INTERNATIONAL JOURNAL OF MS CARE

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Collage from the 2025 Art Showcase from the Multiple Sclerosis Association of America

2025 Annual Meeting of the Consortium of Multiple Sclerosis Centers

May 28-31, 2025 · Phoenix, Arizona

2025 OFFICIAL ABSTRACTS

ABSTRACTS FROM THE 39TH ANNUAL MEETING OF THE CMSC

Scan the QR code or click here to view the full-text Abstract Supplement or view it online at IJMSC.org.

Dear CMSC Community,

At Sanofi, **innovation fuels our pioneering spirit every day**. For over two decades, we have been committed to breaking new ground in our pursuit of solutions for people living with Multiple Sclerosis. As a main sponsor of CMSC, we are proud to stand alongside dedicated healthcare professionals who share our vision of transforming lives through scientific advancement.

Throughout this year's congress, you will witness **Sanofi's continued commitment to address key unmet needs in the MS community,** especially disability accumulation. We are not settling for established pathways—instead, we are actively pursuing the miracles of science to make a meaningful difference in patients' lives through innovation. Our teams are driven by the belief that by challenging conventional thinking, **we can discover breakthrough approaches** to benefit people living with MS.

The opportunity to gather for this 39th annual CMSC meeting is made possible by the extraordinary dedication of the CMSC team and faculty, to whom we extend our deepest gratitude. Your commitment to improving the lives of people impacted by MS continues to inspire our work. We are honored to support this community and remain keenly committed in collaborating to address the challenges that lie ahead.

Our sincere appreciation for your dedication to the MS community. It is our privilege to continue on this journey of discovery alongside each of you.

Best regards,

François-Xavier (FX) Etaix
General Manager, US Neurology - Sanofi

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INTERNATIONAL JOURNAL OF MS CARE
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2025 ANNUAL MEETING OF THE CMSC

The editorial team is pleased to present this supplement to the *International Journal of MS Care* (*IJMSC*) containing the abstracts from the 2025 Annual Meeting of the Consortium of Multiple Sclerosis Centers (CMSC). These abstracts include platform, poster, and Whitaker Research Track presentations. In the spirit of the age, a limited number of this supplement will be printed and available at the meeting and a digital version, including late-breaking abstracts, will be available to all on the *IJMSC* website at IJMSC.org. We would like to thank Sanofi for their support, which made this publication possible. I want to express my gratitude to all of the authors who are con- tributing, through their posters and presentations, to innovation and discovery in the field of comprehensive MS care. We hope that you will find ideas to explore in your own research or apply in your daily clinical practice in what is presented at this meeting.

—Francois Bethoux, MD
IJMSC Editor in Chief

Cover Art: 2025 MSAA Art Showcase

The Multiple Sclerosis Association of America (MSAA) proudly celebrates the artwork and stories of individuals with multiple sclerosis in the MSAA Art Showcase. For more than 15 years, MSAA has received many heartfelt and inspiring pieces from artists across the country. They are honored to share these stories and works of art with the MS community.

To view all of the artwork, please visit: **mymsaa.org/artshowcase2025**.

IJMSC is grateful for our continued partnership with the Multiple Sclerosis Association of America (MSAA) and is excited to feature the 2025 Art Showcase collage on this year's abstract books and on our covers throughout the year. Our sincere thanks to MSAA and the artists for allowing us to feature them.

Scan the QR code to view all of the artwork from MSAA's 2025 Art Showcase.

Please join us at a reception in honor of our partnership on Wednesday, May 28, at 5 pm in room 229B.

WHITAKER RESEARCH TRACK

(WH101) Anti-CD20 Therapies Mitigate the Impact of Social Drivers of Health on Multiple Sclerosis Outcomes

Alexandra Balshi,[1] John Dempsey,[2] Jacob Sloane[2]
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BACKGROUND: Disparities in social drivers of health (SDoH), such as race, ethnicity, employment status, educational attainment, marital status, health insurance coverage, and tobacco use, have been independently linked to disability accrual in people with multiple sclerosis (PwMS).OBJECTIVES: To determine if highly effective anti-CD20 therapies may attenuate disparities in multiple sclerosis (MS) outcomes along SDoH lines.
METHODS: We used multivariable linear mixed-effects modeling to evaluate if SDoH are associated with changes in Expanded Disability Status Scale (EDSS) scores and Timed 25-Foot Walk (T25FW) times during anti-CD20 treatment, controlling for age, sex, MS subtype, body mass index, pre-CD20 medication possession ratio, annualized relapse rate, and radiographic disease burden. We also evaluated how the Area Deprivation Index (ADI), a measure of neighborhood-level socioeconomic disadvantage, influences these outcomes when substituted for individual-level SDoH.
RESULTS: In a cohort of 239 PwMS receiving anti-CD20 therapies, we found that non-White racial identity, educational attainment, marital status, insurance type, and ADI were not significantly associated with EDSS or T25FW progression after adjusting for MS severity indicators. Instead, employment (β=−0.91, *P*<.001) was associated with EDSS decreases, while tobacco use was associated with EDSS and T25FW worsening (EDSS: β=0.59, *P*=.007; 25FTW: β=1.98, *P*=.003).
CONCLUSIONS: Anti-CD20 therapy may attenuate the effects of race, education, marital status, insurance coverage, and ADI on MS disability accrual and ambulatory impairment. Employment and tobacco use may still contribute to progression while individuals are on these high-efficacy DMTs.
DISCLOSURES: *Alexandra Balshi, John Dempsey: Nothing to disclose. Jacob Sloane: Banner, Biogen, Celgene, Genentech, Sanofi, Teva (consulting fee); National Multiple Sclerosis Society (contracted research).*
KEYWORDS: Disease-Modifying Treatments in MS, Economic Issues and MS, Employment in MS

(WH102) Exploring the Brain Networks Underlying Concern About Falling in MS: Amygdala, Hippocampal, and Cerebellar Connectivity

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BACKGROUND: Concern about falling (CAF) is a common and debilitating issue in multiple sclerosis (MS), contributing to poor health outcomes and diminished quality of life. While CAF is related to poor motor functioning, cognition, and emotional well-being, the underlying neural correlates remain unknown. Given the multifactorial nature of CAF, we hypothesized that neural correlates may involve interactions between core brain regions involved in emotional processing (eg, the amygdala) and those involved in motor (eg, cerebellum) and cognitive functions (eg, hippocampus).
OBJECTIVES: This study examined the associations between CAF and resting-state functional connectivity (FC) in the amygdala-hippocampal and amygdala-cerebellar circuits in individuals with MS.
METHODS: Participants with relapsing-remitting MS completed the Falls Efficacy Scale-International to assess CAF, followed by a functional MRI scan. Region of interest (ROI)-to-ROI analyses were used to examine associations between CAF and FC within the amygdala-hippocampal and amygdala-cerebellar circuits. Significant connections were identified using false discovery rate (FDR) correction at *P*<.05.
RESULTS: Forty-one individuals (33 women, ages 31-65 years, mean=47.56, SD=10.17) participated in our study. CAF was significantly associated with greater amygdala-hippocampal FC (L amygdala–L hippocampus: T[39]=5.88, *P*-FDR<.001; L amygdala–R hippocampus: T[39]=7.27, *P*-FDR<.001; R amygdala–R hippocampus: T[39]=6.97, *P*-FDR<.001; R amygdala–L hippocampus: T[39]=3.76, *P*-FDR=.001) and lower amygdala-cerebellar FC (L amygdala–L cerebellum: T[39]=−2.77, *P*-FDR=.016; L amygdala–R cerebellum: T[39]=−2.52, *P*-FDR=.026).
CONCLUSIONS: These findings highlight the neural correlates of CAF in MS, revealing distinct resting-state FC patterns in circuits relevant to motor, cognitive, and emotional processes. Higher CAF was associated with greater connectivity between the amygdala and hippocampus, suggesting that neural circuits underlying fear-related memories and emotional processing may play a crucial role in perceived fall risk. In contrast, lower amygdala-cerebellar connectivity in individuals with greater CAF may reflect diminished integration of emotional and motor responses, potentially compromising environmental assessment and fall-related hazard recognition. Gaining further insights into the neural underpinnings of CAF could identify specific brain regions and circuits that may benefit from interventions targeting CAF and its negative consequences in MS.
DISCLOSURES: *Taylor N. Takla, Reem Tamimi, Hilary A. Marusak, Nora E. Fritz: Nothing to disclose.*
KEYWORDS: Imaging and MS, Psychological Issues and MS

(WH103) Oral Microbiome Alterations in Multiple Sclerosis Characterized by Long Amplicon Sequencing

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BACKGROUND: Dysbiosis in the oral microbiome is associated with various inflammatory, hypersensitivity, and autoimmune disorders. Recent studies indicate that the oral microbiome may differ in people with MS (PwMS), but its characteristics and the interpretation of these differences remain poorly understood. Given the shared drainage of the oropharyngeal cavity and brain to the deep cervical lymph nodes, oral antigens may influence immune responses involved in MS. This makes the oral microbiome in PwMS an intriguing area for further investigation.
OBJECTIVES: To characterize and compare the oral microbiome of PwMS with healthy controls to identify changes that may affect MS pathophysiology.
METHODS: Gingival swabs were collected from newly diagnosed, untreated PwMS (n=55) and healthy controls (n=38). Bacterial DNA was amplified to generate 16S-ITS-23S long amplicons and sequenced using the PacBio system. K-mers, or short DNA sequences, were selected as initial biomarkers using statistical filters (total number of misclassifications, fold change, t-test) and refined collectively. Eight key k-mers were expanded into virtual probe sets, from which reads were extracted to form Amplicon Sequence Variants (ASVs). These ASVs, representing sequences differentially abundant between PwMS and controls, were matched to bacterial taxa using the Basic Local Alignment Search Tool (BLAST).
RESULTS: ASVs corresponding to *Haemophilus*, *Streptococcus*, *Neisseria*, and *Veillonella* were enriched in PwMS, while *Selenomonas* variants were depleted. BLAST analysis identified species matches with high similarity (> 99%) and coverage (100%). Certain proinflammatory species, such as *Veillonella parvula* and *Veillonella rogosae*, were enriched in PwMS.
CONCLUSIONS: Long amplicon sequencing revealed significant differences in the oral microbiome of PwMS, offering high taxonomic resolution to identify bacterial taxa that were enriched and depleted. Enrichment of proinflammatory species in PwMS may modulate immune function, providing insights into potential mechanisms of MS pathogenesis. Notably, the *Veillonella* species identified here have also been implicated in inflammatory bowel disease exacerbations, supporting their role in immune-mediated disease. Collectively, these microbial differences suggest oral dysbiosis in PwMS and highlight candidate taxa for further investigation. Future studies should validate these findings in larger cohorts and explore their impact on immune responses and disease progression.
DISCLOSURES: *Jordan Shaked, Stephen Vaughn, Nick Buitrago-Pocasangre: Nothing to disclose. Daniel Fasulo: Intus Biosciences (salary). Erin E. Longbrake: Alexion, Bristol Myers Squibb, EMD Sereno, Novartis, TG Therapeutics (consulting fee); Biogen (research support); Genentech (consulting fee, research support).*
KEYWORDS: Etiology of MS, Immunology and MS, Oral Microbiome

(WH104) Association Between Perceived Pain During Exercise and Neuromuscular Fatigue in People With Multiple Sclerosis

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BACKGROUND: Pain is a common symptom in people with MS (PwMS), affecting both physical and psychological functions. A theoretical model of the relationship between pain and neuromuscular fatigue suggests that under certain conditions, pain

experienced during exercise—a subcategory of movement-evoked pain (MEP)—may reduce central motor drive, leading to increased neuromuscular fatigue. Despite the prevalence of pain in PwMS, the relationship between perceived pain during exercise and neuromuscular function remains unclear.

OBJECTIVES: To investigate the association between perceived pain during exercise and neuromuscular fatigue in PwMS.

METHODS: Thirty-two PwMS (women=15) and 15 age- and sex-matched controls (women=7) were recruited. The experimental protocol involved maximal voluntary contractions (MVCs) of the dorsiflexors, time-to-task-failure (TTF) of an isometric fatiguing exercise sustained at maximal strength (neuromuscular fatigue), and a postexercise MVC. The twitch interpolation technique quantified voluntary activation (VA) pre- and post-exercise, with pre-to-post reductions in VA indicating central fatigue. Perceived leg pain (Numeric Pain Rating 0-10) was assessed pre-exercise (pre-ex), mid-exercise (mid-ex), and post-exercise (post-ex), with temporal changes and pre-to-post changes analyzed. Disease severity was evaluated using the Expanded Disability Status Scale.

RESULTS: The time-to-task-failure of exercise and central fatigue were not statistically different between PwMS and controls. However, PwMS with more severe disease (N=12) exhibited a significantly shorter TTF (PwMS: 71.6 ± 78.1 sec, controls: 110.1 ± 71.8 sec, P=.05) and higher central fatigue (12.6 ± 18.8% post-exercise reduction in VA in PwMS vs 1.6 ± 7.2% reduction in VA in controls, P=.02) compared with controls. Both PwMS and controls experienced a significant increase in leg pain during exercise (PwMS: pre-ex 0.3 ± 0.8, mid-ex 2.4 ± 2.7, post-ex 3.9 ± 3.7; controls: pre-ex 0.0 ± 0.0, mid-ex 2.6 ± 2.3, post-ex 4.1 ± 3.4), with no significant differences in temporal changes in pain observed between the groups (P=1.0). Among PwMS, pre-to-post exercise changes in pain correlated with TTF (r= 0.51, P=.003), central fatigue (r=0.4, P=.05), and disease severity (r=−0.41, P=.03).

CONCLUSIONS: In contrast to controls, perceived pain during exercise was related to neuromuscular fatigue in PwMS, possibly through pain avoidance adaptations within the nervous system to prevent muscle dysfunction. This suggests that pain may be an overlooked mechanism contributing to neuromuscular fatigue in PwMS. Both PwMS and controls exhibited increased pain perception with higher exercise intensity, possibly related to metabolite accumulation. These insights are valuable for researchers and clinicians in developing tailored pain-management strategies to improve neuromuscular function in PwMS.

DISCLOSURES: *Mitra Rouhani, Marie K. Hoeger Bement, Kathleen M. Zackowski, Sandra K. Hunter, Alexander V. Ng: Nothing to disclose. Ahmed Z. Obeidat: Alexion Pharmaceuticals, Amgen, AstraZeneca, Banner Life Sciences, Biogen, Bristol Myers Squibb, EMD Serono, Sanofi Genzyme, TG Therapeutics (consulting fee, speakers' bureau); BD Biosciences, Biologix Solutions, Celgene, Genentech, GW Pharmaceuticals, Horizon Therapeutics, Jazz Pharmaceuticals, Novartis, Sandoz, Viela Bio (consulting fee).*

KEYWORDS: Pain and MS, Neuromuscular Function and MS, Muscle Fatigue and MS

(WH105) Real-World Efficacy of Cladribine Tablets in a Canadian Tertiary Center Beyond 4 Years After Initiation

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BACKGROUND: Cladribine tablets are a widely-used treatment for relapsing multiple sclerosis (MS). Clinical trial data have demonstrated efficacy of cladribine up to 4 years after initiation, but there are limited real-world efficacy data beyond 4 years.

OBJECTIVES: To evaluate clinical and radiological disease activity and use of subsequent disease-modifying therapies (DMTs) in people with MS (PwMS) who received cladribine at a tertiary MS center.

METHODS: This was a retrospective study evaluating the first 111 PwMS who received cladribine at our MS center and were followed for up to 6.6 years after initiation. Data were extracted from the clinic registry. The proportions of PwMS with disease activity 18 months after cladribine initiation and the use of additional DMT over the follow-up period were assessed. Time to disease activity was evaluated using survival analysis. Cox-proportional hazards evaluated associations between clinical variables and disease activity.

RESULTS: Patients had a mean age of 36.6 years (SD=8.8), were predominately women (n=78, 70.3%), had a mean disease duration of 8.2 years (SD=6.1), and had a median Expanded Disability Status Scale (EDSS) score of 2.0 (range, 0.0-6.0). At a median follow-up of 5.3 years after cladribine initiation, 32.4% of patients (n=36) had a relapse, 64.0% (n=71) had MRI activity, and an additional DMT was required by less than half of participants (47.7%, n=53). Of participants who received additional DMT, an anti-CD20 agent (50.9%, n=27) or a third course of cladribine tablets (43.3%, n=23) were the most common sequencing strategies. At 6 years after initiating cladribine, 42.8% (95% CI, 29.2-62.7) of patients were relapse-free. Longer disease duration was associated with a lower risk of relapse (HR: 0.66, 95% CI, 0.44-0.98, P=.04). There were no associations with other demographic and clinical variables, including sex, age, spinal cord lesions, relapse in the year prior to cladribine initiation, annualized relapse rate, and baseline EDSS (all HRs 95%, CIs overlapping=1).

CONCLUSIONS: Cladribine demonstrates a favorable and durable efficacy profile in the real world 4 to 6 years after initiation. An additional DMT was required by less than half of individuals, with most going on to receive either a third cycle of cladribine or an anti-CD20 agent. Additional studies will be useful to fully understand the real-world durable efficacy and safety profile of cladribine tablets.

DISCLOSURES: *Katherine M. Sawicka, Arshia Vosoughi, Fasna Raufdeen, Melanie Guenette: Nothing to disclose. Reza Vosoughi, Daniel Selchen: Please complete/edit (consulting fee). Jiwon Oh: Biogen Idec, F. Hoffmann-La Roche (consulting fee, contracted research); Bristol Myers Squibb, Eli Lilly, EMD Serono, Novartis, Sanofi Genzyme (consulting fee).*

KEYWORDS: Cladribine, Disease-Modifying Treatments in MS, Epidemiology of MS

(WH106) B-Cell Repopulation and Biomarker Pathways in Multiple Sclerosis: Insights From Ofatumumab Therapy

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BACKGROUND: Anti-CD20 disease-modifying therapies (DMTs) like ofatumumab (Ofb) are effective in controlling disease activity in multiple sclerosis (MS). The long-term effects on B-cells and serum biomarkers are not fully understood. Analyzing these biomarkers can help refine personalized treatment strategies for people with MS (PwMS) on Ofb therapy.

OBJECTIVES: This study aims to investigate CD19+B cells and serum biomarkers in PwMS on Ofb.

METHODS: A retrospective cohort study was conducted at the University of Cincinnati Waddell Center for Multiple Sclerosis and included center patients with relapsing-remitting MS and active secondary-progressive MS who received at least 3 Ofb doses between January 2021 and November 2024. Variables collected included demographics, prior DMTs, relapses (steroid-treated), MRI activity (new T2 or contrast-enhancing lesions), and laboratory biomarkers. CD19+B-cell repopulation was defined as any CD19+count greater than 0. Biomarkers (Octave Bioscience) categorized pathway scores, and Multiple Sclerosis Disease Activity (MSDA) provided an overall disease activity score.

RESULTS: A total of 166 patients were included, with a mean (± SD) treatment duration of 585 (± 337) days. The mean (± SD) age was 43.92 (± 11.3) years; 80.7% were women, and 68% identified as White. Following Ofb initiation, mean CD19+B-cell counts and percentages were 2.22 ± 7.07 and 0.40 ± 1.87, respectively, with a significant reduction compared with prior anti-CD20 therapies (P<.001). No significant correlations were observed between B-cell repopulation and relapse rates (P=.3) or MRI activity (P=.4). CD19+B-cell levels showed no correlation with age, sex, body mass index, ethnicity, or disease duration. Serum biomarker analysis revealed significant decreases in Immunomodulation (P=.01), Neuroinflammation (P=.03), and Neuroaxonal Integrity Scores (P=.001), while Myelin Biology Scores were unchanged (P=.24). MRI activity was significantly correlated with Myelin Biology Scores (P=.02). Neurofilament light levels significantly decreased post-switch (P=.02), while fibronectin leucine-rich transmembrane protein 2, B cell-attracting chemokine 1, and C-C motif chemokine ligand 20 were associated with MRI activity (P<.05). Myelin oligodendrocyte glycoprotein levels were positively correlated with relapse rates (P=.01).

CONCLUSIONS: This study suggests that Ofb may reduce B-cell counts after switching from prior anti-CD20 therapies and may control inflammation through serum biomarker changes. However, small sample sizes and data variability limit the study's statistical power, warranting cautious interpretation.

DISCLOSURES: *Sara Esmaeili, Ravneet S. Sangha, Kiret S. Sangha, Alexander Mirzoev, Joseph LaPorta: Nothing to disclose. Kiranpal S. Sangha: TG Therapeutics (advisory board). W. Daniel Chapman: Amgen, EMD Serono/Merck (consulting fee); Biogen*

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KEYWORDS: Disease-Modifying Treatments in MS, Immunology and MS, Serum Biomarker

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PLATFORMS

DISEASE-MODIFYING THERAPIES

(PLA-A1) No Rebound Observed Following Ozanimod Discontinuation in Female and Male Participants in the DAYBREAK Open-Label Extension Study

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BACKGROUND: Patients discontinuing multiple sclerosis (MS) disease-modifying therapy (DMT) are at risk of disease reactivation. Rebound, characterized by severe disease activity and physical disability, is a concern with some DMTs. Compared with men, women with MS have higher relapse rates in general and, therefore, may be at greater risk of posttreatment relapse.

