walk velocity (r = .51), and between CST FA and TUG (r = −.47), T25FW (r = −.58), and walk velocity (r = .49). Both CST MTR and FA were only weakly correlated with the 2MWT. Hip flexion strength is correlated with CST MTR (r = .42), but walking measures demonstrated stronger associations. Although EDSS is also highly correlated with walking measures, it is only minimally related to CST MTR or FA, which may reflect the specificity of the CST for walking measures. Conclusions: CST measures of MTR and FA are highly correlated with clinical walking performance in our MS cohort. Surprisingly, our data links brain CST to walking measures and highlights MTR as an important addition to structural MRI protocols. Evaluating structure-function relationships is a first step in the development of appropriate quantitative outcome measures; our next step is to determine the predictive value of these measures in evaluating intervention responsiveness.

Supported by: National Multiple Sclerosis Society

Disclosure: Nora E. Fritz, Rhul Marasigan, Jennifer Keller, Chen Chun Chiang: Nothing to disclose. Peter A. Calabresi: Biogen IDEC, Novartis (grant/research support); MedImmune, Prothera, Vaccinex, Vertex (consulting fees). Kathleen M. Zackowski: National Multiple Sclerosis Society (grant/research support).

Keywords: Imaging and MS, Magnetization transfer imaging

CHANGES IN STEP-DOWN KINEMATICS FOLLOWING 16 WEEKS OF SUPERVISED PROGRESSIVE RESISTANCE TRAINING FOR PEOPLE WITH MULTIPLE SCLEROSIS

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Background: Progressive resistance training (PRT) has been reported to increase strength and gait velocity in people with relapsing-remitting multiple sclerosis (RRMS), indicating an improvement to their functional ability. However, it is unclear whether increased strength in people with RRMS will result in similar changes to other functional tasks such as stepping off a curb or going down a step. Objectives: Determine the kinematic changes of a step-down task for people with RRMS who participate in 16 weeks of PRT. Methods: Nine individuals (8 females, 1 male) diagnosed with RRMS with an Expanded Disability Status Scale (EDSS) score of ≤6 participated in 16 weeks of PRT (mean age, 44 ± 12 years; height, 1.7 ± 0.1 m; mass, 77 ± 23 kg; EDSS, 2.8 ± 1.5). The PRT program followed the American College of Sports Medicine’s resistance training guidelines modified for people with RRMS. The program included three supervised sessions per week on nonconsecutive days. Resistance exercises were performed for all major muscle groups. Prior to and following 16 weeks of PRT, motion (100 Hz) and ground reaction force signals (1000 Hz) were collected while participants performed five step-down trials at a self-selected speed. Step-down height was set to 16 cm to mimic the average height of a sidewalk curb. Research variables of interest included step-down time and sagittal plane angular displacements for the lead and trailing legs. Mean differences and standard error of the mean differences were calculated to provide a descriptive analysis of the pre-post intervention changes. Variables displaying a pre-post mean difference of ≥0.1 second for step-down time and ≥3° for angular displacements were considered clinically meaningful. Results: Following the PRT program, people with RRMS displayed an 18% increase in leg strength (reported in a previous abstract) and a 10% decrease in step-down time (mean difference, 0.162 ± 0.070 second). No other clinically meaningful kinematic changes were detected. Conclusions: People with RRMS were able to increase leg strength and perform the step-down task more quickly, indicating a possible improvement in locomotor function following a 16-week PRT program. Furthermore, the ability to perform the step-down task faster without losing balance may also indicate improved balance and possibly more confidence in their ability to step down from a raised surface. Although changes to sagittal plane angular displacements went undetected, people with RRMS appear to benefit from participating in supervised PRT.

Supported by: Mary Ella Lunday Soule Scholarship

Disclosure: Nothing to disclose

Keywords: Disease-modifying treatments in MS, Resistance training

International Journal of MS Care
MULTIFOCAL VISUAL EVOGED POTENTIALS (MFVEP) AND GANGLION CELL INNER PLEXIFORM THICKNESS (GCIPT) IN RELAPSING-REMITTING MULTIPLE SCLEROSIS

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Background: The primary visual pathway is a good model for studying demyelination and neurodegeneration in multiple sclerosis (MS).

Objectives: To detect structural and functional damage using optical coherence tomography (OCT), multifocal visual evoked potentials (mVEP), and contrast sensitivity (CS) in relapsing-remitting multiple sclerosis (RRMS) eyes without active optic neuritis (ON).

Methods: SD-OCT, mfVEP, and Pelli-Robson CS were obtained in 90 RRMS patients. There were 105 eyes (no-ON) without a history of ON and 58 eyes (ON) with last ON ≥ 6 months. 40 age-matched normals had mfVEP and CS. MFVEP recorded with a 60-sector cortically scaled stimulus (22° radius, VERIS 5.1) provided local response amplitude (AMP) (logSNR) and relative latency (LAT) (ms). Global mfVEP AMP and LAT were calculated as mean logSNR and median LAT from 60 sectors. Mean GCIPT, average retinal nerve fiber layer thickness (ARNFLT), and temporal RNFLT (TRNFLT) from OCT were analyzed. Traditional pattern-reversal VEP (tVEP) was recorded (22° radius) in 30 patients and 34 normals; p100 AMP and LAT were calculated for 15', 60', and 120' checks. For mfVEP, CS, and tVEP, responses worse than 5% of norms were classified as abnormal. For OCT, values below 5% of age-matched machine norms were abnormal. Statistical analyses used proc Genmod (SAS 9.2) to account for age and intrasubject inter-eye correlation.