OBJECTIVES: This post hoc subgroup analysis assessed risk of relapse and relapse characteristics in women and men after ozanimod discontinuation during the DAYBREAK trial.

METHODS: DAYBREAK (NCT02576717) was a single-arm, open-label extension trial of ozanimod 0.92 mg/d for up to ~7 years that enrolled patients with relapsing MS who completed a phase 1 to phase 3 ozanimod trial (database lock: April 2023). During the study, the safety follow-up period was increased from an initial 28 days to 75 days and then 90 days. Confirmed MS relapses after permanent ozanimod discontinuation were analyzed for severity and disability in women and men who had safety follow-up and did not transition to commercial ozanimod.

RESULTS: Of 2494 DAYBREAK participants, 1679 (n =1120 women; n =559 men) were analyzed. After discontinuing ozanimod, 42 women (3.8%) and 13 (2.3%) men had an MS relapse during follow-up. Few participants (4.6% of women; 4.6% of men) initiated another DMT during the follow-up period; 1 female participant relapsed while using another DMT (fingolimod). Relapses occurred a median of 69 days (range, 3-141 days) after ozanimod discontinuation in women vs 43 days (range, 16-90) in men. Median increase in Expanded Disability Status Scale (EDSS) score at relapse vs before relapse was 1.0 (range, 0-3.0) in women and 0.5 (range, 0-2.0) in men; 6 of 42 (14.3%) women and 1 of 13 (7.7%) men had EDSS increases of greater than or equal to 2.0. The only relapse deemed severe by the investigator was in a woman whose EDSS score increased by 0.5 points; she partially recovered within 36 days. A larger proportion of women who relapsed were hospitalized compared with men (28.6% vs 15.4%), but a larger proportion of women completely recovered from relapse (81.0% vs 61.5%). An additional 16.7% of women and 30.8% of men had a partial recovery; 1 woman (2.4%) and 1 man (7.7%) did not recover.

CONCLUSIONS: Relapse rates after ozanimod discontinuation were low in both women and men, but a slightly larger proportion of women relapsed, consistent with previously reported higher relapse rates among women with MS vs men with MS. There was no evidence of higher-than-expected disease activity indicative of a rebound effect in either women or men.

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DISCLOSURES: *Ralf Gold: Abbott, Bayer Schering, Biogen, Bristol Myers Squibb, Chugai, Eisai, EMD Serono/Merck, Janssen, Nikkiso Pharma, Sanofi-Genzyme, Teva (contracted research, speakers' bureau); Baxter, Talecris, ZLB Behring (consulting fee); Bayer, Merck, Pfizer (personal stock); Novartis, Roche (contracted research, speakers' bureau, personal stock). Krzysztof W. Selmaj: Biogen, Celgene, Genzyme, Merck, Novartis, Ono Pharma, Roche, Synthon, Teva (consulting fee). Regina Berkovich: Alexion, Biogen, Bristol Myers Squibb, EMD Serono, Horizon, Johnson & Johnson, Mallinckrodt, Novartis, Sanofi (consulting fee). Jeffrey A. Cohen: Astoria, Atara, Biogen, Bristol Myers Squibb, Convelo, Viatris (consulting fee). Eva K. Havrdová: Actelion, Celgene, Sanofi Genzyme (advisory boards); Biogen, EMD Serono/Merck, Novartis (advisory boards and honoraria/research support); Czech Ministry of Education Project Cooperatio LF1, National Institute for Neurological Research (Programme EXCELES, ID project No LX22NPO5107), European Union-Next Generation EU (support); Roche, Teva (honoraria/research support). Hetal Desai, Zhaohui Liu, Corey Cusack, Shafeeq Dugger, Jon V. Riolo, Erik DeBoer: Bristol Myers Squibb (employee and/or shareholder). Andrew Thorpe: Bristol Myers Squibb (salary, shareholder). Bruce A.C. Cree: Alexion, Atara, Autobahn, Avotres, Biogen, Boston Pharma, EMD Serono, Gossamer Bio, Hexal/Sandoz, Horizon, Immunic AG, Neuron23, Novartis, Sanofi, Siemens, TG Therapeutics (consulting fee); Genentech (contracted research). Kyverna (consulting fee, contracted research).*

KEYWORDS: Disease-Modifying Treatments in MS, Women with MS

(PLA-A2) Placental and Breastmilk Transfer of Ocrelizumab From Women With Multiple Sclerosis to Infants and Potential Impact on B-Cell Levels: The Minore and Sopranino Trials

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BACKGROUND: Multiple sclerosis (MS) pregnancy and breastfeeding management prioritizes infant safety over the mother's risk of increased disease activity upon disease-modifying therapy discontinuation; prospective data to establish safety for mother and baby are lacking. Ocrelizumab (OCR) labeling advises use of contraceptives during treatment and for 6 months after the last administration.

OBJECTIVES: To measure placental and breastmilk transfer of OCR in women with MS and evaluate the impact on B-cell levels in infants potentially exposed during pregnancy (Minore NCT04998812) or breastfeeding (Sopranino NCT04998851).

METHODS: In Minore, 35 pregnant women with MS (≤ gestational week [W] 30), whose last OCR infusion occurred less than or equal to 6 months prior to the last menstrual period/during the first trimester, were enrolled. Primary end point was the proportion of infants with B-cell levels below the lower limit of normal (LLN) at W6 of life. In Sopranino, 13 breastfeeding women receiving OCR and their infants were enrolled (W2-W24 at first postpartum infusion). Co–primary end points were proportion of infants with B-cell levels less than LLN 30 days post infusion and OCR average daily infant dose (ADID) over 60 days post infusion. Key secondary end points were serum concentration of OCR in the infant's umbilical cord blood at W6 of life (Minore) and 30 days post maternal infusion (Sopranino).

RESULTS: Minore: OCR was undetectable in most infants' serum, both at birth in umbilical cord (33/35, 94.3%) and at W6 (32/33, 97.0%). When detectable, OCR levels were close to the limit of quantification and below therapeutic levels. Sopranino: OCR levels in breastmilk were negligible (mean ADID, 64.5 µg) and undetectable in infant serum at 30 days post infusion (9/9, 100%). All infant B-cell levels were above the age-specific LLN in Minore (W6 of life: 34/34, 100%) and Sopranino (30 days post infusion: 10/10, 100%). Adverse events were typical for delivery, postpartum, and infancy and aligned with the established OCR safety profile.

CONCLUSIONS: The results indicate that pregnancy planning and breastfeeding are compatible with OCR treatment and can support clinicians caring for women with MS in making evidence-based treatment decisions.

DISCLOSURES: *Riley Bove: Alexion, EMD Serono, Horizon, Janssen, Sanofi, TG Therapeutics (consulting fee); Biogen, Department of Defense, Eli Lilly, F. Hoffmann-La Roche, National Institutes of Health, National Multiple Sclerosis Society Harry Weaver Award, Novartis (funded by). Celia Oreja-Guevara: Alexion, Amgen, Biogen Idec, Bristol Myers Squibb, F. Hoffmann-La Roche, Horizon, Janssen, Merck, Neuraxpharm, Novartis, Sandoz, Sanofi-Genzyme, Teva Pharmaceuticals, Viatris (consulting fee, speaker fee). Sandra Vukusic: Biogen, EMD Serono/Merck, F. Hoffmann-La Roche, Novartis, Sanofi-Genzyme (consulting fee, contracted research, lectures or speaking); Bristol Myers Squibb/Celgene, Sandoz, Teva Pharmaceuticals (consulting fee, lectures or speaking); Janssen (consulting fee). Anna Shah: EMD Serono/Merck, Novartis, TG Therapeutics (consulting fee, speaking and advisory board compensation); F. Hoffmann-La Roche*

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KEYWORDS: Disease-Modifying Treatments in MS

(PLA-A3) A Phase 1 Dose-Escalation Study of BMS-986353, a CD19 NEX-T, Evaluating Safety and Tolerability in Relapsing or Progressive Forms of Multiple Sclerosis: Breakfree-2

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BACKGROUND: Therapies for relapsing (R) and progressive (P) multiple sclerosis (MS) have long-term toxicities and limited effect on disease progression. Novel chimeric antigen receptor (CAR) T-cell therapies may exert anti-inflammatory and immunomodulatory effects in multiple sites, such as the central nervous system, and induce an immune reset, leading to durable, treatment-free disease control (Müller F, Taubmann J, Bucci L, et al. CD19 CAR T-cell therapy in autoimmune disease-a case series with follow-up. *N Engl J Med*. 2024;390(8):687-700. doi:10.1056/NEJMoa2308917). BMS-986353 is a CAR T-cell therapy expressing the CD19-directed CAR used in US Food and Drug Administration–approved lisocabtagene maraleucel; the NEX-T® manufacturing process shortens manufacturing time and optimizes phenotypic attributes. We report data on BMS-986353 for the first 2 treated patients with MS from Breakfree-2 (NCT06220201).

OBJECTIVES: Evaluate safety and tolerability of BMS-986353 in MS and determine recommended phase 2 dose.

METHODS: This phase 1 multicenter study investigates BMS-986353 in RMS or PMS. Disease-modifying therapies were not administered after leukapheresis. A single BMS-986353 infusion (5×10^6 CAR+T cells [dose level 1]) was administered 2 to 9 days after lymphodepletion.

RESULTS: As of September 24, 2024, 6 patients had undergone leukapheresis; 2 patients with highly active relapsing-remitting MS (RRMS) were treated with BMS-986353. One was a 33-year-old man diagnosed in 2011 with an Expanded Disability Status Scale (EDSS) score at screening of 3.0; his prior MS treatments included alemtuzumab, glatiramer acetate, Iβ-1a, fingolimod, natalizumab, ocrelizumab, ofatumumab, and ublituximab. The other was a 30-year-old woman diagnosed in 2022 with an EDSS score at screening of 3.5; her prior MS treatments included ocrelizumab. Low-grade treatment-emergent adverse events occurred in both patients. One had grade 1 cytokine release syndrome (CRS) treated with paracetamol that lasted 1 day. Neither had dose-limiting toxicities, immune effector cell–associated neurotoxicity syndrome (ICANS), infections, or transient/reversible grade 3 or greater neutropenia or thrombocytopenia. At day 29, week 8, and week 12, MRI showed no new T2 or gadolinium-enhanced lesions in the man, and no other lesions concerning for infectious or other demyelinating etiology were observed. Follow-up MRI data were not available for the woman. Both had complete B-cell depletion.

CONCLUSIONS: BMS-986353 showed promising initial safety in patients with highly active RRMS, with no ICANS observed and 1 patient with transient low-grade CRS. Enrollment is ongoing. Updated safety, pharmacokinetic, and translational data will be presented.

DISCLOSURES: *Refik Pul: Alexion, Amgen, Hexal, Merck Serono, Novartis, Sanofi Aventis (consulting fee); Apurano, Bristol Myers Squibb, Merck Serono, Novartis, Roche, Sanofi Aventis (contracted research); German Multiple Sclerosis Society (speakers' bureau). Bastian von Tresckow: AbbVie, AstraZeneca, Bristol Myers Squibb/Celgene, Gilead Kite, Incyte, Janssen-Cilag, Lilly, Merck Sharp & Dohme, Novartis, Roche, Takeda (honoraria); AbbVie, AstraZeneca, Gilead Kite, Janssen-Cilag, Lilly, Merck Sharp & Dohme, Novartis, Pierre Fabre, Roche, Takeda (travel support); Allogene, Amgen, Bristol Myers Squibb/Celgene, Cerus, Gilead Kite, Incyte, IQVIA, Janssen-Cilag, Lilly, Merck Sharp & Dohme, Miltenyi, Noscendo, Novartis, Pentixapharm, Pfizer, Pierre Fabre, QualWorld, Regeneron, Roche, Sobi, Takeda (consulting fee); Esteve (Inst), Merck Sharp & Dohme (Inst), Novartis (Inst), Takeda (Inst) (contracted research); Regeneron, Takeda (steering committee). Swathi Namburi: GSK, Janssen, Pfizer, Sanofi (consulting fee). Claire S. Riley: Amgen, Bristol Myers Squibb, Cabaletta Bio, EMD Serono, Genentech, Immunic AG, Novartis, Roche, TG Therapeutics, Viracta (consulting fee). Bonaventura Casanova: Nothing to disclose. Ran Reshef: Allogene, Autolus, Bayer, Gilead Sciences, Incyte, Orca Bio, Quell Therapeutics, Sana Biotechnology, TScan (consulting fee); AbbVie, Allogene, Atara Biotherapeutics, Bristol Myers Squibb, Cabaletta, CareDx, Genentech, Gilead Sciences, Immatics, Imugene, Incyte, Johnson & Johnson, Sanofi, Synthekine, Takeda, TCR2, TScan, (contracted research); Novartis (fees for non-CME/CE services). Francisco Pérez Miralles: Amgen (speakers' bureau); Bristol Myers Squibb, Janssen, Neuraxpharm, Novartis, Roche, Sanofi (consulting fee, speakers' bureau). Lisa Kelly, Lingyun Lyu, Alexis Melton, Burhan Chaudhry, Ashley Koegel: Bristol Myers Squibb (salary). Rafael Sarmiento, Sharmila Das, Jerill Thorpe, Samantha By: Bristol Myers Squibb (ownership interest, salary). Pavle Repovic: Alexion/AstraZeneca (speakers' bureau); Biogen, Bristol Myers Squibb (contracted research, speakers' bureau); EMD Serono/Merck (consulting fee); Genentech (consulting fee, contracted research, speakers' bureau); Horizon/Amgen, Novartis, TG Therapeutics (consulting fee, speakers' bureau).*

KEYWORDS: CAR T-Cell Therapy, Disease-Modifying Treatments in MS, Immunology and MS

(PLA-A4) Disability Outcomes in Tolebrutinib Phase 3 Trials in Nonrelapsing Secondary Progressive Multiple Sclerosis and Relapsing Multiple Sclerosis

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BACKGROUND: Tolebrutinib is a brain-penetrant and bioactive Bruton tyrosine kinase inhibitor that modulates immune mechanisms within the central nervous system, including those driven by disease-associated microglia and B cells. Therefore, tolebrutinib may affect chronic smoldering neuroinflammation, thought to be a key driver of disability accrual.

OBJECTIVES: To evaluate disability outcomes and safety results from phase 3 trials of tolebrutinib in nonrelapsing secondary progressive multiple sclerosis (nrSPMS) and relapsing multiple sclerosis (RMS).

METHODS: HERCULES (NCT04411641), GEMINI 1 (NCT04410978), and GEMINI 2 (NCT04410991) were phase 3, double-blind, event-driven trials of tolebrutinib 60 mg once daily. In HERCULES, participants with nrSPMS were randomly assigned 2:1 to receive tolebrutinib or placebo. In GEMINI, participants with RMS were randomly assigned 1:1 to receive tolebrutinib or teriflunomide (14 mg once daily), each with matching placebo. Time to onset of 6-month confirmed disability progression (CDP) was the primary end point in HERCULES, and time to onset of 6-month confirmed disability worsening (CDW) in the pooled GEMINI 1 and GEMINI 2 data sets was a key secondary end point in the GEMINI trials. Time to onset of 6-month confirmed disability improvement (CDI) was a secondary end point in all trials.

RESULTS: HERCULES enrolled 1131 participants with a mean age of 48.9 years and mean Expanded Disability Status Scale (EDSS) score of 5.5 (median, 6.0). GEMINI 1 and GEMINI 2 enrolled 1873 participants with a mean age of 36.5 years and mean EDSS score of 2.4 (median, 2.0). Tolebrutinib demonstrated a 31% risk reduction in 6-month CDP vs placebo ($P = .0026$) in HERCULES and a 29% risk reduction in 6-month CDW vs teriflunomide (nominal $P = .0225$) in GEMINI 1 and 2. The probability of achieving 6-month CDI was 88% greater with tolebrutinib vs placebo (nominal $P = .0206$) in HERCULES and numerically higher with tolebrutinib vs teriflunomide in GEMINI 1 and 2. Alanine aminotransferase increases greater than 20 times the upper limit of normal were observed in 0.5% of participants with tolebrutinib across all trials, all occurring within 90 days of treatment start.

CONCLUSIONS: Tolebrutinib had a consistent impact on disability across phase 3 trials involving participants with nrSPMS and RMS. This is the first evidence of a significant slowing of disability accrual in people with nrSPMS.

DISCLOSURES: *Robert J. Fox: AB Science, Bristol Myers Squibb, Eli Lilly, EMD Serono, Genentech, Greenwich Biosciences, Immunic, INmune Bio, Janssen, Siemens, TG Therapeutics (consulting fee); Biogen, Novartis, Sanofi (consulting fee, research support). Bruce A.C. Cree: Alexion, Atara, Autobahn, Avotres, Biogen, Boston Pharmaceuticals, EMD Serono, Gossamer Bio, Horizon, Immunic, Neuron23, Novartis, Sandoz, Sanofi, Siemens, TG Therapeutics, Therini (consulting fee); Genentech (research). Amit Bar-Or: Accure, Atara, Biogen, BioTherapeutics, Bristol Myers Squibb, GSK, Gossamer, Janssen, MedImmune, Sanofi (speaking and/or consulting); Biogen Idec (grant support to institution); EMD Serono, Novartis, Roche Genentech (grant support to institution, speaking and/or consulting). Sana Syed, Wendy S. Vargas, Zhixing Xu, Timothy J. Turner: Sanofi (employees). Jiwon Oh: Amgen, Eli Lilly, EMD Serono, Novartis, Sanofi (consulting and/or speaking); Biogen, Roche (consulting and/or speaking; research).*

KEYWORDS: Clinical Trial, Tolebrutinib, Disease-Modifying Treatments in MS

(PLA-A5) Fenebrutinib Maintains Low Disease Activity in Relapsing Multiple Sclerosis: Results From the FENopta Open-Label Extension

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BACKGROUND: Fenebrutinib (FEN) is a potent, highly selective, noncovalent, reversible Bruton tyrosine kinase inhibitor. In the phase 2 FENopta study (NCT05119569), FEN reduced acute inflammatory disease activity and showed central nervous system penetrance in people with relapsing MS (PwRMS).

OBJECTIVES: To evaluate efficacy, safety, and exploratory biomarkers after FEN treatment in the FENopta open-label extension (OLE) through week (W) 48.

METHODS: PwRMS received FEN 200 mg or placebo (PBO) orally twice daily during the double-blind treatment period (DBTP). All received FEN during the OLE. Disease activity was evaluated through protocol-defined relapses and brain MRI. Adverse events (AEs) and exploratory biomarkers (B-cell and immunoglobulin [Ig] levels) were also assessed.

RESULTS: The OLE enrolled 99 PwRMS (DBTP: 65 FEN, 34 PBO); 96 (97%) remain in the study. Annualized relapse rate was 0.04, and 96% were relapse free. At OLE W48, the mean number of new T1 gadolinium-enhancing lesions (Gd+Ls) was 0.015 lesions per scan (n = 67) and 99% of pwRMS were free of new Gd+Ls. At OLE W48, the adjusted annualized rate of new or enlarging T2 lesions was 0.16 (95% CI, 0.044-0.60) in the FEN-FEN arm and 0.13 (95% CI, 0.022-0.78) in the PBO-FEN arm. In the DBTP, T2 lesion volume (T2LV) increased with PBO (0.36 cm^3; 95% CI, −0.081 to 0.79) but decreased with FEN (−0.11 cm^3; 95% CI, −0.43 to 0.21) relative to baseline (BL). In the OLE, T2LV reversed to near BL with PBO-FEN (0.03 cm^3; 95% CI, −0.28 to 0.35) and continued to improve with FEN-FEN (−0.33 cm^3; 95% CI, −0.57 to −0.095) relative to BL. There was no change in median Expanded Disability Status Scale score at OLE W48 vs BL. In the OLE through W48, no evidence of disease activity with 3 components was achieved by 89.6% of PwRMS. At OLE W24, the FEN-FEN arm had reductions from BL in $CD3^-CD19^+$ B-cell counts (n = 62; 21%; 95% CI, 17%-25%), IgM (22.7%), and IgG (n = 63; 5.8%). One PwRMS (1%) experienced 2 serious AEs (urinary tract infection, nephrolithiasis). Most common AEs (> 5% of PwRMS) were urinary tract infection (8%), COVID-19 (7%), and pharyngitis (5%). An asymptomatic alanine transaminase elevation newly occurred in 1 OLE PwRMS (1%) at 16 weeks of treatment and resolved with treatment discontinuation.

CONCLUSIONS: PwRMS treated with FEN for 1 year had near complete suppression of acute inflammatory disease activity. FEN maintained a favorable safety profile, with high OLE patient retention. Reductions in B-cell and Ig levels were observed. Three phase 3 clinical trials are underway in MS.

DISCLOSURES: *Amit Bar-Or: Abata, Accure, Atara Biotherapeutics, Bristol Myers Squibb/Celgene/Receptos, GSK, Gossamer, Horizon Therapeutics, Immunic, Janssen/Actelion, MedImmune, Novartis, Sangamo, Sanofi-Genzyme, Viracta (consulting fee); Biogen Idec, F. Hoffmann-La Roche, Merck/EMD Serono (consulting fee, contracted research); Genentech (contracted research). Jiwon Oh: Biogen Idec, F. Hoffmann-La Roche (consulting fee, contracted research); BMS, Eli Lilly, EMD Serono, Novartis, Sanofi Genzyme (consulting fee). Michal Dufek: Nothing to disclose. Hrvoje Budincevic: Bayer, Medis, Novartis, Pliva/Teva (fees for non-CME/CE services). Mario Habek: Biogen, F. Hoffmann-La Roche, Merck, Novartis, Pliva/Teva, Sanofi Genzyme (consulting fee). Maresa Caunt Mitzner, Christopher Harp, David Clayton, Ying-Fang Chen, John N. Ratchford, Alexandra Goodyear: F. Hoffmann-La Roche (royalty); Genentech (salary). Malgorzata Sierzega: F. Hoffmann-La Roche (royalty, salary). Jelena Drulovic: Amicus, AstraZeneca, Bayer Schering Pharma, Biogen Idec, Hemofarm, Janssen, Medis, Novartis, Sanofi Genzyme, Teva (speakers' bureau); F. Hoffmann-La Roche, Merck Serono (contracted research, speakers' bureau).*

KEYWORDS: Disease-Modifying Treatments in MS

(PLA-A6) Safety and Efficacy of Frexalimab From the Phase 2 Open-Label Extension in Participants With Relapsing Multiple Sclerosis: Two-Year Results

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BACKGROUND: Frexalimab, a second-generation anti-CD40L antibody, blocks the CD40/CD40L pathway, which is important in regulating both adaptive and innate immunity. In the double-blind period of a phase 2 trial (NCT04879628) involving participants with relapsing multiple sclerosis (PwRMS), frexalimab was well tolerated and efficacious at reducing disease activity, with an 89% reduction in new gadolinium-enhancing (Gd+) T1 lesions with 1200-mg intravenous (IV) frexalimab treatment vs placebo at week (W) 12.

OBJECTIVES: To report safety and efficacy of frexalimab at W96 in the phase 2 open-label extension (OLE).

METHODS: The 129 participants were randomly assigned (4:4:1:1) to IV frexalimab 1200 mg every 4 weeks or subcutaneous (SC) frexalimab 300 mg every 2 weeks or matching placebo. After W12, participants receiving placebo switched to respective frexalimab arms and entered the OLE. During OLE, the SC dose was increased to 1800 mg every 4 weeks (first high dose administered August 21, 2023), resulting in a similar frexalimab exposure to the 1200-mg IV dose every 4 weeks. Of the participants in the SC arms, 36 of 57 (63%) had their W96 MRI assessments after receiving this high-dose frexalimab. Key end points included safety and efficacy outcomes (number of Gd+ T1 lesions, new/enlarging T2 lesions, annualized relapse rate [ARR]).

RESULTS: As of July 22, 2024, 106 study participants (82%) remained on treatment (W96 cutoff). At W96, total number of Gd+ T1 lesions (mean [SD]) remained low in participants who continued receiving frexalimab and those who switched from placebo to frexalimab at W12 (IV arms: IV frexalimab 1200 mg, 0.1 [0.5]; IV placebo/IV frexalimab 1200 mg, 0.1 [0.3]; SC arms: 0.4 or below across all groups). New/enlarging T2 lesion monthly count remained low with IV frexalimab 1200 mg through W96. ARR (baseline through W96) was low (0.08; 95% CI, 0.03-0.18) in the IV frexalimab 1200-mg arm; 92% of participants were relapse free. Frexalimab was well tolerated through W96. The most

common adverse events in the OLE were nasopharyngitis, headache, and COVID-19.

CONCLUSIONS: Frexalimab continues to show favorable safety and sustained reduction in disease activity in PwRMS through W96, supporting its further development in phase 3 trials as a potential high-efficacy, non–lymphocyte-depleting therapy.

DISCLOSURES: *Patrick Vermersch: AB Science, Ad Scientiam, Biogen, Bristol Myers Squibb, Celgene, Imcyse, Janssen, Merck, Novartis, Roche, Sanofi, Teva (honoraria and/or consulting fees); Novartis, Roche, Sanofi (research support). Cristina Granziera: Actelion, GeNeuro, Hoffmann La Roche, Novartis, Sanofi, Siemens (advisory boards/consulting fees to institution); Biogen, Hoffmann La Roche, Janssen, Merck, Novartis, Sanofi, Teva (speaker fees); Biogen, GeNeuro, Hoffmann La Roche, Sanofi (research grants). Yang Mao-Draayer: Acorda, Bayer, Biogen, Bristol Myers Squibb/Celgene, Chugai, EMD Serono, Genentech-Roche, Horizon/Amgen, Janssen, Novartis, Sanofi, Teva (consulting and/or speaker fees); Chugai, Genentech-Roche, National Institute of Allergy and Infectious Diseases Autoimmune Center of Excellence, National Institutes of Health National Institute of Neurological Disorders and Stroke, Novartis, Patient-Centered Outcomes Research Institute, Sanofi (research support). Gary Cutter: Alexion, Antisense Therapeutics, Biogen, ClinTrialSolutions LLC, Entelexo Biotherapeutics, Genentech, GW Pharmaceuticals, Immunic, Immunosis, Klein Buendel, Merck/Serono, Novartis, Perception Neuroscience, Protalix BioTherapeutics, Regeneron, Roche, SAB Biotherapeutics, Sanofi (consulting/advisory boards); AI Therapeutics, AMO Pharma, Applied Therapeutics, AstraZeneca, AveXis, BioLineRx, BrainStorm Cell Therapeutics, Bristol Myers Squibb/Celgene, CSL Behring, Galmed, Green Valley, Horizon, Immunic, Karuna Therapeutics, Mapi Pharma, Merck, Mitsubishi Tanabe Pharma Holdings, National Heart, Lung, and Blood Institute Protocol Review Committee, Novartis, Opko Biologics, Prothena Biosciences, Reata, Regeneron, Sanofi, Teva, University of Texas Southwestern, University of Pennsylvania, Visioneering Technologies (data and safety monitoring boards). Pythagoras Birmingham (president): University of Alabama-Birmingham (employee). Oleksandr Kalbus: Bristol Myers Squibb/Celgene, Genentech, GeNeuro, Mapi Pharma, Merck, Novartis, Roche, Sanofi, Teva, Viela Bio (honoraria, consulting and/or speaker fees). Ivan Staikov: Adapt, Bayer, Boehringer Ingelheim, Ewopharma-Biogen, F. Roche, Gedeon Richter, Gerot Lannach, Medochemie, Merck, Mylan, Nobelpharma, Novartis, Penumbra, Pfizer, Polpharma, Sanofi, Shire, Teva, Viatris (travel funding, consulting fees, and/or speaker honoraria). Michal Dufek: Sanofi (study coordinator). Xavier Montalban: AbbVie, Actelion, Alexion, BIAL, Biogen, Bristol Myers Squibb/Celgene, European Committee for Treatment and Research in Multiple Sclerosis, EMD Serono, Excemed, Genzyme, Hoffmann-La Roche, Immunic Therapeutics, Janssen Pharmaceuticals, MedDay, Medscape, Merck, Multiple Sclerosis International Federation, Mylan, National Multiple Sclerosis Society, NervGen, Neuraxpharm, Novartis, PeerVoice, Samsung-Biosys, Sandoz, Sanofi-Genzyme, Teva Pharmaceuticals, TG Therapeutics, or any of their affiliates (lecture honoraria, travel expenses, scientific meetings, clinical trial steering committee membership, or clinical advisory board fees to institution). Stephen Krieger: Biogen, Novartis (grant and research support); Biogen, EMD Serono, Genentech, Novartis (nonpromotional speaking); Biogen, EMD Serono, Genentech, Genzyme, Mallinckrodt, MedDay, Novartis, Octave, Teva, TG Therapeutics (consulting or advisory work). Stephane Saubadu, Xiaodong Luo, Brendan Smyth, Biljana Djukic, Philippe Truffinet, Erik Wallstroem: Sanofi (employee). Gavin Giovannoni: AbbVie, Actelion, Atara Biotherapeutics, Biogen, Canbex, Celgene, EMD Serono, Genentech, GSK, GW Pharma, Japanese Tobacco, Merck, Novartis, Roche, Sanofi, Synthon BV, Teva (research support/consulting/speaker fees).*

KEYWORDS: Disease-Modifying Treatments in MS

DISEASE MANAGEMENT

(PLA-B1) Impact of Relapses on Quality of Life and Economic Disease Burden in Patients With Neuromyelitis Optica Spectrum Disorder in the United States

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BACKGROUND: Anti–aquaporin-4 antibody-positive (AQP4-Ab+) neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune disease characterized by repeated, unpredictable relapses, often leading to irreversible neurological disability. Evaluation of the incremental impact of relapses on quality of life (QOL) and indirect costs is needed to understand the full impact of NMOSD.

OBJECTIVES: To assess the impact of relapses on QOL and economic burden in patients with AQP4-Ab+ NMOSD in 2023 in the United States.

METHODS: An independent, electronic survey (January-April 2024) was used to collect QOL data (Euro-QoL 5-dimension 5-level [EQ-5D-5L] index score and "health today" scores per the EQ-5D-5L visual analogue scale [0-100, with 100 being "the best health you can imagine"]) and indirect cost data among patients with self-reported AQP4-Ab+ NMOSD. Data were compared between patients who experienced 1 or more relapses in 2023 vs those who did not. EQ-5D-5L index score (0 ["a state as bad as being dead"] to 1 ["full health"]) and health today scores (0 ["worst"] to 100 ["best"]) were also compared across treatments and treatment groups, regardless of relapses.

RESULTS: Data were available for 209 patients (female, 76%; mean ± SD age, 45.1 ± 12.6 years; 44% reported a relapse in 2023). For all patients, regardless of relapses, mean EQ-5D-5L index score was 0.45 and mean health today score was 53. Mean EQ-5D-5L index score was 0.43 for patients with a relapse in 2023 vs 0.57 for those without ($P < .01$). Mean health today score was 51.5 for patients with a relapse vs 62.1 for those without ($P < .01$). EQ-5D-5L index scores ranged from 0.31 for patients on plasma exchange (PLEX) to 0.59 for those on eculizumab, and health today scores ranged from 49 for patients on either PLEX or intravenous immunoglobulin to 62 for those on eculizumab. Mean (± SD) total indirect cost was significantly higher for patients with a relapse than for those without ($57,327 [± 39,564] vs $44,423 [± 36,042]; $P = .016$), with lost productivity accounting for 74% of the total indirect costs ($42,051 [± 34,478] vs $32,755 [± 32,673]; $P = .049$). Patients with relapses received higher government and other financial assistance than those without ($21,609 vs $10,632; $P = .023$).

CONCLUSIONS: Patients with AQP4-Ab+ NMOSD who experienced relapse in 2023 reported significantly worse QOL and higher indirect costs than patients who did not experience relapse. Patients currently on eculizumab reported the highest QOL in the sample. Given the impact of relapses on QOL, health care providers should strive for 0 relapses in patients with AQP4-Ab+ NMOSD.

DISCLOSURES: *Benjamin J. Osborne: Alexion, Amgen, AstraZeneca Rare Disease (speakers' bureau, medical scientific advisory boards); TG Therapeutics (medical scientific advisory boards); UCB (speakers' bureau); UpToDate (royalty). Mayvis Rebeira, Justin Lee, Martin Kleman, Sami Fam: Alexion, AstraZeneca Rare Disease (salary, stock). Evanthia Bernitsas: Biogen, Janssen (speakers' bureau); Roche/Genentech (research support to institution).*

KEYWORDS: Comprehensive Care and MS, Economic Issues and MS, NMOSD

(PLA-B2) The MS-Link Outcomes Study: Study Design and Descriptive Analyses of Patient-Reported Outcomes, Disease, and Sociodemographic Characteristics

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BACKGROUND: There are currently few multiple sclerosis (MS) observational studies in North America focused on collecting comprehensive longitudinal real-world data with an emphasis on patient-reported outcomes (PROs). Here we describe the MS-LINK Outcomes Study, a multicenter, prospective, longitudinal real-world study focused on collecting both patient- and provider-reported outcomes in sites across the US, which aims to develop a comprehensive and representative source of data on patients with MS.

OBJECTIVES: To describe the design of the MS-LINK Outcomes Study and provide an overview of the sociodemographic characteristics of the study population and key provider- and patient-reported outcomes.

METHODS: The MS-LINK Outcomes Study aimed to enroll adults with MS from diverse centers across the US to be followed for up to 3 years, with patient and disease characteristics, clinical and functional outcomes, and PRO measures collected at baseline and subsequent regular intervals. Electronic medical record data, if available, were collected on a regular basis via automated extraction; otherwise, provider-reported data were collected by manual online entry. Patient-reported data were collected digitally, and participating patients had ongoing access to their own data via a web-based patient portal.

RESULTS: As of study completion in May 2024, a total of 2172 patients were enrolled. The study population was diverse in terms of age, race, and ethnicity. Approximately 85% of patients reported using a disease-modifying therapy at baseline; infusion ther-

apies were most frequently used. Baseline completion rates were greater than 85% for each of the key PRO questionnaires, indicating high patient engagement. Longitudinal PRO scores and clinical tests are described for the entire cohort and for subgroups of interest, such as by age.

CONCLUSIONS: The MS-LINK Outcomes Study uniquely utilized a decentralized trial approach. The use of digital dashboards in the patient and provider portals provides real-time tracking of outcomes and a comprehensive view of the patient experience, allowing the patients and providers to use up-to-date monitoring in clinical or personal settings, whereas the diverse patient population improves the generalizability of study findings and facilitates future subgroup analyses.

DISCLOSURES: *Jeffrey English: Atlanta Neuroscience Institute (medical director); Biogen Idec, Celgene, EMD Serono, Genentech, Genzyme, Mallinckrodt, Novartis, Teva (advisory boards and speaker panels); Healthcare Impact Partners, HIPnation Operations & Solutions (creator, partner, stockholder). Carlo Tornatore: Atara, Biogen, EMD Serono, Genentech, Sanofi, TG Therapeutics (advisory boards); Biogen, EMD Serono, Sanofi (research funding). Emily Riser: Nothing to disclose. Gabriel Pardo: AbbVie, Adamas, Alkermes, Biogen Idec, EMD Serono, Novartis, Roche/Genentech, Sanofi-Genzyme, Teva (research support); Alexion, Biogen Idec, Celgene/Bristol Myers Squibb, EMD Serono, Horizon/Amgen, Novartis, Roche/Genentech, Sanofi-Genzyme, TG Therapeutics (speaker honoraria and/or consulting fees); Cadenza Bio, Progentec Diagnostics (advisory board). Léorah Freeman: EMD Serono, Genentech, Hoffmann La Roche, Horizon Therapeutics, Sanofi, TG Therapeutics (advisory board, consulting fees); Genentech, Medscape, Merck, Multiple Sclerosis Association of America (honoraria); EMD Serono, Genentech, National Institutes of Health National Institute of Neurological Disorders and Stroke, Patient-Centered Outcomes Research Institute, Sanofi (grant support). Jacob Sloane: Banner, Biogen, Celgene, Genentech, Sanofi, Teva (consulting fee); National Multiple Sclerosis Society (contracted research). Jeanie Cote: Biogen, Bristol Myers Squibb, EMD Serono, Novartis, Sanofi, TG Therapeutics (consulting fees, honoraria for education, speaking fees). Rana Zabad: Adamas, Biogen, EMD Serono, Genentech, Novartis, Patient-Centered Outcomes Research Institute, Sanofi, Sun Pharma (site investigator/principal investigator for clinical trials); Bayer, Biogen, Celgene/Bristol Myers Squibb, EMD Serono, Genentech, Genzyme, TEVA Neuroscience, TG Therapeutics (consulting fee); MedDay Pharmaceuticals, Parexel (adjudication committee for clinical trial); Bristol Myers Squibb, Genentech, Novartis, Sanofi, TEVA Neuroscience (sponsored unbranded lectures). Tania Reyna: Alexion, Biogen, EMD Serono, TG Therapeutics (consulting fee); Biogen, EMD Serono, Novartis, TG Therapeutics, UCB (research support). Elizabeth Piette, Christina Caon: EMD Serono (salary). Terrie Livingston: EMD Serono (former employee); Octave Bioscience (salary).*

KEYWORDS: MS-LINK Outcomes Study, Patient-Reported Outcomes, Disease-Modifying Treatments in MS

(PLA-B3) Reduce Your Risk of Falls: A Group Coaching Program to Increase Mobility Confidence and Reduce Fall Risk in People With Multiple Sclerosis

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BACKGROUND: Over 50% of people with multiple sclerosis (MS) fall at least once in 6 months, with many falling repeatedly.[1] In MS, fall incidence is similar to that of adults older than 80 years (~ 50%).[2] Falls cause injuries, loss of mobility confidence, social isolation, and reduced quality of life. All-falls medical costs in the United States are estimated at $80 billion.[3] Can Do MS (CDMS) provides programs with actionable information and connection opportunities to help people meet the challenges of MS. In 2023, CDMS developed and delivered a 4-session group coaching program on reducing fall risk.

OBJECTIVES: To help people with MS (1) reduce factors that contribute to falls, (2) become knowledgeable about tools and strategies that reduce fall risk, (3) increase mobility confidence, and (4) report fewer falls and/or near-falls.

METHODS: Four weekly, 75-minute sessions were held virtually and coached by psychologists and physical therapists with MS expertise. Participants viewed presession videos on causes of and prevention of falls. Exercise videos on strength and balance, developed by CDMS, were viewed during sessions and were encouraged to be viewed between sessions. A virtual falls resource dashboard was available to all participants before, during, and after coaching. Three monthly meetup sessions were held post program to reinforce behavior change. Participants were asked to complete pre- and postprogram questionnaires and a daily falls questionnaire.

RESULTS: Postprogram respondents (n = 41) reported feeling confident that they could turn to family/friends for support (83%), participate in home/community activities (93%), manage their MS symptoms (95%), and collaborate with health care providers (85%). Most (95%) reported at least 1 positive behavior change to prevent falls: 44% made their daily environment safer, 61% exercised to reduce falls, 46% worked with a physical therapist, and 59% used a mobility aid. Following the program, participants reported a 35% decrease in days with fall events.

CONCLUSIONS: The CDMS fall risk reduction coaching program resulted in increased confidence to safely perform daily activities and reductions in falls. Improvements were observed immediately following the coaching sessions and continued through the final meetup session. Results support the impact of this unique program to prevent falls in people with MS.

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DISCLOSURES: *Laura Allen, Abbey J. Hughes, Kathleen Costello, Rosalind Kalb, Paige Kennon: Nothing to disclose. Mandy Rohrig: BridgeBio (salary).*

KEYWORDS: Comprehensive Care and MS, Management of Activities of Daily Living in MS, MS and the Caregiver/Family

(PLA-B4) Disparities of Hypertension Awareness in Multiple Sclerosis: Age, Sex, and Severity

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BACKGROUND: Hypertension (HTN) and vascular comorbidities worsen outcomes in people with multiple sclerosis (MS). High rates of HTN unawareness have been noted in Hispanic individuals with MS but remain unexplored in other populations.

OBJECTIVES: To evaluate risk factors for HTN unawareness in a multiethnic population with MS.

METHODS: Retrospective chart review was performed using records from 199 people with MS with at least 1 visit from 2020 to 2023. Data included demographics, insurance, Area Deprivation Index (ADI), past medical history (PMH), medical problem list (PL), blood pressure (BP), and medications. BP averages were classified into American Heart Association (AHA) categories. HTN by vital signs (HTNv) was defined as 2 or more BP readings greater than or equal to 130/80 mm Hg on separate visits. Patients with HTNv were *HTN aware* if HTN was in PMH or PL or if antihypertensives were prescribed. Patients were *HTN unaware* if none of those were present. Disability measures included the Timed 25-Foot Walk and serum neurofilament light chain levels. *T* or *z* tests evaluated group differences between those with and without any HTN. Regression analysis evaluated associations for HTN unawareness (logistic) or disability measures (linear). Final models were adjusted for age, sex, race/ethnicity, AHA BP category, MS phenotype, disease-modifying therapy (DMT) category, insurance type, and ADI.

RESULTS: The 199 patients (69.8% female; mean age, 44 years) were 88.4% White, 8.5% Black, 1% Asian, 0.5% Hispanic, and 0.5% Indigenous. Most had relapsing MS (95%) and were on DMT at follow-up (84%). HTNv was present in 134 of 194 people with available BP (69.1%). Any HTN diagnosis was present for 136 people, 133 of whom had complete data. Of patients with HTNv, 21.6% had an established HTN diagnosis and 41% were on antihypertensives. Among those with HTNv, 55% were HTN unaware. Patients with HTN were more likely to be on teriflunomide (12.8% vs 4.2%; $P < .05$) or S1P inhibitors (15.4% vs 4.2%; $P < .05$). Multifactor logistic regression showed women were 7.02 times more likely to be HTN unaware than men (95% CI, 2.48-19.86; $P < .01$). Stage II HTN (≥ 140/90 mm Hg) decreased odds of HTN unawareness by 3.8 times (expB, 0.26; 95% CI, 0.08-0.88; $P = .03$), and unawareness decreased with age (expB, 0.96; 95% CI, 0.92-1.0; $P = .03$). DMT class, race, or ADI were not associated with HTN unawareness. No associations were found between HTN awareness and disability.