Results: MFVEP showed lower AMP and longer LAT in no-ON (P < .01) and ON (P < .0001) than normal (mean ± SE logSNR: 0.61 ± 0.02, 0.56 ± 0.01, 0.42 ± 0.02; relative LAT: 0.7 ± 0.5, 3.2 ± 0.7, 9.0 ± 1.6 in no-ON, and ON). Compared to normal (1.61 ± 0.01), mean CS was reduced in ON (1.40 ± 0.04, P < .001) but similar in no-ON (1.60 ± 0.01, P = .90). Mean GCIPT (µm) was 77.9 ± 0.9 in no-ON and 69.7 ± 1.7 in ON (P < .001). For no-ON, 23% had abnormal mfVEP in AMP, 25% in LAT and 47% in AMP or LAT. Among those with abnormal LAT, 65% had significant delay within the central 5.6°, the mfVEP region that corresponds best with the region measured by GCIPT. More no-ON eyes had abnormal GCIPT (20%) than ARNFLT (12%) or TRNFLT (13%) (P = .03 for both). 8% of no-ON had abnormal CS. For tVEP (120'), 3% of no-ON had abnormal AMP, 17% abnormal LAT, 23% abnormal AMP or LAT. Results of 15' and 60' were similar. For ON, percentages of abnormal AMP were 5% for mfVEP, 5% for GCIPT, 51% for ARNFLT, 44% for TRNFLT, and 38% for CS, and 74% for tVEP 120' AMP/LAT.

Conclusions: GCIPT and mfVEP offer complementary information on the integrity of the visual pathway and are useful for detecting subclinical neuronal defects in MS.

Supported by: National Institutes of Health (grants P30 EY07551 and T35 007088), Fight for Sight Summer Student Fellowship, Minnie Flaura Turner Memorial Fund for Impaired Vision Research

Disclosure: Divya Narayanan, Han Cheng, Laura Frishman: Nothing to disclose. Rosa Tang: Biogen, Serono (grant/research support, lecture fees), Novartis (grant/research support).

Keywords: Etiology of MS, Natural history of MS, Optical coherence tomography

RIGHT UNDER OUR NOSES: OLFACTORY PATHOLOGY IN CENTRAL NERVOUS SYSTEM DEMYELINATING DISEASES

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Background: Olfactory dysfunction is a common feature of multiple sclerosis (MS). Previous radiographic and pathological studies have attributed olfactory disturbance in MS to demyelination of the olfactory brain with the olfactory bulb and tract to be relatively spared.

Objectives: To determine whether olfactory bulb and tract pathology is a feature of MS and other inflammatory demyelinating diseases.

Methods: A human autopsy cohort of pathologically confirmed cases encompassing the spectrum of demyelinating disease (MS, n = 17; neumyelitis optica, n = 3; acute disseminated encephalomyelitis, n = 7) was compared to normal (n = 8) controls. For each case, olfactory bulbs and/or tracts were stained for myelin, axons, and inflammation.

Results: Olfactory bulb/tract demyelination was frequent in all demyelinating diseases (MS 12/17 [70.6%], acute disseminated encephalomyelitis 3/7 [42.9%], neuromyelitis optica 2/3 [66.7%]) but was absent in herpes simplex virus encephalitis, Alzheimers disease, and non-neurologic (n = 8) controls. For each case, olfactory bulbs and/or tracts were stained for myelin, axons, and inflammation.

Conclusions: Olfactory bulb/tract demyelination was frequent in all demyelinating diseases (MS 12/17 [77.6%], acute disseminated encephalomyelitis 3/7 [42.9%], neuromyelitis optica 2/3 [66.7%]) but was absent in herpes simplex virus encephalitis, Alzheimers disease, and non-neurologic controls. Inflammation was significantly greater in the demyelinating diseases compared to non-neurologic controls. Olfactory bulb/tract axonal loss was detected in all demyelinating diseases, being more severe in MS, where it correlated significantly with the extent of demyelination (r = 0.610, P = .009) and parenchymal inflammation (r = 0.681, P = .003). The extent of olfactory bulb/tract demyelination and inflammation mirrored that found in superficial cortical layers where subpial demyelination and inflammation were observed.

Disclosure: Nothing to disclose.

Keywords: Etiology of MS, Immunology and MS, Olfaction
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WHERE:  Product Theater Area (between Poster Boards and Exhibitor Lounge)
TIME:   12:00 pm-1:00 pm

TOPICS:
• Why patient preferences are an important consideration in MS
• Ways to successfully discuss and evaluate efficacy and safety
• Examples of effective shared decision-making

PANELISTS:

Christopher LaGanke, MD
Director, LaGanke, Multiple Sclerosis Center, Cullman, AL

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