CONCLUSIONS: Most individuals with MS meeting AHA HTN criteria are HTN unaware, representing a significant care gap for people with MS. Female sex, younger age, and less severe HTN significantly increase the risk of HTN unawareness. Further research is needed to explore the long-term effects of HTN unawareness.

DISCLOSURES: *Maya A. Jayaram: Nothing to disclose. Michael V. Robers: Genentech, TG Therapeutics (consulting fee); Sanofi (speakers' bureau).*

KEYWORDS: Comprehensive Care and MS, Disparities in MS

(PLA-B5) Wearable Devices for Monitoring Incomplete Bladder Emptying in Multiple Sclerosis

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BACKGROUND: Over 85% of people with multiple sclerosis (PwMS) experience various forms of bladder dysfunction (BD), including difficulty with voiding. Incomplete emptying can increase the risk of urinary tract infections (UTIs), which have been associated with high rates of hospitalization, mortality, and pseudorelapses in PwMS. Standard practice in identifying UTIs involves screening with urinalysis and culture after patients report having symptoms. Urinary retention is assessed via clinic-based postvoid residual volume (PVR). Given the fluctuation in MS symptoms, including BD, the ability to remotely capture urinary retention could enhance the monitoring of UTIs.

OBJECTIVES: Examine the association between urinary retention, as measured by clinical and remote PVR, and the presence of UTIs in PwMS.

METHODS: Female individuals referred to pelvic health physical therapy were provided a novel wearable bladder ultrasound device (DFree), which records bladder fullness on a scale of 0 to 10. Its spot-check function allows users to perform on-demand bladder scans, which participants used after voiding to obtain remote PVR values. Data were sent to a mobile app and viewed online by the clinician. Participants wore the device for at least 3 to 5 days per month over 3 months. Standard clinical PVR measurements (average of 3 readings within 5 minutes) were recorded at baseline, and patients' electronic medical records were reviewed to identify self-reported or culture-confirmed UTIs within the year leading up to the study. Linear regression was used to examine the relationship between remote PVR values and UTIs.

RESULTS: Ultrasound data were available for 86.4% (19 of 22) of participants; 8 reported experiencing at least 1 UTI (42.1%). Mean age was 51.5 years (SD, 9.5), median disability (Expanded Disability Status Scale) score was 4.0 (range, 1.0-8.0), and median disease duration was 16.0 years (IQR, 11.0). Linear regression analysis showed that increased remote PVR significantly related to UTI outcomes ($r = 0.46$; $F[1,17] = 4.57$; $P = .04$), with an effect estimate of 28.4.

CONCLUSIONS: Results suggest that greater residual volume, as measured by both clinic and remote PVR, may contribute to higher risk of experiencing a UTI. Remote PVR showed similar trends to clinic PVR values, highlighting the potential utility of wearable devices in assessing retention in the home environment. Further research is needed to assess the utility of wearables for predicting the likelihood of developing UTIs in PwMS.

DISCLOSURES: *Anne M. Suskind: Flume Catheter Company (consulting fee). Riley Bove: Alexion, EMD Serono, Genzyme, Horizon, Janssen, Sanofi, TG Therapeutics (consulting fee). Chelyn Park, Leah McIntyre, Gabby B. Joseph, Michelle E. Van Kuiken, Valerie J. Block: Nothing to disclose.*

KEYWORDS: Bladder Wearables, Equipment in MS, Management of Activities of Daily Living in MS

(PLA-B6) No Association Between Decreases in Serum Immunoglobulin Levels and Serious Infections With Long-Term Ublituximab Treatment in Patients With Relapsing Multiple Sclerosis

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BACKGROUND: In people with relapsing forms of multiple sclerosis (RMS), ublituximab (UBL) provides sustained clinical benefit over 5 years of treatment. The impact of long-term exposure to anti-CD20 therapies on immunoglobulin (Ig) levels and concomitant serious infections (SIs) remains an important topic. This analysis quantified the incidence of SI and the effect of prolonged UBL treatment on Ig levels and evaluated any potential association between hypogammaglobulinemia and SI.

OBJECTIVES: To evaluate the immunological safety profile of prolonged UBL treatment.

METHODS: After 2 years in a double-blind period, patients with RMS either continued UBL treatment or switched from teriflunomide to UBL during open-label extension. At 5 years, mean serum Ig levels were calculated. Lower limit of normal (LLN) thresholds were (g/L) as follows: 5.65 (IgG), 0.4 (IgM), and 0.7 (IgA). Severity of hypogammaglobulinemia (g/L) was classified as mild (< 5.65 to ≥ 4.0), moderate (< 4.0 to ≥ 2.0), or severe (< 2.0) for IgG and mild (< 0.4 to ≥ 0.36), moderate (< 0.36 to ≥ 0.2), and severe (< 0.2) for IgM. Exposure-adjusted incidence rates for SI were calculated as the number of SI events per 100 patient-years, excluding terms *COVID-19* and *COVID pneumonia*.

RESULTS: Mean serum IgG and IgM levels remained stable and above LLN after continuous UBL treatment for 5 years (mean [SD], 8.1 [2.23] g/L and 0.7 [0.66] g/L, respectively). At year 5, IgG decreases were limited and mild (12.6%) to moderate (0.3%); none were severe. Also, at year 5, IgM decreases were mild (4.9%), moderate (18.9%), or severe (11.2%). For UBL-treated patients, rates of SI per 100 patient-years less than LLN or greater than or equal to LLN were 3.26 (95% CI, 2.10-5.05) and 2.44 (95% CI, 1.94-3.07) for IgM, 2.92 (95% CI, 0.94-9.06) and 2.57 (95% CI, 2.09-3.16) for IgG, and 3.66 (95% CI, 1.37-9.76) and 2.55 (95% CI, 2.07-3.13) for IgA, respectively, indicating no significant difference in the incidence of SI regardless of Ig levels above or below LLN. The rate of SIs occurring within 1 month of less than LLN or equal to or greater than LLN Ig value did not differ, further supporting lack of relationship between decreases in Ig below LLN and SI occurrence.

CONCLUSIONS: Mean Ig levels remained stable and above LLN at year 5, and no association between decreased Ig and risk of SI was observed. UBL confers a benefit-risk balance suitable for the long-term clinical management of RMS.

DISCLOSURES: *Lawrence Steinman: 180 Life Sciences, AbbVie, Atreca, EMD Serono, Novartis, Pasithea, Teva, TG Therapeutics (consulting fee); Atara (contracted research); Bristol Myers Squibb (consulting fee, contracted research). Edward J. Fox, Koby Mok, Yanzhi Hsu, Yihuan Xu, Chris Rowland, Karthik Bodhinathan, Peter Sportelli, Jackie Parker, Hari Miskin: TG Therapeutics (salary). Hans-Peter Hartung: Bayer Pharma AG, Biogen, Merck Serono, Novartis, Roche, Sanofi, Teva (consulting fee). Enrique Alvarez: Atara, Biogen, Bristol Myers Squibb, Genentech/Roche, National Institutes of Health, National Multiple Sclerosis Society, Novartis, Patient-Centered Outcomes Research Institute, Rocky Mountain Multiple Sclerosis Center, Sanofi, TG Therapeutics (research support); Biogen, Celgene/Bristol Myers Squibb, Cionic, EMD Serono/Merck, Genentech/Roche, Horizon/Amgen, Novartis, Sanofi, TG Therapeutics (consulting fee). Peiqing Qian: Biogen, Bristol Myers Squibb, Genentech, Sanofi, TG Therapeutics, Viela Bio (consulting fee). Sibyl Wray: Biogen, Bristol Myers Squibb, EMD Serono, Novartis, Roche/Genentech, Sanofi (consulting fee). Derrick Robertson: Anokion, Atara Biotherapeutics, Biogen, CorEvitas, EMD Serono, Genentech, GW Pharmaceuticals, Janssen, Novartis, Patient-Centered Outcomes Research Institute, PRIME CME, Sanofi, TG Therapeutics (consulting fee). Krysztof W. Selmaj: Biogen, Celgene, Genzyme, Merck, Novartis, Ono Pharma, Roche, Synthon, Teva (consulting fee). Daniel Wynn: EMD Serono, Genentech, Novartis, Sanofi (consulting fee). Bruce A. C. Cree: TG Therapeutics (consulting fee).*

KEYWORDS: Disease-Modifying Treatments in MS, Immunology and MS

REHABILITATION

(PLA-C1) Is There a Threshold or Dose-Response Association Between Physical Activity and Cognitive Function in Multiple Sclerosis?

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BACKGROUND: Cognitive impairment is prevalent, disabling, and poorly managed in people with multiple sclerosis (MS). Physical activity, often expressed as steps per day, has been associated with cognitive function in this population. However, researchers have not focused on the nature of the association between physical activity and cognition in MS, and this has implications for the design of randomized controlled trials and public health promotion of physical activity behavior.

OBJECTIVES: This study examined the possibility of a (1) steps per day threshold associated with the absence of cognitive impairment or (2) dose-response relationship between steps per day and cognitive function in MS.

METHODS: The sample included 358 people with MS who provided demographic (age, sex, race) and clinical (MS type, disease duration, disability status) information,

and who completed the Symbol Digit Modalities Test (SDMT) for cognitive processing speed and the California Verbal Learning Test-Second Edition (CVLT-II) for verbal learning and memory. Participants wore an ActiGraph wGT3X and an accelerometer above the nondominant hip during waking hours over a 7-day period to measure steps per day.

RESULTS: The receiver operating characteristic (ROC) curve analysis did not identify a steps-per-day threshold associated with cognitive impairment on SDMT (area under the curve [AUC] range, 0.606-0.691). In addition, the ROC curve analysis did not identify a threshold of steps per day associated with cognitive impairment based on CVLT-II (AUC range, 0.606-0.691). The regression analysis indicated significant linear relationships between steps per day and SDMT (R^2=.06; β=.251; P<.001) and CVLT-II (R^2=.06; β=.247; P<.001) z scores.

CONCLUSIONS: The observed linear relationship suggests that focusing on increasing steps per day across all levels of physical activity might be beneficial for cognitive function in MS.

DISCLOSURES: *Brenda Jeng, Gary R. Cutter, Robert W. Motl: Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Health Behavior, Management of Activities of Daily Living in MS

(PLA-C2) Long-Term Efficacy of Translingual Neurostimulation by a Portable Neuromodulation Stimulator on Gait Deficit Improvement in Multiple Sclerosis: Results From the PoNSTEP Study

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BACKGROUND: Noninvasive cranial nerve translingual neural stimulation (TLNS) combined with physical therapy (TLNS therapy) has been shown to improve gait deficit in people with multiple sclerosis (MS) by upregulating central motor control mechanisms and, presumably, contributing to enhanced neuroplasticity.[1-3]

OBJECTIVES: The PoNS Therapeutic Experience Program (PoNSTEP) study sought to better understand the dose-response dynamics and durability of the previously observed improvements.

METHODS: PoNSTEP enrolled 43 people with MS with gait deficit who received 14 weeks of TLNS therapy at a target dose of 100 to 120 min per day, daily, in clinic for the first 2 weeks (phase 1), then unsupervised at home for 12 weeks (phase 2) with a 6-month follow-up (phase 3). We used correlation analyses to evaluate associations between phase-specific adherence and Dynamic Gait Index (DGI) improvements and paired t-tests with 95% CIs to determine changes in DGI during phase 1 and phase 2 (primary end point), as well as from the end of phase 2 to the end of phase 3 (secondary end point).

RESULTS: Of the 43 participants, 41 started and 38 completed the 14-week TLNS protocol. The 38 participants who completed the treatment protocol showed a statistically significant mean increase of 5.00 points (95% CI, 4.1-5.9, P<.001) at week 14. In phase 1, average therapy adherence was 89.5% and improvement was not associated with adherence. In phase 2, adherence was 71% and improvement was linearly associated with adherence (r=0.345; P=.034). Participants with greater than or equal to 85% adherence improved 3.7 points (1.8 SD); those with less than 85% adherence improved 2.0 points (1.8 SD); this difference was statistically significant (P=.008). Of those who completed the 14 weeks of therapy, 28 of 41 (70.7%) were reassessed at 6 months. One of 28 showed greater than or equal to 30% decline in DGI (95% exact binomial CI, 0.09%-18.4%). Mean decline (%) in DGI was −4.1 (95% CI, −9.4% to 1.1%; range −35.7% to 25.0%) with the 95% CI's lower bound showing statistically reliable evidence that the true mean decline was no more than −9.4% (P=.12).

CONCLUSIONS: The study shows that adherence to the recommended TLNS therapy dose is associated with gait improvement and supports its effectiveness in sustaining improvements 6 months post therapy, suggesting that TLNS therapy makes a contribution to neuroplasticity's role in promoting a lasting gait function enhancement in MS.

DISCLOSURES: *Deborah Backus: Helius Medical (consulting fee, contracted research). Christopher Langston: Biogen, EMD Serono, Genentech (consulting fee). Christopher Langston, VJ Yadav, Prudence Plummer, Leigh E. Charvet: Helius Medical (contracted research). Greg Maislin: Helius Medical (salary). Brad Willingham: Nothing to disclose. Salvatore Napoli: Biogen, Bristol Myers Squibb, EMD Serono, Genentech (consulting fee). Expert witness (for vaccine injury).*

KEYWORDS: Clinical trials, Comprehensive Care and MS, Equipment in MS

(PLA-C3) Effectiveness of Facility-Based and Home-Based Exercise Programs for Multiple Sclerosis: The STEP for MS Trial

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BACKGROUND: Exercise training improves mobility and may slow disability progression in people with multiple sclerosis (MS), but barriers like limited access to facilities and lack of MS expertise can reduce participation. Home-based programs may address some of these issues, but the impact of exercise location and the individual's location choice on outcomes remains unclear.

OBJECTIVES: The STEP for MS trial evaluated short- and long-term effects of individualized exercise programs based on the Guidelines for Exercise in Multiple Sclerosis (GEMS) delivered in-person at a facility (GEMS-F) or with remote coaching at home (GEMS-H).

METHODS: Participants (N=379) were randomly assigned to RANDOM (assigned: GEMS-F n=92, GEMS-H n=97) or CHOICE (selected: GEMS-F n=106, GEMS-H n=84) and completed 16 weeks (wks) of twice-weekly aerobic and resistance training. The Timed 25-Foot Walk Test (T25FW; primary outcome measure), 6-Minute Walk Test (6MWT), Expanded Disability Status Scale (EDSS), and MS Walking Scale-12 (MSWS-12) were assessed at 16 wks and 52 wks.

RESULTS: Participants were mostly female (75.7%), White (64.9%) or Black (29.3%), and had relapsing-remitting MS (72.7%). As reported previously, all groups improved T25FW speed and EDSS scores at 16 wks. Using a repeated measures model with time by treatment interaction adjusted for age, sex, site, baseline EDSS, and random effect for participant, least squares means show all groups improved T25FWT from baseline to 52 wks, and all lost some of the 16-wk improvement by 52 wks. EDSS scores worsened between 16 and 52 wks in all groups, significantly in RANDOM GEMS-H (+0.3, P=.03) and CHOICE GEMS-F (+0.2, P=.03). 6MWT distance improved at 16 wks, but at 52 wks all groups walked fewer feet and the decline (−115.1 feet) in CHOICE GEMS-F was significant (P<.01). MSWS-12 improved in all groups at 16 wks but worsened an average 5 points at 52 wks, nonsignificantly for RANDOM GEMS-F and GEMS-H (P=.06), but significantly for CHOICE GEMS-F (P=.02). CHOICE GEMS-H worsened by 7 points (P<.01).

CONCLUSIONS: Findings show that facility- and home-based exercise programs yield similar short- and long-term benefits, suggesting home-based programs can be viable alternatives to facility-based programs. Variability in CHOICE groups suggests participant preference may influence outcomes, but further research is required. The decline in outcomes at 52 wks highlights the need for strategies to sustain benefits, such as ongoing exercise support, booster sessions, or behavioral interventions.

DISCLOSURES: *Deborah Backus: Helius Medical (contracted research, consulting fee). Robert W. Motl, Gary R. Cutter, Jeffrey Hebert, Alexander V. Ng, Kevin McCully, Casey Kandilakis, Jonathan Lowman, Whitney N. Neal: Nothing to disclose. Francois Bethoux: Bristol Myers Squibb (consulting fee, advisory board member); MedRhythms (consulting fee, contracted research, scientific advisory board member); Qr8 (intellectual property rights). Prudence Plummer: Helius Medical (contracted research).*

KEYWORDS: Comprehensive Care and MS, Exercise, Physical Activity

(PLA-C4) Balancing Fatigue Mechanisms in Multiple Sclerosis Through Low Load Blood Flow Restriction Resistance Exercise

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BACKGROUND: Muscle fatigue is a prevalent and debilitating symptom among

people with multiple sclerosis (PwMS). Relative to asymptomatic controls, fatigue typically manifests as increased central (eg, reduced corticospinal excitability or responsiveness) but reduced peripheral (eg, metabolites) fatigue. Consequently, PwMS may have diminished capacity to derive comparable benefits from exercise. An innovative strategy to accelerate peripheral fatigue is through the application of blood flow restriction (BFR).

OBJECTIVES: This study examined the prevalence and magnitude of central and peripheral fatigue following acute bouts of high load (HL), low load (LL), and LL with BFR (LLBFR) resistance exercise.

METHODS: Twelve women (mean age ± SD=42 ± 12 yrs) and 3 men (41 ± 10 yrs) with relapsing-remitting MS performed unilateral, isotonic, leg extension muscle actions with an HL (70% of 1 repetition maximum [1RM]), LL (30% of 1RM), and LLBFR (30% of 1RM with BFR applied at 60% of the total arterial occlusion pressure required to restrict blood flow to the working muscle). Prior to and immediately after each exercise bout, maximal voluntary isometric contraction (MVIC) torque, as well as indexes of central (surface electromyographic [sEMG] amplitude, superimposed twitch torque [STT], V_{WAVE}/M_{WAVE}) and peripheral (potentiated twitch torque [PTT]) fatigue were assessed via motor nerve stimulation. A 3 (Condition [HL, LL, LLBFR]) × 2 (Time [pretest, posttest]) repeated measures analysis of variance and post hoc Pearson correlations were used to examine central and peripheral fatigue.

RESULTS: All conditions elicited decreases in MVIC torque (−21.0% relative to baseline; $P<.001$, $g=1.486$). LLBFR resulted in greater PTT reductions (−37.1%; $P<.001$, $g=1.135$) compared to HL (−14.2%; $P=.093$, $g=0.440$) but was not different than LL (−26.8%; $P<.001$, $g=1.203$). STT increased (+24.5%, $P=.018$, $g=0.650$), while there were decreases in sEMG amplitude (−9.7%; $P=.004$, $g=0.852$) and V_{WAVE}/M_{WAVE} (−7.9%; $P<.001$, $g=1.037$) that were not different among conditions. Muscle fatigue was primarily characterized as peripheral for LLBFR (PTT, $r=0.811$), central for HL (STT, $r=0.763$), and both for LL (PTT, $r=0.668$; sEMG amplitude, $r=0.515$).

CONCLUSIONS: These findings demonstrate that resistance exercise induces distinct changes in central and peripheral fatigue indexes among PwMS. Applying BFR to LL resistance exercise enhanced peripheral fatigue development and was associated with reduced central fatigue compared to HL resistance exercise. Future research should explore optimal resistance exercise protocols to maximize clinical feasibility, adherence, and therapeutic outcomes.

DISCLOSURES: *Ethan C. Hill: Suji (contracted research). Christopher E. Proppe, Sean M. Lubiak, Mason A. Howard, Anuj J. Prajapati, Niriham M. Shah, Nihar N. Patel, Paola M. Rivera, Jeffrey T. Schmidt: Nothing to disclose.*

KEYWORDS: Complementary/Alternative Therapies in MS, Equipment in MS, Rehabilitation

(PLA-C5) Psychometric Properties of Free-Living Step-Based Metrics (Daily Steps and Peak Cadence) in Multiple Sclerosis

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BACKGROUND: Walking represents an important clinical end point in people with multiple sclerosis (MS). Clinical measures of walking performance have been crucial for monitoring disease progression and evaluating the efficacy of disease-modifying agents and rehabilitation interventions. However, assessments conducted in controlled settings (eg, performance-based tests) may not reflect real-world capacity and movement in a natural environment. Step-based metrics (daily steps and peak cadence) via accelerometry have emerged as promising measures of real-world walking performance in MS, yet data on their psychometric properties remain limited.

OBJECTIVES: We examined the reliability, precision, and clinically detectable change of daily steps, peak 30-minute cadence (Peak-30_{CAD}), and peak 1-minute cadence (Peak-1_{CAD}) over a 6-month period in the absence of intervention among persons with MS. We further evaluated the construct validity through correlations with laboratory-assessed walking and gait performance.

METHODS: Seventy-eight participants underwent the Timed 25-Foot Walk, 6-Minute Walk, and gait assessment (ie, gait velocity, step time, and step length) in the laboratory, and then wore an ActiGraph GT3X and accelerometer for 7 days in a free-living condition; the same procedure was repeated after 6 months without any intervention. Accelerometer data were processed using custom R scripts to generate step-based metrics, including daily steps (steps/day), Peak-30_{CAD} (step/min; the average cadence of the 30 highest nonconsecutive minutes in a day), and Peak-1_{CAD} (step/min; the highest cadence recorded for a single minute in a day) across all valid days. We calculated intraclass correlation coefficient (ICC), standard error of measurement (SEM), and minimal detectable change (MDC_{95}), and performed paired samples t tests and Spearman correlations.

RESULTS: Step-based metrics were stable with no significant changes across time ($P>.05$) and demonstrated good test-retest reliability (ICCs: 0.80-0.85) and acceptable precision (SEM%s: 14.4%-24.3%). The MDC_{95} values for Peak-30_{CAD}, Peak-1_{CAD}, and daily steps were 25.6 steps/min, 31.0 steps/min, and 2909.2 steps/day, respectively. There were consistent, strong associations between peak cadence with walking tests, gait parameters, and disability status at both time points ($|r_s|=0.52$-0.79), even after controlling for daily steps ($|pr_s|=0.25$-0.58; $P<.05$).

CONCLUSIONS: Our findings support step-based metrics via accelerometry as reliable and valid measures of free-living ambulatory performance in MS and may inform the inclusion of these metrics in clinical trials among people with MS.

DISCLOSURES: *Peixuan Zheng, Robert W. Motl: Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Management of Activities of Daily Living in MS, Walking; Accelerometry; Reliability, Validity, and Precision; Clinical Change

(PLA-C6) Walk It Out: Acute Treadmill Walking Exercise Reduces State Anxiety in People With Multiple Sclerosis Who Have Generalized Anxiety Disorder

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BACKGROUND: Generalized anxiety disorder (GAD) is prevalent among people with multiple sclerosis (MS), yet poorly treated and understudied. Exercise training may be an effective intervention to manage anxiety symptoms among people with MS who have GAD, and a foundational step in developing chronic exercise training interventions is the study of acute bouts of exercise on state anxiety in people with MS prescreened for GAD.

OBJECTIVES: We examined the effects of an acute bout of moderate-intensity treadmill walking exercise on state anxiety in persons with MS and GAD.

METHODS: The study followed a within-subject, randomized, and counterbalanced design. The sample was prescreened for GAD and independent ambulation using the Generalized Anxiety Disorder 7-item scale and the Patient-Determined Disease Steps scale, respectively. We compared the effects of an experimental condition (moderate-intensity treadmill walking exercise) with a control condition (seated quiet rest) on state anxiety as measured by the State-Trait Anxiety Inventory, State subscale (STAI-S). The STAI-S was administered before, immediately after, and 20 minutes after each 20-minute condition. The data were analyzed using a 2-way, condition-by-time repeated measures analysis of variance (ANOVA).

RESULTS: Twenty participants with mean age of 37.4 (8.4) years, predominantly female (80%), were included in the study. The repeated measures ANOVA indicated a statistically significant condition-by-time interaction on STAI-S scores ($F[2,38]=7.95$, $P=.001$, $n^2=.295$). There was a reduction in STAI-S scores immediately after the exercise condition compared with scores before exercise ($d=1.0$), and STAI-S scores remained reduced compared with scores before exercise for 20 minutes after the exercise bout ($d=.75$). There were no changes in STAI-S scores immediately after ($d=.06$) and 20 minutes after ($d=-.13$) the control condition compared with scores before the condition.

CONCLUSIONS: We provide initial evidence for the beneficial effect of acute, moderate-intensity walking exercise for improvement in state anxiety symptoms among people with MS who have GAD, and this exercise stimulus might be appropriate for long-term management of GAD in MS.

DISCLOSURES: *Petra Šilić, Robert W. Motl: Nothing to disclose.*

KEYWORDS: Acute Exercise and State Anxiety, Psychological Issues and MS

IMAGING, COGNITIVE, AND PSYCHOSOCIAL FEATURES OF MULTIPLE SCLEROSIS AND RELATED DISORDERS

(PLA-D1) Toward Precision Medicine in Multiple Sclerosis: Subjective Cognitive Fatigability Is Related to Psychosocial Fatigue, Cognitive Impairment, and Disability.

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BACKGROUND: Among the most common and debilitating symptoms of multiple sclerosis (MS) is fatigue, characterized by pervasive exhaustion, reduced motivation and, relatedly, declines in performance with sustained effort (ie, fatigability). Cognitive fatigue and fatigability have been well-studied objectively (eg, via neuropsychological tests) and are linked to other secondary disease characteristics (eg, mood) and physical functioning in people with MS (PwMS). However, less is known about the relationship between *subjective* cognitive fatigability (SCF), an individual's perception of reduced capacity to maintain cognitive effort, and well-being among PwMS.

OBJECTIVES: The present study used a data-driven approach to identify the best-fitting secondary disease characteristics contributing to SCF and disability.

METHODS: PwMS (N=85) completed the Modified Fatigue Impact Scale, Pittsburgh Fatigability Scale, Hospital Anxiety and Depression Scale, Perceived Deficits Questionnaire, Pittsburgh Sleep Quality Index, and Patient-Determined Disease Steps (PDDS). *T*-tests and Fisher exact tests were used to compare secondary disease characteristics and disability by SCF (high or low). Multivariate regressions with an exhaustive search of the model space were conducted using the lowest Bayesian information criterion to identify the strongest indicators of SCF and disability status.

RESULTS: PwMS with high SCF (n=43) had higher rates of unemployment (P=.002) and worse depression (P<.001), perceived cognitive impairment (P<.001), sleep quality (P=.002), physical fatigue (P<.001), cognitive fatigue (P<.001), and psychosocial (P<.001) fatigue, as well as greater PDDS scores (P=.006) compared with PwMS with low SCF (n=42). The best-fitting indicators of SCF included psychosocial fatigue (P<.001) and perceived cognitive impairment (P=.020), while disability status included age (P=.008) and SCF (P=.002).

CONCLUSIONS: Perceived cognitive impairment and psychosocial fatigue were key indicators of high SCF over other secondary disease characteristics (ie, mood, sleep, physical fatigue). Further, SCF emerged as the strongest indicator of PDDS. These results suggest that cognitive challenges and fatigue associated with social interaction contribute to perceived performance declines after sustained cognitive effort. Screening for SCF may identify patients at risk for cognitive-emotional factors contributing to increased disability. Finally, this study identifies SCF as a potential intervention target to improve well-being among PwMS.

DISCLOSURES: *Candice L. Craft, Tamanna Islam, Jason A. Berard, Lisa A.S. Walker: Nothing to disclose.*

KEYWORDS: Fatigue and MS, Psychological Issues and MS

(PLA-D2) Sulcal Morphometry Associated With Cognitive Performance and Cognitive Fatigue in Multiple Sclerosis

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BACKGROUND: Cognitive impairment and cognitive fatigue are 2 of the most pervasive symptoms of multiple sclerosis (MS). Structural neural correlates have been linked to cognition and fatigue in MS, although limitations exist in their sensitivity and predictive power. Measures of sulcal morphometry have demonstrated greater sensitivity for predicting outcomes in several neurological groups, however, their ability to predict outcomes in MS is much less understood.

OBJECTIVES: To investigate the association of sulcal measures (ie, sulcal length, sulcal span, sulcal surface area) with cognitive performance and cognitive fatigue in people with MS (PwMS).

METHODS: Sixty-nine PwMS (56 women; mean age 52.48 years) underwent structural neuroimaging, cognitive testing (Brief International Cognitive Assessment for MS), and an evaluation of cognitive fatigue (Modified Fatigue Impact Scale subscale). Structural T1 MRI scans were segmented using FreeSurfer 6.0, and outputs were imported into BrainVISA's Morphologist toolbox to obtain sulcal measures. Sulcal maps and values were inspected for gross errors. Six sulci (L, R separate)—superior frontal sulcus, central sulcus, anterior and posterior lateral sulci, superior temporal sulcus, and intra-parietal sulcus—were selected based on previous literature examining reliability, universal presence, size, and ease of identification. Raw scores for sulcal measures, cognitive testing, and fatigue were used in all analyses.

RESULTS: To account for collinearity among sulci, linear ridge regressions were conducted within RStudio. Age, sex, education, and estimated intracranial volume were included as covariates. Longer length of the right posterior lateral sulcus was associated with better visual and verbal memory performance. Shorter length in the right anterior lateral sulcus, left posterior lateral sulcus, and right central sulcus was associated with greater cognitive fatigue. Greater sulcal span in the left posterior lateral sulcus and left intraparietal sulcus was associated with poorer verbal memory and processing speed. Greater cognitive fatigue was associated with greater sulcal span in the left and right posterior lateral sulci and left superior frontal sulcus. Lastly, sulcal surface area in the right posterior lateral sulcus and left anterior lateral sulcus were positively associated with visual memory and processing speed, respectively.

CONCLUSIONS: Measures of sulcal morphometry hold promise for predicting cognitive performance and fatigue in MS. Examining sulci in MS advances the field by providing unique, detailed information regarding cortical folding as it relates to critical MS outcomes. Also, based on work in other neurological groups, sulcal measures may provide a more sensitive and nuanced picture of structural brain changes in MS that more conventional measures (eg, cortical thickness) miss. Future work would benefit from larger samples and longitudinal designs.

DISCLOSURES: *Cristina A.F. Román, Chirag Motwani, Fabrizio Pizzagalli, Glenn R. Wylie, Carly LA Wender, Brian M. Sandroff, Bing Yao: Nothing to disclose. John DeLuca: Biogen (consulting fee, speakers' bureau, grant funding); Bristol Myers Squibb (consulting fee, grant funding); EMD Serono (speakers' bureau); Janssen, MedRhythms, Novartis, Roche (consulting fee).*

KEYWORDS: Cognition, Imaging and MS, Psychological Issues and MS

(PLA-D3) Cognitive Concerns and Work: A Collaborative Occupational Therapy and Speech and Language Pathology Approach to Assessment and Treatment

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BACKGROUND: Work has many benefits, including financial security, improved mental health, and access to medical benefits, among others. Multiple sclerosis (MS) can affect a person's ability to work in many ways, with a major barrier being cognitive concerns, which can be further impacted by fatigue. In our MS outpatient clinic, occupational therapists (OTs) and speech and language pathologists (SLPs) collaboratively work with people with MS (PwMS) who have cognitive issues that interfere with their work. OTs are experts in functional cognition, activity analysis, fatigue management, and assessing the impact of the environment on the performance of meaningful occupations. SLPs offer expertise in cognitive communication. By combining these 2 lenses, PwMS can be more comprehensively supported in their needs at work.

OBJECTIVES: To show how OTs and SLPs can collaboratively support PwMS with their needs in the workplace when there are cognitive concerns.

METHODS: Interviews gather information regarding issues at work (ie, work history and job demands, cognitive concerns, impact of fatigue, work environment, or other symptoms/barriers that may require a referral for further collaboration [eg, physiotherapist, social worker]) and outside of work (ie, social history, informal supports, ability to manage basic and instrumental activities of daily living).

NEXT steps can include formal assessments to quantify strengths/weaknesses in memory, attention, executive function, verbal/written expression, and auditory/reading comprehension; education on MS and work (ie, diagnosis disclosure, rights in the workplace, accommodations, return-to-work process, disability benefits, etc); symptom management education; education/practice using cognitive/cognitive-communication compensatory and/or fatigue management strategies; advocacy for formal workplace accommodations; development of a gradual return-to-work plan incorporating cognitive symptom and fatigue management; and discussion about considering a medical leave of absence from work.

RESULTS: Using these specialists in combination, PwMS who have cognitive issues can be best supported in their needs at work.

CONCLUSIONS: OTs and SLPs offer expertise that, when applied collaboratively, can best support PwMS who have cognitive issues with their needs at work.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Allied Health, Comprehensive Care and MS, Employment in MS

(PLA-D4) Management of Psychological Comorbidities in Neuroimmunologic Disease

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BACKGROUND: It is estimated that between 30% and 50% of people with multiple sclerosis (MS) have comorbid mental health disorders, compared with an estimated 11% of the general population. There are mixed data for neuromyelitis optica (NMO).

Some reports suggest that mental health conditions are more common in NMO than in MS and others suggesting they are less common. Despite the prevalence, there is little evidence for the management of mental health disorders in patients with neuroimmunologic (NI) disease.

OBJECTIVES: To explore practice patterns for the treatment of anxiety and depression in patients with MS and NMO, including referral to behavioral health clinicians and choice of pharmacotherapy.

METHODS: Using the Federated Clinical Analytics Platform, we performed an analysis of all patients with a diagnosis of NMO or MS presenting to a tertiary care institution. Psychiatric comorbidities, frequency of behavioral health referrals, and treatment patterns were assessed.

RESULTS: We identified 8020 patients with MS and 325 patients with NMO. Mental health disorders were documented in over 30% of patients with MS and 24% of patients with NMO vs 8.4% of all patients receiving medical care at the institution. In patients with comorbid anxiety or depression, 37% of patients with MS were referred to behavioral health vs 43% of patients with NMO and 19% of all patients. Psychiatric medications are prescribed significantly more often in patients with NMO/MS when compared with the institution population. Of patients with MS or NMO and mental health comorbidities, 88% and 84% are prescribed antidepressants, respectively, compared with 77% within the institution. Bupropion and duloxetine are used most often in patients with NI disease, while sertraline or escitalopram are used significantly more often in the general population. In patients with NMO, 46% are prescribed antipsychotics vs 31.1% of patients with MS and 19.5% of overall patients. Patients with MS are significantly more likely to be placed on quetiapine, lamotrigine, haloperidol, or aripiprazole. Patients with NMO are significantly more likely to be placed on quetiapine (17%) and haloperidol (15%) vs 7.5% and 6.5% of all patients presenting with anxiety or depression, respectively.

CONCLUSIONS: Our study confirmed the increased prevalence of psychiatric comorbidities in patients with neuroimmunologic disease. These patients are more likely to be referred to behavioral health services and to be placed on psychiatric medications, with different preferred agents used in NMO or MS.

DISCLOSURES: *Virginia Baker: Nothing to disclose. Suma Shah: Novartis, TG Therapeutics (consulting fee).*

KEYWORDS: Comprehensive Care and MS, Epidemiology of MS, Psychological Issues and MS

(PLA-D5) The Importance of Super-Resolution and Harmonization in a Pragmatic Clinical MRI Dataset

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BACKGROUND:MRI plays a critical role in monitoring people with multiple sclerosis (PwMS). However, variability in clinical image acquisition—due to scanner differences, accessibility, and nonstandard protocols—presents challenges for longitudinal analysis. This is particularly problematic for deep learning algorithms, which struggle with inconsistencies in resolution and contrast.

OBJECTIVES:TO evaluate the impact of super-resolution (SR) and harmonization techniques on analyzing a pragmatic clinical MRI dataset for PwMS.

METHODS:WE analyzed longitudinal MRI data from 3 imaging sites within the TRaditional Versus Early Aggressive Therapy for MS (TREAT-MS) pragmatic clinical trial (NCT03500328), each involving 9 PwMS with at least 3 follow-up sessions over 5 years. There were a total of 112 different imaging sessions among the 27 PwMS. Images were preprocessed using ECLARE for SR and HACA3 for harmonization (enhanced preprocessing) and compared to a baseline preprocessing approach lacking these techniques. Downstream analyses included total intracranial volume (TICV), total brain volume via SLANT, and lesion volume via UniSELF. After processing, each session was designated as *pass* or *fail* based on the downstream results.

RESULTS:THE enhanced preprocessing improved downstream consistency. In total, we observed 35 failures out of the 112 imaging sessions in the baseline preprocessing, a 31% failure rate. When using the enhanced preprocessing, the number of failures decreased to 3 out of 112, 2.7%. Most failures observed in TICV computation for the baseline images were resolved with the enhanced preprocessing. Total brain volume estimates were robust, though baseline results showed minor inconsistencies. Lesion volume estimations varied substantially using the baseline preprocessing, which underestimated the lesion sizes.

CONCLUSIONS: These findings highlight the necessity of SR and harmonization for accurate and consistent image processing in clinically acquired MRI. By addressing variability in resolution and contrast, the enhanced preprocessing pipeline significantly reduced failure rates, enabling more reliable longitudinal analyses for PwMS. While our study primarily focused on identifying major processing failures, future work could explore methods to quantify and address minor inconsistencies, especially in the absence of ground truth references. Overall, incorporating SR and harmonization holds promise for improving the robustness of deep learning applications in clinical MR imaging.

DISCLOSURES: *Savannah P. Hays, Blake E. Dewey, Samuel W. Remedios, Jinwei Zhang, Lianrui Zuo, Sandra D. Cassard, Carolyn Koch, Ann Fishman, Aaron Carass, Jerry L. Prince: Nothing to disclose. Ellen M. Mowry: Biogen, Genzyme (research funding); Teva (medication for a clinical trial); UpToDate (royalty). Scott D. Newsome: Autobahn (advisor); Biogen, Genentech (consulting fee, research funding); Bristol Myers Squibb, EMD Serono, Greenwich Biosciences, Horizon Therapeutics, Novartis, TG Therapeutics (consulting fee); medDay Pharmaceuticals (clinical adjudication committee member); Roche (contracted research, research funding).*

KEYWORDS: Imaging and MS

(PLA-D6) Remote Cognitive Monitoring in Multiple Sclerosis: A Path Toward Holistic Care With the icometrix Platform

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BACKGROUND: Cognitive dysfunction is a debilitating aspect of multiple sclerosis (MS), yet routine assessment in clinical practice remains limited by time and resource constraints. Digital cognitive assessments offer a scalable solution for regular, remote cognitive monitoring, enabling a comprehensive approach to MS care management.

OBJECTIVES: This study aimed to evaluate the usability and acceptance of digital cognitive assessments by patients and their potential for integration into the icometrix MS care platform. Additionally, the study investigated the correlation between cognitive test results and neuroimaging biomarkers, emphasizing the clinical value of the icognition Symbol Test for tracking disease progression.

METHODS: In this fully remote cross-sectional study, 205 people with MS (PwMS) completed cognitive assessments (Symbol Digit Modalities Test [SDMT], Dot Test, and Backwards Digit Span Test) through the icompanion app. Usability was assessed using the System Usability Scale (SUS) and a custom questionnaire comparing preferences for digital vs uploaded formats via the icompanion portal were analyzed using icobrain to quantify volumetric biomarkers.

RESULTS: Patients rated the digital cognitive tests with an acceptable SUS score of 70.65 and significantly preferred them over paper-based assessments (eg, SDMT: t=5.48, P<.001). The SDMT demonstrated strong correlations with MRI volumetric biomarkers, including thalamic volume (ρ=0.49, P=.023), underscoring its ability to reflect neurodegenerative changes in MS.

CONCLUSIONS: The study highlights the high usability, patient preference, and clinical relevance of the digital icognition SDMT, supporting its integration into the icometrix MS care platform. This integration aims to deliver a holistic care solution that combines digital cognitive monitoring with measures of symptom tracking, finger dexterity, visit preparation, and quantitative imaging biomarkers. The SDMT's strong correlation with thalamic volume further validates its role as a valuable tool for tracking disease progression, enhancing personalized care, and potentially improving outcomes for PwMS. These findings pave the way for incorporating digital cognitive assessments as a cornerstone of comprehensive MS care.

DISCLOSURES: *Guy Nagels: icometrix (ownership interest). Augusto Miravalle: Alexion, Celgene, EMD Serono, Genentech, Genzyme, Novartis (consulting fee, speakers' bureau). Lars Costers, Rebecca Bartz, Diana M. Sima, Dirk Smeets: icometrix (salary). Enrique Alvarez: Atara, Biogen, Bristol Myers Squibb, Genentech/Roche, National Institutes of Health, National Multiple Sclerosis Society, Novartis, Patient-Centered*

Outcomes Research Initiative, Rocky Mountain MS Center, Sanofi, TG Therapeutics (research support); Biogen, Celgene/Bristol Myers Squibb, Cionic, EMD Serono/Merck, Genentech/Roche, Horizon/Amgen, Novartis, Sanofi, TG Therapeutics (consulting fee). Wissam Elmalik, Hanan Al Halawani, Maarten Dewil, Melissa Cambron, Matthias Grothe, Delphine Van Laethem, Stijn Denissen: Nothing to disclose. Aaron L. Boster: Amgen, Sanofi, Serono (speakers' bureau); Amgen, Biogen, Novartis, Roche, Sanofi, Serono (research).

KEYWORDS: Cognition, Imaging and MS, Psychological Issues and MS

EPIDEMIOLOGY AND SOCIAL DETERMINANTS OF HEALTH

(PLA-E1) Disease Severity and Disparities in Black and White People With Multiple Sclerosis: Sociodemographic and Modifiable Lifestyle Factors in a New York Population

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BACKGROUND: A more severe disease course has been described in Black people with multiple sclerosis (BPwMS) without definitive biological underpinnings; sociodemographic and modifiable lifestyle factors warrant investigation. We analyzed the relationship between race and multiple sclerosis (MS) outcomes in BPwMS and White people with MS (WPwMS) and how socioeconomic and modifiable factors may affect it.

OBJECTIVES: Establish the MS-diverseCITY cohort to investigate sociodemographic and modifiable lifestyle factors impacting disease severity in BPwMS and WPwMS living in New York City (NYC).

METHODS: Chart review identified BPwMS ages 18 to 65 years and 1:1 age-and-sex matched WPwMS; all underwent neuropsychological evaluation (Multiple Sclerosis Functional Composite [MSFC], cognitive Symbol Digit Modalities Test [SDMT], verbal/nonverbal memory and physical measures Timed 25-Foot Walk [T25-FW], Nine-Hole Peg Test [NHPT], dynamic balance) as part of routine care. Patient-reported outcomes assessed gait disturbance, mood, sleep, and adherence to a Mediterranean diet. The socioeconomic status (SES) index included neighborhood deprivation index, educational attainment, and literacy. Single/parallel mediation analyses explored the extent to which these factors accounted for the relationship between race and MS outcomes.

RESULTS: The MS-diverseCITY cohort includes 150 BPwMS (36 Black/Hispanic) and 150 WPwMS (9 White/Hispanic), mean age 42.7 (± 10); 78% women. There were no group differences in disease duration, MS phenotype, or use of high-efficacy therapies. The percentage of participants holding bachelor's degrees—although higher than the NYC population—was lower in BPwMS (59%) vs WPwMS (77%) ($P < .001$). BPwMS had lower SES index ($P<.001$, Cohen $d=0.84$) and diet adherence ($P<.001$, $d=0.69$) and worse performance on cognitive and physical measures (P range, .004 to < .001; d range, 0.41-0.63) and MSFC ($P<.001$, $d=0.74$). SES and diet partially mediated the relationship between race and MSFC (48.7%), SDMT (43.1%), NHPT (47.9%), and T25-FW (57.1%).

CONCLUSIONS: Despite higher-than-average educational attainment and equivalent use of high-efficacy treatments in this NYC-based cohort, BPwMS experienced disparate disease outcomes. Our work explicated substantial group differences using detailed cognitive measures and established significant mediation using a composite SES proxy. These results provide an initial roadmap toward targeting these disparities in clinical practice.

DISCLOSURES: *Mitzi J. Williams: Amgen, EMD Serono, Genentech, Sanofi/Genzyme (consulting fee, speakers' bureau); Biogen, Bristol Myers Squibb, TG Therapeutics (consulting fee). Annette F. Okai: Alexion, Biogen, Bristol Myers Squibb, EMD Serono, Roche Genentech, Sanofi Genzyme (consulting fee); Alexion, Biogen, Novartis, Roche Genentech, Sanofi Genzyme, TG Therapeutics. (research support). Aaron E. Miller: BVF Partners, Cell Gene Therapeutics, Frictionless Solutions (for Horizon Therapeutics), MJH Life Sciences, PSL Group, Research America, Sangamo, Slingshot Insights, Third Bridge, Viatris (Mylan) (consulting fee). Sarah Levy, Sylvia Klineova, Claire Wigley, Marwa Baalbaki, Ilana Katz Sand, Michelle Fabian, James F. Sumowski: Nothing to disclose. Stephen Krieger: Baim Institute, Cleveland Clinic, MedRX, Octave (consulting fee); Biogen (consulting fee, contracted research, speakers' bureau); Bristol Myers Squibb (contracted research); EMD Serono, Genentech, TG Therapeutics (consulting fee, speakers' bureau); Novartis, Sanofi/Genzyme (consulting fee, contracted research).*

KEYWORDS: Comprehensive Care and MS, Economic Issues and MS, Psychological Issues and MS

(PLA-E2) Characterizing Disability and MRI Outcomes in Latinx People With Multiple Sclerosis Before and After the COVID-19 Pandemic

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BACKGROUND: In the United States, COVID-19 was disruptive for people with multiple sclerosis (PwMS) and more severely impacted people from racial/ethnic minority backgrounds. The extent to which this disparity affected Latinx PwMS is important to discern due to their increased risk for worse MS outcomes compared to non-Hispanic White (NHW) PwMS.

OBJECTIVES: To assess the impact of the COVID-19 pandemic on disability and MRI activity in US Latinx PwMS and how that impact differed from other racial/ethnic groups.

METHODS: Analysis included PwMS who self-identified as Latinx, non-Hispanic Black (NHB), or NHW in the Multiple Sclerosis Partners Advancing Technology and Health Solutions US sites with 1 or more visits within 1 year prior to March 2020 (pre-COVID), between March 2020 and February 2021 (during COVID peak), and between March 2021 and February 2022 (post-COVID peak). Performance outcomes included Patient-Determined Disease Steps (PDDS), Walking Speed Test (WST), Manual Dexterity Test (MDT), and Processing Speed Test (PST). MRI activity was defined as new T2/gadolinium-enhancing (GdE) lesions. Linear mixed-effects models assessed the impact of the periods on disability and MRI measures in Latinx PwMS, adjusting for age, disease duration, MS phenotype, and smoking status. The same models were applied across all groups, adjusting for race. Outcomes were compared between racial/ethnic groups; interactions between periods and race/ethnicity were explored.

RESULTS: There were 589 Latinx, 1422 NHB, and 8446 NHW PwMS in the study. Baseline characteristics in Latinx, NHB, and NHW were, respectively: women 75%, 80%, 73%; median (IQR) age of diagnosis 31 (24-39), 34 (27-42), 36 (29-44) years; relapsing-remitting 40%, 37%, 42%; and current smoker 13%, 14%, 16%. In Latinx PwMS, MDT (dominant) worsened post pandemic ($P<.001$); PST worsened during the pandemic ($P=.02$); WST worsened post pandemic ($P=.03$) compared to the prepandemic period. Latinx PwMS had worse MDT, WST, and PST vs NHW (all $P<.001$) and better performance measures vs NHB (MDT and WST, $P<.001$; PST, $P=.02$). There was no significant worsening in PDDS or MRI activity in Latinx PwMS across time periods. There were no significant interactions between race and period across PDDS and new T2 lesions.

CONCLUSIONS: Latinx PwMS had worsened disability measures over the pre- to postpandemic period and demonstrated greater disability worsening than NHW but less than NHB. Findings suggest differences in social determinants of health between Latinx PwMS and other racial/ethnic groups during the height of the COVID-19 pandemic.

DISCLOSURES: *Carrie M. Hersh: Alexion, EMD Serono, Genentech, Genzyme, Horizon, TG Therapeutics (consulting fee); Biogen, Bristol Myers Squibb, Novartis (consulting fee, contracted research). Mengke Du, Sarah Worley, Farren B.S. Briggs: Nothing to disclose. Daniel Ontaneda: Bristol Myers Squibb, Genentech, Genzyme, National Institutes of Health, National Multiple Sclerosis Society, Novartis, Patient-Centered Outcomes Research Institute, Race to Erase MS Foundation (contracted research). Devon S. Conway: Alexion, TG Therapeutics (consulting fee); Amgen, EMD Serono (contracted research); Biogen (contracted research, speakers' bureau); Bristol Myers Squibb, Novartis (consulting fee, contracted research).*

KEYWORDS: Health Care Disparities in MS

(PLA-E3) Optical Coherence Tomography Hyper-Reflective Foci in Pediatric Onset Multiple Sclerosis

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BACKGROUND: Youth with multiple sclerosis (MS) experience higher disease activity and earlier onset of disability than adults with MS. Optical coherence tomography (OCT) is a well-established noninvasive method by which to monitor retinal changes

in MS via evaluation of retinal nerve fiber layer (RNFL) thickness and the ganglion cell inner plexiform layer (GCIPL). Recent research in adult MS has identified correlations between measures of disease severity and number of hyper-reflective foci (HRF) on OCT. HRF are thought to represent activated microglia and, therefore, may serve as a surrogate marker for disease activity. Little is known about the extent or relevance of HRF in pediatric-onset multiple sclerosis (POMS).

OBJECTIVES: To compare hyper-reflective foci in POMS to a healthy population.

METHODS: We performed a cross-sectional analysis of children who met McDonald 2017 MS diagnostic criteria and had an OCT performed within 1 year of diagnosis and at least 5 months after an episode of acute optic neuritis. We excluded those with acute optic neuritis, refraction worse than+/− 6 diopters, or those unable to complete the OCT. Healthy controls (HC) had no history of ocular disease, no history of psychiatric or neurological disease, and a refraction better than+/− 6 diopters. OCT scans were performed by a trained technician using the spectral-domain OCT Cirrus scanner (Carl Zeiss Meditec). All scans were reviewed to ensure they satisfied OSCAR 1B criteria modified for Cirrus. To evaluate HRF, the retinal layers were segmented using OCTExplorer, and the retinal layer volumes were calculated using the Early Treatment Diabetic Retinopathy Study (ETDRS) grid. For each eye, HRF were counted on 1 foveal b-scan, 1500um temporally and nasally from the fovea. Hyper-reflective foci were expressed as total number and as a density of the retinal layer volume per mm^3. Descriptive statistics and independent *t* tests were performed to compare the distribution and characteristics of retinal thickness and hyper-reflective foci between the POMS and HC groups.

RESULTS: 36 POMS (27 girls; median age 15, IQR 3 years) and 22 HC (10 girls; median age 14, IQR 4 years) were included. POMS patients had lower ganglion cell layer volume (0.826 vs 0.955 mm^3, $P<.0001$) and inner plexiform layer volume (1.064 vs 1.103 mm^3, $P<.0095$) than HC. Children with MS had more HRF compared to HC in the GCIPL (11.07 vs 9.84 foci, $P=.023$) and the inner nuclear layer (INL, 7.08 vs 4.43 foci, $P<.00001$). The density of HRF was also higher in children with MS compared to HC in the GCIPL (5.92 vs 4.79 foci/mm^3, $P<.001$) and the INL (7.80 vs 4.82 foci/mm^3, $P<.00001$).

CONCLUSIONS: HRF are increased in POMS when compared to HC. These findings corroborate the results seen in adult MS. Whether the frequency of HRF is associated with pediatric disease activity, disability, or markers of progression is unknown and should be the subject of future investigations.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Glial Biology, Imaging and MS

(PLA-E4) Accelerated Metabolomic Aging and Its Association With Social Determinants of Health in Multiple Sclerosis

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BACKGROUND: Biological age, a measure of age-related cell/tissue dysfunction rate determined by different omics data, including metabolomics, estimates health outcomes more accurately than chronological age (cAge). In diseases other than multiple sclerosis (MS), accelerated biological aging may mediate the effects of social determinants of health (SDOH) on disease progression and outcomes. Metabolomics, which captures molecular changes reflective of internal and external factors, enables the estimation of biological age; its association with SDOH indexes, such as the Area Deprivation Index (ADI), may offer insights into how these nonmedical factors influence the outcomes and progression of MS.

OBJECTIVES: To assess differences in metabolomic age (mAge) between people with multiple sclerosis (PwMS) and healthy controls (HC) and investigate the association between accelerated metabolomic aging and SDOH.

METHODS: mAge was calculated for 389 adults (683 serum samples): 66 HCs (142 samples, 20.79%) and 323 PwMS (541 samples, 79.21%) (median age: 45.09 years; IQR: 35.13-53.77; 72.62% women). It was also calculated from 131 pediatric serum samples: 67 HCs (51.15%) and 64 pediatric-onset MS or clinically isolated syndrome (POMS/CIS) (48.85%) (median age: 14.7 years, IQR: 12.35-16.32; 47.33% girls). mAge was calculated using an age estimation model previously developed based on the metabolomic profiles of 11,977 healthy individuals measured using the same untargeted platform utilized for both datasets. Accelerated aging was defined as the difference between mAge and cAge. Between-group comparisons were performed using *t* tests, and the association between mAge and ADI in the adult cohort was examined using linear regression.

RESULTS: Cross-sectionally, age acceleration was 9.48 years (95% CI, 6.29-12.67; $P<.0001$) greater in adults with PwMS and 7.05 years (95% CI, 1.71-12.40; $P=.01$) greater in POMS/CIS compared to HCs. Longitudinally, PwMS (n=131 with longitudinal data) showed a faster biological aging rate than HCs (1.01 biological years per chronological year, 95% CI, 0.00-2.00; $P=.04$). Greater social deprivation was associated with faster biological aging. In PwMS, a 10-percentile increase in ADI was associated with a 0.71-year (95% CI, 0.17-1.25) increase in age acceleration ($P=.01$).

CONCLUSIONS: We demonstrated accelerated biological aging in PwMS and its association with social disadvantage, offering insights into how SDOH may influence MS severity and progression.

DISCLOSURES: *Fatemeh Siavoshi, Rezvan Noroozi, Gina Chang, Vinicius Schoeps, Farren B.S. Briggs: Nothing to disclose. Jennifer Graves: ABM, ATARA Biotherapeutics, Biogen, EMD Serono (contracted research); Google (consulting fee); Horizon, TG Therapeutics (advisory board participation); Novartis (contracted research, pediatric clinical trial steering committee). Emmanuelle Waubant: Advanced Curriculum, NeurologyLive (speakers' bureau); Alexion, Biogen (contracted research); Bristol Myers Squibb (volunteer for data and safety monitoring board); Roche (contracted research, advisory board participation). Pavan Bhargava: Amylyx Pharmaceuticals, GSK (contracted research); EMD Serono, Genentech (contracted research, speakers' bureau). Kathryn C. Fitzgerald: SetPoint Medical (consulting fee).*

KEYWORDS: Metabolomic Age

(PLA-E5) Race-Based Identity and Its Relationship With Neighborhood Marginalization and Mental Health in Pediatric-Onset Multiple Sclerosis

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BACKGROUND: Individuals with pediatric-onset multiple sclerosis (POMS) experience high levels of depression. Disparities in mental health outcomes between individuals of different racial and ethnic backgrounds have been linked to disadvantages in socioeconomic status experienced by different groups. Associations between race-based identity, neighborhood marginalization, and outcomes have not been investigated in individuals with POMS.

OBJECTIVES: To determine the relationship between race-based identity, neighborhood marginalization, and depression in POMS.

METHODS: Patients with POMS (N=97; age=17 yrs, IQR:16-18; 64 girls) attending the Neuroinflammatory Disorders Clinic at The Hospital for Sick Children were included. The Center for Epidemiologic Studies Depression Scale (CES-D; dichotomized with a cutoff score >10 for higher depressive symptoms) and the Canadian Institute for Health Information racial and ethnic categories were used for analysis. Neighborhood marginalization scores (Canadian Marginalization Index 2016) were linked to participant CES-D Scale for Children scores. Descriptive and inferential analyses were conducted.

RESULTS: The marginalization scores for Material Resources (ES=0.25, $P=.039$) and Immigration and Visible Minority (0.52, $P<.001$) were higher for individuals from various racial and ethnic backgrounds with POMS than for White individuals. Black individuals with POMS had the highest marginalization score for Material Resources (median=4.5, IQR=2.0) and Households and Dwellings and had higher odds of living in a neighborhood with the highest quintile of marginalization for Material Resources (OR=7.00, (95% CI, 1.48-33.1, $P=.01$) and Immigration and Visible Minority (OR=4.85, 95% CI, 1.08-21.8, $P=.04$) compared to White individuals with POMS. In comparison to White individuals with POMS (n=41, age=17, IQR16-18, 29F), individuals with POMS from different racial and ethnic backgrounds (n=56, age=17, IQR 16-18, 35 girls) had higher RR for depressive symptoms (RR=1.43, 95% CI, 1.02-2.00; Asian individuals: RR=1.76, 95% CI, 1.22-2.53; Black individuals: RR=1.60, 95% CI, 1.06-2.40).

CONCLUSIONS: Individuals with POMS from different racial and ethnic backgrounds have higher risk for depressive symptoms than White individuals. Black individuals with POMS have higher odds of living in highly marginalized neighborhoods compared to White individuals with POMS. Future studies should investigate intersections between these factors and their influences on health outcomes.

DISCLOSURES: *Paul Y. Yoo, Auva Zarandi, Samantha Stephens, Teresa To, Ruth Ann Marrie, Marcia Finlayson, Robert W. Motl: Nothing to disclose. E. Ann Yeh: Alexion, Hoffman-LaRoche (consulting fee); Pipeline Therapeutics (data safety monitoring board).*
KEYWORDS: Psychological Issues and MS, Social Determinants of Health

(PLA-E6) Clinical and Radiological Features in MOG-Negative vs MOG-Positive Pediatric Acute Demyelinating Syndromes: One Entity or Multiple?

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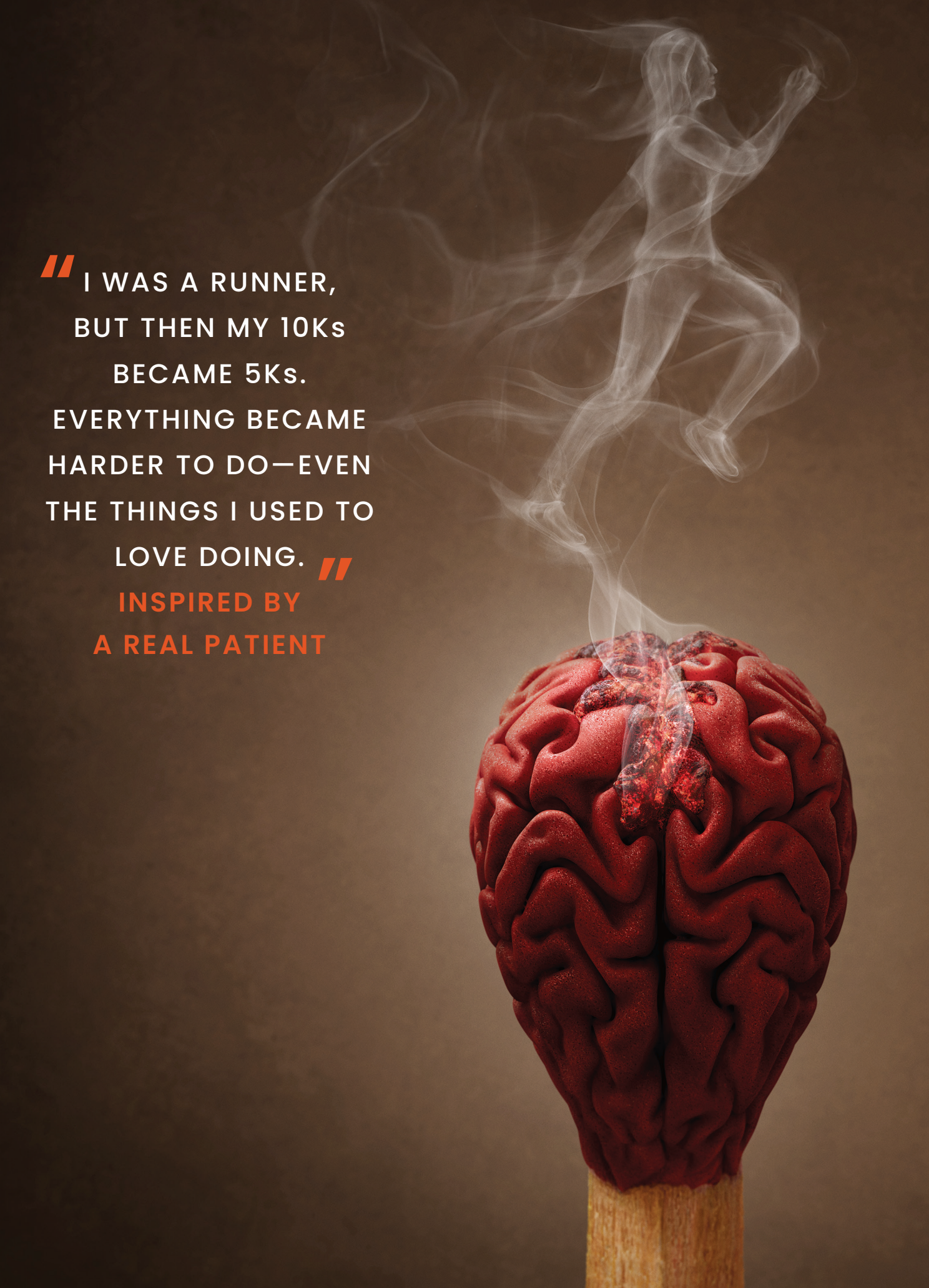
BACKGROUND: Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) relies on clinical and radiological features combined with the presence of myelin oligodendrocyte glycoprotein-immunoglobulin G (MOG-IgG) antibodies. The sensitivity of the MOG IgG assay is uncertain, leading to potential overlap between seropositive and seronegative cases.
OBJECTIVES: To compare clinical and radiological features between children with MOG-negative and MOG-positive assays who meet the diagnostic criteria for MOGAD.
METHODS: Children with acute demyelinating syndromes who presented at a tertiary pediatric hospital in Toronto, Canada, between 2014 and 2024 were included. Eligible patients met clinical and radiological criteria for MOGAD, irrespective of their MOG antibody status, and underwent standardized neuroinflammatory evaluation, including live and fixed cell-based MOG-IgG assays. Patients meeting diagnostic criteria for multiple sclerosis, aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder, acute flaccid myelitis, or other identified neuroinflammatory conditions were excluded. Demographic, clinical, and radiological data were collected through chart review. Descriptive statistics were used to compare the groups. Informed consent was obtained (REB# 1000005356).
RESULTS: The study included 160 patients (124 MOG-positive and 36 MOG-negative), with 79 girls and 81 boys, aged 2 months to 17 years. MOG-negative patients were more likely to present with myelitis than those who were MOG-positive (36% vs 10%; $P<.001$). MOG-positive patients were more likely to present with optic neuritis associated with longitudinal optic nerve involvement and perineural enhancement on MRI ($P<.001$). The relapse rate was higher in MOG-positive compared to MOG-negative (25% vs 5%; $P<.001$). Additionally, elevated white blood cell count in cerebrospinal fluid (CSF) is more likely in MOG-positive compared to MOG-negative (77% vs 54%). There were no significant differences in CSF protein levels, presence of oligoclonal bands, or prodromal infection between groups.
CONCLUSIONS: Children with MOG-negative clinical and radiological features with acute demyelinating syndromes are distinct from their counterparts who are MOG-positive. Further research is essential to elucidate whether double-seronegative syndromes (MOG/AQP4) have unique pathophysiological mechanisms.
DISCLOSURES: *Nothing to disclose.*
KEYWORDS: Glial Biology



"I WAS A RUNNER, BUT THEN MY 10Ks BECAME 5Ks. EVERYTHING BECAME HARDER TO DO—EVEN THE THINGS I USED TO LOVE DOING."

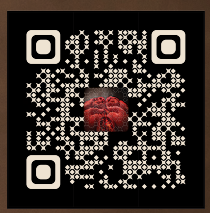
INSPIRED BY A REAL PATIENT

EVEN IF YOU CAN'T SEE

SMOLDERING NEUROINFLAMMATION,

YOU CAN HEAR IT IN PATIENTS' STORIES.

Smoldering neuroinflammation starts at disease onset and may increasingly drive disability accumulation across the MS spectrum.[1,2]



WATCH STORIES INSPIRED BY REAL PATIENTS EXPERIENCING MS DISABILITY PROGRESSION

MS=multiple sclerosis.

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POSTERS

COMPLEMENTARY AND ALTERNATIVE THERAPIES

(CAM01) Is Higher Arterial Stiffness Independent of Body Composition in People With Multiple Sclerosis?

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BACKGROUND: Arterial stiffness is higher in people with multiple sclerosis (PwMS) than controls, and this may be explained by differences in body composition.
OBJECTIVES: This study compared arterial stiffness controlling for body composition in PwMS (n = 81) and control (n = 51) samples matched for age and sex.
METHODS: We measured arterial stiffness based on heart rate–normalized augmentation index (AIx75) and pulse wave velocity (PWV) using applanation tonometry. Body composition was assessed based on total fat mass, body fat percentage, and lean mass using dual-energy x-ray absorptiometry.
RESULTS: The MS sample had higher AIx75 (24.2% vs 19.5%; $P = .04$) and PWV (7.3 m/s vs 6.6 m/s; $P = .02$) than controls, but the samples did not differ based on body composition. AIx75 was associated with all 3 markers of body composition (total fat mass: $r = 0.30$; body fat percent: $r = 0.49$; total lean mass: $r = -0.38$), whereas PWV was only associated with lean mass ($r = 0.33$) in the combined MS and non-MS control samples. The regression analyses indicated that group differences in AIx75 and PWV largely persisted after controlling for age, blood pressure, and markers of body composition.
CONCLUSIONS: Our findings suggest that body composition generally does not explain differences in arterial stiffness between MS and controls.
DISCLOSURES: *Nothing to disclose.*
KEYWORDS: Complementary/Alternative Therapies in MS, Etiology of MS, Management of Activities of Daily Living in MS

CASE REPORTS/ CASE SERIES

(CRS01) Central Neurological Manifestations of Epstein-Barr Virus–Associated Kikuchi-Fujimoto Disease: A Case Study

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BACKGROUND: Kikuchi-Fujimoto disease (KFD) is a rare necrotizing lymphoproliferative disease with a suspected autoimmune etiology, which infrequently has neurological involvement including clinical presentations of meningoencephalitis, acute cerebellar ataxia, and central nervous system vasculitis.
OBJECTIVES: To describe a case of a young patient with new-onset refractory status epilepticus (NORSE) with post–Epstein-Barr virus, biopsy-supported Kikuchi-Fujimoto disease.
METHODS: Chart and literature review.
RESULTS: A 20-year-old right-handed Black man with a history of biliary atresia status post Kasai procedure presented with concerns of persistent fevers and odynophagia, which rapidly progressed to acute respiratory failure requiring emergency intubation. CT imaging revealed acute tonsillitis/adenitis and diffuse lymphadenopathy involving cervical, axillary, mediastinum, retroperitoneal, and femoral regions. Severe transaminitis and hepatic vein thrombosis with subsequent liver ischemia were also observed. By hospital week 4, he developed new-onset tonic-clonic seizure with gaze fixation, requiring initiation of antiseizure medications (ASMs). Electroencephalogram (EEG) results revealed focal to secondarily generalized seizures arising from the left hemisphere. Five days later, he developed facial twitching, and at this time, EEG recordings revealed right hemispheric epileptiform discharges concerning for nonconvulsive status epilepticus. He required up-titration of ASMs to an eventual maximum dosage on 3 agents, necessitating prolonged sedation with multiple intravenous (IV) infusions. Ongoing workup revealed high positive titers of serum Epstein-Barr virus (60,200). Cervical lymph node biopsy results revealed extensive necrosis with necrotic lymphocytes. Cerebrospinal fluid analysis showed pleocytosis (white blood cell count of 11 with lymphocytic predominance). MRI of the brain and autoantibody/paraneoplastic panels was unrevealing. Seizure control was ultimately achieved after 5 days of high-dose IV steroids and 5 sessions of plasmapheresis. In addition, his fever profile and transaminitis also improved. After a prolonged hospital and long-term acute care stay, he was discharged home with decannulation and a modified Rankin Scale score of 3.
CONCLUSIONS: Kikuchi-Fujimoto disease is a rare entity with lymph node necrosis in histopathology and a varying neurological presentation, if present, that may include NORSE. In severe cases, early recognition and treatment with plasmapheresis and steroids may be warranted.
DISCLOSURES: *Nothing to disclose.*
KEYWORDS: Kikuchi-Fujimoto Disease, Epstein-Barr Virus, New Onset Refractory Status Epilepticus (NORSE), Lymphadenopathy, Necrotizing Lymphoproliferative Disease, Lymphocyte Necrosis

(CRS02) Mitigation Strategies to Reduce Allergic Reactions to Ublituximab: A Multicenter Case Series Analysis

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BACKGROUND: Ublituximab (Briumvi®), a monoclonal antibody targeting CD20, has demonstrated efficacy in treating relapsing forms of multiple sclerosis (RMS). However, infusion-related allergic reactions (IRRs) remain a notable concern, particularly during the first or second dose. Effective risk mitigation strategies, including premedications, are crucial for minimizing these reactions and ensuring patient safety during therapy.
OBJECTIVES: To evaluate the effectiveness of risk mitigation strategies, including premedication protocols, in reducing allergic reactions to ublituximab among patients with RMS across multiple centers.
METHODS: This multicenter study analyzed a case series of patients treated with ublituximab. Patients were categorized into 2 groups: those who experienced an allergic reaction during the first or second dose of ublituximab (group A) and those who did not (group B). Detailed data on premedication regimens, infusion protocols, clinical characteristics, and outcomes were collected from participating centers. Prior exposure to B-cell–depleting drugs was recorded, as it also predicted the risk of allergic reactions. For patients in group A, adjustments to premedication and infusion protocols were implemented to prevent the recurrence of IRRs.
RESULTS: The study included 10 patients (5 in group A, 5 in group B) from multiple centers. Common premedications included corticosteroids, antihistamines, and antipyretics. In group A, adjustments such as increased premedication doses, lengthened infusion times, and additional antihistamine administration reduced IRR recurrence, with participants reporting no further allergic events. In group B, adherence to standard premedication protocols was sufficient to prevent IRRs.
CONCLUSIONS: This multicenter case series demonstrates that implementing individualized premedication regimens and modifying infusion protocols effectively mitigate the risk of allergic reactions to ublituximab, enhancing treatment tolerability and patient safety. These findings emphasize the importance of proactive risk management strategies in administering ublituximab for patients with RMS. Further studies are warranted to optimize premedication protocols and standardize practices across clinical settings. Additionally, we will continue to add more patients before the abstract presentation as we continue to identify this issue.
DISCLOSURES: *Anza B. Memon: Connected Research & Consulting, Inlightened (consulting fee). Jacob B. Rube, Mazure Izabela, Tesiley Ash, Ryan Havens, Rebecca Spain, Patti Yager-Stone, Melinda Hungerford, Carey DeLuca, Francesca R. Bagnato, Mitchell T. Wallin: Nothing to disclose. Sam Hooshmand: Amgen, EMD Serono, Genentech, Sanofi Genzyme, TG Therapeutics (scientific advisory boards and/or speaking); Amgen, EMD Serono (research funding to institution).*
KEYWORDS: Immunology and MS, Ublituximab, Briumvi, Allergic Reactions, Infusion-Related Reactions, Risk Mitigation

(CRS03) Myelin Oligodendrocyte Glycoprotein Antibody Disease Misdiagnosis Rates and Associated Factors: Lessons Learned

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BACKGROUND: Myelin oligodendrocyte glycoprotein antibody disease (MOGAD) is a rare inflammatory condition of the central nervous system. Despite the growing

availability of antibody testing, MOGAD remains underrecognized, leading to frequent misdiagnosis and delays in care. This study aims to assess the rate of misdiagnosis and delayed diagnosis in people with MOGAD.

OBJECTIVES: The primary objective was to characterize the frequency and impact of initial misdiagnosis and delayed diagnosis in people with MOGAD. Additionally, we sought to identify factors associated with prolonged time to diagnosis and their effect on patient management.

METHODS: A retrospective review of people with MOGAD at the University of South Florida Neuroimmunology Clinic was conducted. Statistical analyses assessed associations between misdiagnosis and diagnostic delays. **RESULTS:** Of 26 people with MOGAD, 11 (42%) were initially misdiagnosed with an alternative neurologic condition. Alternative initial diagnoses included multiple sclerosis (MS) (6), migraine (2), neuromyelitis optica (1), encephalitis (1), and stroke (1). Misdiagnosis was associated with diagnostic delay (median of 75.5 days in those correctly diagnosed vs 1273.5 days in those misdiagnosed) as well as delayed access to neuroimmunology subspecialty evaluation (median of 104 days in those correctly diagnosed vs 691 days in those misdiagnosed). Median time to initial serum MOGA testing was 19.0 days in those correctly diagnosed vs 313.5 days in those misdiagnosed. Chi-square analysis showed an association between misdiagnosis and delayed serum MOGA testing ($P=.068$). In those with available MOGA indices, misdiagnosis was more common at low levels (rate of misdiagnosis of 29% at index of 1:160 or greater vs 75% at index less than 1:160). Analyzing patterns of radiologic involvement, those with gray matter involvement on MRI were more likely to be initially misdiagnosed ($t=2.278$; $P=.031$). Of note, those initially misdiagnosed with MS were exposed to several disease-modifying therapies, including interferons, glatiramer acetate, teriflunomide, natalizumab, and ocrelizumab.

CONCLUSIONS: Misdiagnosis and delayed diagnosis remain significant challenges in the management of MOGAD, leading to delays in care and inappropriate treatment exposure. Earlier recognition of typical clinical presentations and broadened availability of MOGA testing could help reduce diagnostic delays and prevent neurologic disability accrual.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: MOGAD Diagnosis

(CRS04) What Next When It Becomes a Dual Diagnosis of Amyotrophic Lateral Sclerosis and Multiple Sclerosis: A Case Report

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BACKGROUND: A dual diagnosis of amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS) remains a challenge. The co-occurrence of these 2 distinct neurological diseases in the same individual is rare. ALS is a progressive, fatal neuromuscular disease involving both upper and lower motor neurons, leading to muscle weakness progressing to death. MS is a chronic disease that leads to a weakened central nervous system, affecting musculoskeletal function, and can be progressive. Once the dual diagnoses are established, what is next?

OBJECTIVES: We report a case of co-occurrence of ALS and MS in a 55-year-old right-handed White man who is a military veteran. He was diagnosed by a community provider in 2005 with relapsing-remitting MS after presenting with optic neuritis.

METHODS: Case management revealed that he was treated with steroids for his optic neuritis and started on glatiramer acetate. He continued this immunomodulator until 2014, when he developed weakness on his left side and new lesions in his cervical spinal cord. He was switched to fingolimod. In August 2022, he noticed worsening weakness in his extremities, limiting his ability to ambulate. Initially, the thought was MS relapse, but when dyspnea was noted, his workup was expanded to include electromyography (EMG). Repeated EMGs led to the diagnosis of ALS.

RESULTS: The veteran was started on triple ALS therapy (riluzole, edaravone, and sodium phenylbutyrate/taurursodiol). Soon after, fingolimod was stopped due to thrombocytopenia, leukopenia, and elevated liver function test results. He was referred to the Veterans Health Administration system for continued care. He elected to remain off all MS disease-modifying therapies (DMTs). His symptoms progressed to include dysphagia, neurogenic bladder, loss of musculoskeletal function, and respiratory insufficiency requiring ventilatory support. He is currently at home on invasive ventilatory support.

CONCLUSIONS: We highlight the need for providers caring for people living with MS to keep a high index of suspicion of ALS developing when symptoms similarly seen in both diseases present themselves. Co-occurrence of MS/ALS has been reported. We emphasize the need to pay deliberate attention to relapses to avoid delays in the diagnosis of ALS. The challenge of disease management in codiagnoses with existing treatments is recognized. Should MS DMTs be continued along with the medications for ALS? What discussions are to be held with the patients about disease management? As both diagnoses have several similar symptoms, should the focus be only on symptom management and not on slowing down MS disease progression? When is it prudent to continue MS DMTs and for how long? Providers and patients are faced with many questions, requiring further purposeful exploration because the literature suggests an increased co-occurrence of both diseases.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Natural History of MS, Nursing Management in MS, ALS

(CRS05) Impact of Prompt Diagnosis of Neuromyelitis Optica Spectrum Disorders on Expanded Disability Status Scale Scores in 21 Hispanic Patients: A Retrospective Single-Center Case Series

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[1]Escuela de Medicina y Ciencias de la Salud, Tecnológico de Monterrey, Monterrey, Nuevo León, Mexico; [2]Neurology, MS and Neuroimmunology Center at DHR Health, McAllen, TX

BACKGROUND: Neuromyelitis optica spectrum disorder (NMOSD) is an immune-mediated inflammatory condition affecting astrocytes, resulting in secondary demyelination. NMOSD often mimics multiple sclerosis (MS), leading to frequent misdiagnosis. NMOSD is characterized by stepwise deterioration with each relapse, resulting in increased disability. The antibodies associated with NMOSD target aquaporin 4 on astrocytes. Astrocytes play a role in remyelination and the restoration of oligodendrocytes post MS relapse, but they provide limited self-repair. Consequently, patients with NMOSD seldom regain functionality lost during an acute episode, and even a single episode can lead to lifelong disability. Thus, prompt diagnosis of NMOSD is essential for maintaining function and preventing further disability. Due to the clinical similarities between NMOSD and other neurological disorders, diagnosing NMOSD can be challenging, often prolonging the time to diagnosis and increasing the risk of subsequent relapses. Because disability in NMOSD arises from relapses, timely diagnosis is vital.

OBJECTIVES: This study examines the differences in Expanded Disability Status Scale (EDSS) scores among patients diagnosed with NMOSD before and after the establishment of a neuroimmunology clinic in a predominantly Hispanic community in South Texas. EDSS scores were recorded for each patient at their first NMOSD episode and at their most recent outpatient appointment, focusing on the relationship between time to diagnosis, initiation of disease-modifying therapy (DMT), and EDSS progression.

METHODS: Over a 4.5-year period, patients with NMOSD who presented to our center were entered into an institutional review board–approved database. Demographics, time to diagnosis, time to initiation of DMT, and EDSS scores were assessed.

RESULTS: A total of 21 patients were included in this study, 20 of whom were Hispanic individuals. Of these, 13 were diagnosed before 2021, prior to having a local neuroimmunologist, and 8 were diagnosed after. The average time to diagnosis for patients diagnosed before 2021 was 10.7 years, whereas all patients diagnosed after 2021 received their confirmatory diagnosis within 1 year of symptom onset. Of the 13 patients diagnosed before 2021, 7 were misdiagnosed with MS (54%), 1 was misdiagnosed with myasthenia gravis (8%), and 5 (38%) experienced delays in diagnosis due to low clinical suspicion. Regarding EDSS, patients diagnosed before 2021 had an average increase of 2.5 points in their EDSS scores from baseline to their last clinical visit. In contrast, patients diagnosed after 2021 experienced a decrease of 0.5 points in their EDSS scores during the same period.

CONCLUSIONS: Although larger epidemiological studies are needed to gain a deeper understanding of NMOSD in Hispanic individuals, our single-center study indicates that prompt diagnosis is crucial in preventing significant progression and disability associated with this condition.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Neuromyelitis Optica Spectrum Disorders, NMOSD

(CRS06) Neuromyelitis Optica Spectrum Disorders Demographics, Clinical Presentation, and Response to Treatment: Hispanic Experience in South Texas

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BACKGROUND: Neuromyelitis optica spectrum disorder (NMOSD) is a rare neuroinflammatory astrocytopathy with secondary demyelination. This condition is primarily

relapse dependent, with each relapse potentially worsening the patient's disability. The serological hallmark of NMOSD is aquaporin 4 immunoglobulin (AQP4 IgG) antibodies, which target astrocytes in the central nervous system. Common clinical presentations of NMOSD include optic neuritis, longitudinally extensive transverse myelitis, and area postrema syndrome (APS). This study aims to share our experience with NMOSD in a primarily Hispanic community in South Texas.

OBJECTIVES: We reviewed the medical records of 21 patients diagnosed with NMOSD, 20 of whom had positive test results for AQP4 IgG antibodies; 1 patient had seronegative results but had brain biopsy results consistent with NMOSD. We recorded demographic data, clinical presentation, and response to treatment for all patients.

METHODS: Over a 4.5-year period, patients with NMOSD who presented to our center were entered into an institutional review board–approved database. Demographics, clinical syndrome at presentation, MRI findings, and response to disease-modifying therapy (DMT) were assessed. **RESULTS:** Among the 21 patients considered, 20 were Hispanic individuals and 1 was an African American individual. There was a notable predilection for women, with a ratio of 20:1. The median age at symptom onset was 41 years, with ages ranging from 17 to 77. A total of 10 patients (48%) had an initial presentation of optic neuritis, 8 of whom had MRI findings in accordance with their acute **DIAGNOSIS.** At the time of their first diagnostic MRI, 6 patients had a unilateral optic lesion and 2 had bilateral enhancing lesions. Thirteen patients (62%) exhibited lesions in the brain, and 9 patients (43%) had spinal cord lesions. Patients could present with multiple distributed lesions that were not limited to only these categories. Although APS is a common presentation, it was not observed in our population. Of the 20 patients initiated on DMT, 12 (60%) had experienced at least 1 relapse prior to starting their current DMT regimen. Of these relapses, 6 were attributed to nonadherence (50%), 3 were attributed to misdiagnoses of multiple sclerosis (MS) and treatment with MS DMT (25%), 1 patient was not receiving any DMT (8%), and 2 cases represented treatment failures (17%). One patient opted to receive hospice care.

CONCLUSIONS: Further studies are needed to enhance our understanding of NMOSD in Hispanic populations. By sharing our single-center experience, we hope to contribute to narrowing the knowledge gap regarding NMOSD in primarily Hispanic communities.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Neuromyelitis Optica Spectrum Disorders, NMOSD

(CRS07) Case Report of Severe Relapse After Discontinuing Interferon Beta-1a Therapy in a 60-Year-Old Person With Multiple Sclerosis

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BACKGROUND: Evidence of an increased risk of disease activity to support ongoing treatment with interferons for people with multiple sclerosis (MS) without recent inflammatory activity is limited to those 55 years or older.

OBJECTIVES: To report on a severe relapse after a 60-year-old man with MS discontinued interferon beta-1a therapy to highlight an area for future research.

METHODS: Case report.

RESULTS: A 45-year-old man presented with sensory myelitis, and MRIs revealed brain and spinal cord lesions consistent with MS. Cerebrospinal fluid analysis was positive for oligoclonal bands. The patient was diagnosed with relapsing-remitting MS and commenced disease-modifying therapy (DMT) with interferon beta-1a (Rebif). The patient developed secondary progressive MS at 51 years. At this time, he could walk several miles but began using a cane due to left leg weakness. At 55 years, he felt that he was experiencing more weakness in his legs, and MRI found he had an enhancing lesion at the cervicomedullary junction. At 60 years, he could ambulate 1 block with a unilateral gait aid. Given his age, an absence of disease activity for the preceding 5 years, and his transition to the secondary progressive phase, a decision was made to discontinue interferon beta-1a at 60 years. Sixteen months later, the patient was seen and reported confusion, lack of concentration, and short-term memory deficits dating back many months. Brain MRI revealed numerous new, abnormal T2 hyperintense foci in the juxtacortical and periventricular white matter, brainstem, and right cerebellum. The superior right frontal white matter and right cerebellar lesion demonstrated a small amount of enhancement. Several of these larger lesions were thought to be compatible with Balo concentric sclerosis. In addition, new nonenhancing abnormal cord T2 hyperintensities were seen in the left cord at C3-4 level and C5/C5-6 levels, with progression of fairly diffuse bilateral cord signal abnormality at C5-6. The patient was given 1 g of intravenous methylprednisolone daily for 5 days. Plasma exchange was considered, but the patient and family ultimately decided not to pursue this acute treatment. He was then started on ocrelizumab (Ocrevus) for MS.

CONCLUSIONS: A severe rebound of disease activity is possible in people with MS after stopping interferon beta-1a therapy despite advanced age and prolonged clinical and radiologic stability. Further research is needed to identify the risk of rebound disease activity after stopping all DMTs, including interferons, in patients older than 55 years. Close monitoring of patients who are discontinuing interferons should be considered regardless of the indication for discontinuation.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Disease-Modifying Treatments in MS, Natural History of MS

(CRS08) Cognitive Crossroads: Case Report of Alzheimer Disease Mimicking Cognitive Decline in Primary Progressive Multiple Sclerosis

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BACKGROUND: Primary progressive multiple sclerosis (PPMS) is a subtype of MS characterized by a gradual and continuous progression of neurological symptoms and disability from disease onset without distinct relapses or remissions. Although less prominent than physical disability, cognitive decline, particularly in processing speed, attention, and executive functioning, occurs in 40% to 65% of individuals. Cognitive decline as the sole presenting symptom in PPMS is uncommon but presents a diagnostic challenge due to its subtle onset and overlap with other neurodegenerative conditions. Although MS can result in cognitive dysfunction, the degree of cognitive decline observed in some patients may not correlate directly with the extent of lesion burden or disease progression.

OBJECTIVES: This report presents a case of a 51-year-old woman with PPMS and primary symptom of progressive cognitive decline, suggesting the potential presence of an alternative neurodegenerative process, such as Alzheimer disease (AD), despite MS diagnosis.

METHODS: Retrospective chart review.

RESULTS: The patient developed cognitive and mood changes in 2018, including memory loss, disorganization, and impaired attention, leading to loss of employment by 2020. Initial MRI showed mild white matter changes consistent with chronic ischemia, but her symptoms worsened. In 2023, imaging revealed diffuse T2/fluid-attenuated inversion recovery hyperintense brain and cervicothoracic cord lesions and significant atrophy, leading to a PPMS diagnosis. Despite treatment with ocrelizumab, her cognitive decline persisted. Elevated tau biomarkers (T-tau, p-tau181, p-tau217) and amyloid deposition on PET imaging indicated possible AD. Neuropsychological testing results revealed deficits in multiple domains, including memory and executive function, not fully attributable to PPMS. The patient was diagnosed with comorbid AD and treated with rivastigmine, memantine, and mood-stabilizing medications, leading to subjective improvements despite ongoing decline.

CONCLUSIONS: Cognitive impairment in MS and AD differs in pattern and mechanism. MS-related cognitive changes often involve attention, information processing, and executive function, whereas AD predominantly affects episodic memory. Neuroimaging and biomarkers are essential for differentiation. This patient's findings of amyloid plaques, elevated tau levels, and severe cognitive deficits indicated AD alongside PPMS. This case highlights the diagnostic challenge of distinguishing MS-related cognitive impairment from AD, particularly in overlapping presentations. Accurate differentiation is crucial for tailored treatment. PPMS management includes disease-modifying therapies, whereas AD treatments target amyloid and tau pathology. For coexisting conditions, combined approaches are necessary. Comprehensive evaluation and biomarker analysis are critical for optimizing care in such complex cases.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Psychological Issues and MS

(CRS09) Treatment of Neuromyelitis Optica Spectrum Disorders With Ravulizumab Complicated by Stevens-Johnson Syndrome

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BACKGROUND: Neuromyelitis optica (NMO) is a severe relapsing autoimmune demyelinating disease of the nervous system with poor prognosis and increased mortality.[1] Terminal complement inhibitors have been shown to be highly effective in preventing relapses in NMO phase 3 clinical trials.[2,3] Ravulizumab was approved by the Food and

Drug Administration as a treatment for NMO after showing a relapse risk reduction of 98%, the most effective medication in clinical trials to show that effect.[3]

OBJECTIVES: There are no published reports of ravulizumab-induced Stevens-Johnson syndrome (SJS). We are reporting a case of NMO treated with ravulizumab and complicated by SJS.

METHODS: Case study.

RESULTS: A 32-year-old White woman presented to the hospital with progressive weakness in her lower extremities. Inpatient workup included an MRI of the brain and spine that revealed an extensive lesion extending from the brainstem to the conus with edema and enhancement. Laboratory results showed an anti–aquaporin 4 IgG titer of 1:1000 with cell-based assay. In preparation for ravulizumab treatment, the patient received doses of MenACWY and MenB vaccines. She developed a rash after vaccination that resolved with antihistamine and steroid. The patient received the loading dose of ravulizumab without event. She was started on penicillin and sulfamethoxazole-trimethoprim prophylaxis in addition to continued high-dose steroids. The first maintenance dose of ravulizumab was given on schedule 2 weeks after the loading dose. Three days after this dose, she presented to the hospital with a severe rash on her hands, feet, trunk, and neck as well as conjunctivitis and was diagnosed with SJS. All prophylactic antibiotics were discontinued. Cyclosporine was started, and high-dose prednisone was continued. The patient was treated aggressively for her wounds, and her rash stabilized after 1 week and started to improve after 2 weeks. NMO treatment was changed to inebilizumab, with the first dose given 8 weeks after ravulizumab. Antibiotic prophylaxis was changed to azithromycin and will be continued through 5 half-lives of ravulizumab as meningitis vaccination was not completed.

CONCLUSIONS: Treatment for NMO with the most effective agent is not without risk. Allergic reactions can be severe and fatal. Appropriate follow-up with these patients after the treatment is important to provide early interventions and stabilization. A multidisciplinary approach is crucial to ensure good outcomes.

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DISCLOSURES: *Abigail Wiggins: EMD Serono (speakers' bureau). Ghaida Zaid: Nothing to disclose.*

KEYWORDS: Neuromyelitis Optica Spectrum Disorder, NMOSD

(CRS10) Opsoclonus and Ophthalmoplegia Associated With Anti–Glial Fibrillary Acidic Protein Autoimmune Encephalitis

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BACKGROUND: Anti–glial fibrillary acidic protein autoimmune encephalitis (anti-GFAP AE), also known as anti-GFAP meningoencephalomyelitis or autoimmune GFAP astrocytopathy, was first reported by investigators at Mayo Clinic in 2016. Anti-GFAP AE typically presents with clinical features of meningitis, followed by encephalitis, myelitis, and visual disturbances with papillitis or optic neuritis. Various movement disorders have also been reported, including tremor, clonus, and ataxia, in addition to hyponatremia. MRI characteristically shows linear perivascular gadolinium enhancement perpendicular to the ventricles, though this finding is present in less than 50% of cases. Detection of immunoglobulin G autoantibodies against GFAPα is diagnostic in cerebrospinal fluid.

OBJECTIVES: To our knowledge, the literature contains only 1 case of hyperekplexia and oculogyric crises in a patient with anti-GFAP AE. Our case expands the clinical phenotype and MRI findings of this encephalitis syndrome.

METHODS: Case report.

RESULTS: We present a case of a woman in her 40s who presented with headache, neck stiffness, fevers, and generalized malaise. Influenza, COVID-19, and respiratory syncytial virus tests were negative. She was empirically started on vancomycin, cefepime, and acyclovir for suspected central nervous system infection. Cerebrospinal fluid (CSF) studies found 91% lymphocytic predominant pleocytosis of 202, elevated protein of 88, and normal glucose of 51. CSF culture and meningitis-encephalitis panel were negative, and antimicrobial agents were stopped. She was persistently hyponatremic. Three days into her hospitalization, she developed diplopia and became minimally responsive. On neurologic exam, substantial opsoclonus and left medial rectus palsy were discovered. There was no evidence of papilledema or papillitis on ophthalmologic evaluation. Contrasted MRI brain revealed a nonspecific 4-mm nodular focus of enhancement at the most ventral aspect of the temporal horn of the left lateral ventricle. Radiology provided broad differential for this lesion, including focus of choroid plexus, neoplasm, or infarct. GFAP autoantibodies were reactive on immunofluorescence with titer 1:32, as well as positive reflex cell-based assay on CSF autoimmune/paraneoplastic panel. The serum autoimmune/paraneoplastic panel was negative. CT chest/abdomen/pelvis and MRI pelvis showed a uterine fibroid and benign-appearing hepatic cystic lesions without evidence of malignancy. She had clinical improvement with intravenous corticosteroids and was discharged to inpatient rehabilitation.

CONCLUSIONS: Although MRI findings of linear perivascular gadolinium enhancement perpendicular to the ventricles are the most common finding for patients with anti-GFAP AE, we describe a patient with an atypical focus of enhancement at the ventral aspect of the temporal horn. Additionally, our patient had papillitis, optic neuritis, and retinal disease, which have been reported in anti-GFAP AE. To our knowledge, there is only 1 case in the literature of hyperekplexia and oculogyric crises in a patient with anti-GFAP AE. Our case expands the clinical phenotype and MRI findings of this encephalitis syndrome.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Autoimmune Encephalitis

(CRS11) A Case of Aquaporin-4–Positive Neuromyelitis Optica Spectrum Disorder After Treatment With Nivolumab

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BACKGROUND: Neuromyelitis optica spectrum disorder (NMOSD) is a rare central nervous system autoimmune disease affecting 0.07 to 10 per 100,000 individuals globally. Various neurological immune-related adverse events (irAEs) secondary to immune checkpoint inhibitors (ICIs) are documented, though cases of NMOSD resulting from irAEs are rare. It is unknown whether the natural history of ICI-induced NMOSD is different from de novo cases.

OBJECTIVES: To report the onset of aquaporin-4 (AQP4) antibody positive NMOSD after treatment with nivolumab and highlight the risks of ICIs in triggering autoimmune CNS disorders.

METHODS: Case report

RESULTS: A 50-year-old woman experienced subacute onset of bilateral leg weakness, muscle spasms, urinary urgency, blurry vision, and right eye pain after 7 cycles of nivolumab therapy for malignant melanoma. Her clinical condition improved significantly, but she did not return to baseline. An MRI scan done after the acute phase showed a longitudinally extensive, nonenhancing central T2 hyperintense lesion in the thoracic spinal cord (T2-T6), and a lumbar puncture showed elevated cerebrospinal fluid protein with an increased immunoglobulin G index. Serum AQP4 antibodies by cell-based assay were positive with a titer of 1:40. She was started on immunotherapy treatment with inebilizumab and has not had any relapses.

CONCLUSIONS: NMOSD cases induced by nivolumab and other ICIs are rare. Literature documents at least 2 cases of AQP4+ NMOSD linked to nivolumab, 2 cases linked to pembrolizumab, and 1 involving the combination of ipilimumab and nivolumab. The precise mechanism of triggering NMOSD is indeterminate, though ICIs might induce or unmask underlying NMOSD. NMOSD may also be caused by a paraneoplastic process. However, given the chronology of symptoms and association with ICI therapy, an irAE is more plausible. As the use of ICIs becomes more prevalent in oncology, identifying ICI-associated myelitis secondary to NMOSD promptly is crucial for diagnosis and management. Some case reports suggest ICI-induced NMO may have worse outcomes than de novo NMOSD, although more research is necessary to substantiate this. Our patient has had a mild disease course so far. Further research is imperative to understand how ICIs affect AQP4 antibody production and the risks of ICI combination therapies. Additionally, investigation is needed to assess the utility of pre-ICI therapy screening for AQP4 antibodies.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: NMOSD and Immune Checkpoint Inhibitors

(CRS12) Neutropenic Adverse Effects of B-Cell–Depleting Therapies in Patients With Multiple Sclerosis

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BACKGROUND: Patients with multiple sclerosis (MS) are increasingly treated with monoclonal antibodies directed against CD20. Neutropenia and neutropenic fever are poorly studied complications in this unique population. An improved understanding of their incidence, risk factors, severity, and management would benefit patients and their providers.

OBJECTIVES: To improve the understanding and management of neutropenia in patients with MS on B-cell–depleting therapies.

METHODS: A retrospective cohort study identified patients with MS on B-cell–depleting therapy in a 14-hospital health system by systematic query of the electronic medical record. Neutropenia was defined as an absolute neutrophil count (ANC) less than 1.5, severe neutropenia as an ANC less than 0.5, and neutropenic fever as an ANC less than 0.5 with fever. Neutropenic events were not included if they were consequences of other medications or an underlying bone marrow disorder. For each event, information such as ANC nadir, time to recovery, use of granulocyte colony-stimulating factor (G-CSF), and effect on MS treatment was collected via chart review.

RESULTS: We identified 31 patients with MS who had neutropenic complications of B-cell depleting therapy. Ten patients had multiple episodes. There were 21 episodes from ocrelizumab and 23 from rituximab, though work is ongoing to detect neutropenia in other B-cell–depleting therapies. Twenty-five events met the criteria for severe neutropenia, of which 18 met the criteria for neutropenic fever. The 12 patients who received G-CSF had a faster time to ANC recovery of 3.1 days. Eleven patients were switched away from B-cell–depleting agents because of neutropenia. There were no deaths. The average time on a particular agent before an episode was 35.4 months, with an SD of 30.5 months. Two patients had neutropenia on prior therapies, and 1 patient had 3 episodes on ocrelizumab and 1 on fingolimod.

CONCLUSIONS: Neutropenia, severe neutropenia, and neutropenic fever are complications of B-cell–depleting medications in patients with MS that can result in hospitalization, serious infections, invasive procedures, and a switch to less-effective treatment. The significant number of patients with recurrent episodes supports therapy transition after an index event. The timing of developing neutropenia appears unpredictable, given the wide SD in months on an agent before an event. In this cohort, there were no deaths recorded with appropriate treatment, and the use of G-CSF was both well tolerated and effective.

DISCLOSURES: *Matthew D. Doerfler: Nothing to disclose. Enrique Alvarez: Atara Biotherapeutics, Biogen, Bristol Myers Squibb, Genentech/Roche, National Institutes of Health, National Multiple Sclerosis Society, Novartis, Patient-Centered Outcomes Research Institute, Rocky Mountain MS Center, Sanofi, TG Therapeutics (research support); Biogen, Celgene/Bristol Myers Squibb, Cionic, EMD Serono/Merck, Genentech/Roche, Horizon/Amgen, Novartis, Sanofi, TG Therapeutics (consulting fee). Andrew Wolf: Amgen/Horizon, Novartis (fees for non-CME/CE services); EMD Serono, TG Therapeutics (consulting fee); Genentech (consulting fee, contracted research); Sanofi (contracted research).*

KEYWORDS: Disease-Modifying Treatments in MS, Neutropenia

(CRS13) A Case Highlighting the Potential Ambiguity of Antibody Testing for Co-occurring Myasthenia Gravis and Multiple Sclerosis

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BACKGROUND: Myasthenia gravis (MG) and multiple sclerosis (MS) are both autoimmune neurological conditions. Their co-occurrence has been reported more than would be expected by random chance. It is known that patients with MG can exhibit variable seroreactivity for the acetylcholine receptor (AChR) and muscle-specific kinase antibodies. Apparent seronegative MG may be due in part to B-cell–depleting therapies such as ocrelizumab, which targets antibody-producing cells and treats MS. Therefore, there is ambiguity as to the utility of the antibody tests for patients with co-occurring MS and MG. The case presented here highlights the issues surrounding the diagnostic relevance of antibody testing for concurrent MG in MS patients on B-cell–depleting therapies.

OBJECTIVES: To report insights gained by a case of coexisting MS and seronegative MG.

METHODS: Case study.

RESULTS: A 47-year-old woman was diagnosed with MS in 2015 based on positive oligoclonal bands. She was subsequently followed in the outpatient setting and treated with glatiramer acetate followed by oral teriflunomide before transitioning to ocrelizumab in 2020. At the time of establishing care at our center (2023), her MS was clinically stable; her Expanded Disability Status Scale score was 1.5, and she demonstrated mild overall disability. She reported dysphonia, left-sided ptosis, and reduced bilateral upgaze, which first appeared in 2022. Given her history of MS, there was concern that the disease had evolved to include the brain stem; however, MRI revealed no lesions in this area. Several months before the current presentation, pulmonary function testing was concerning for possible neuromuscular disease. These results, combined with her lack of new MS lesions, prompted additional clinical workup for possible MG. Serologic studies in 2023 revealed negative AChR and muscle-specific kinase antibodies. Single fiber electromyography (SF-EMG) found mildly increased jitter consistent with MG. She was started on 60-mg pyridostigmine 3 times daily, with significant resolution of symptoms.

CONCLUSIONS: This case highlighted a patient with co-occurring MG and MS who failed to demonstrate the antibody testing results expected of MG. This diagnostic uncertainty necessitated ancillary SF-EMG testing to confirm MG diagnosis. Given the technical challenge of performing SF-EMG, it may be helpful to investigate new targets for more sensitive AChR assays.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Disease-Modifying Treatments in MS, Immunology and MS

(CRS14) Female-to-Male Transition and Multiple Sclerosis Radiologically Isolated Syndrome

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BACKGROUND: A female 23-year-old started to transition to male by applying testosterone 1% gel on their shoulders daily. They had an elevated body mass index, had smoked 2 cigarettes daily for the past 8 years, and had no family history of multiple sclerosis (MS). Three months later, they experienced numbness and tingling over the upper lip. Two months later, they experienced reduced right eye acuity with painful eye movements and an associated right afferent pupillary defect consistent with right optic neuritis. MRI scanning confirmed the diagnosis of MS.

OBJECTIVES: People undergoing transition are a part of sexual and gender minorities and are understudied and underreported. This case aims to highlight the impact of sex hormones on MS and the need to study that relationship.

METHODS: We report a case of a person with gender dysphoria who visited us at our tertiary care MS clinic in Australia for the first presentation.

RESULTS: Various investigations and multidisciplinary involvement led to a diagnosis of relapsing-remitting MS within 7 months of the transition initiation.

CONCLUSIONS: A series of events within 1 year does not establish causation, but it makes one think about the relationship between hormones and MS. Convention dictates that female hormones play a role in MS. However, that relationship is questioned when such cases with reverse hormonal profiles are brought examined. This patient had other risk factors for MS, such as obesity, smoking, and residing in a country with an MS prevalence of 131.1 per 100,000 people (Australian data from 2021). In the pathophysiology of MS and the interplay of genetic and environmental factors, was transition (exogenous testosterone supplementation) one of the last checkboxes ticked, thus manifesting as a diagnosis of MS? There is a glaring need to study this cohort of patients in all neurological illnesses, especially MS, where hormonal therapy has been tried but the correct link is yet to be established.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Nursing Management in MS, Psychological Issues and MS

(CRS15) Electroencephalogram Pattern Mimicking Epileptic Discharges Induced by Pembrolizumab Therapy

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BACKGROUND: Pembrolizumab is a monoclonal antibody and immune checkpoint inhibitor (PD1 inhibitor) used in the treatment of a variety of malignancies through prevention of T-cell inhibition. Results of previous studies have described encephalopathy induced by pembrolizumab with electroencephalogram (EEG) demonstrated generalized intermittent slowing for diffuse encephalopathy.
OBJECTIVES: To demonstrate a unique EEG pattern associated with pembrolizumab use.
METHODS: A case report and literature review of EEG findings on pembrolizumab.
RESULTS: A 64-year-old woman with recurrent ovarian cancer and hypertension started pembrolizumab therapy 2 weeks prior. Four days after her second infusion cycle, she presented with altered mental status, nausea, vomiting, fatigue, and 1 episode of new-onset generalized tonic-clonic seizure. She was intubated and started on levetiracetam for seizure treatment and prophylaxis. CT head and cerebrospinal analysis were unremarkable. Laboratory tests revealed chronic leukopenia and, thrombocytopenia and transient hyponatremia. EEG monitoring on presentation revealed diffuse background slowing with a unique EEG pattern of generalized periodic discharges with triphasic morphology but with remarkably high amplitude, 1 to 2 Hz/sec, predominating on the central regions and more prominent with stimulation. There were no clinical events or epileptic discharges captured during EEG monitoring. Unfortunately, the patient died within 2 weeks of her presentation.
CONCLUSIONS: Increased autoimmunity caused by immune checkpoint inhibitors can lead to neurological immune-related adverse events such as altered mental status or seizures. Our patient had a unique EEG pattern consistent with diffuse encephalopathy secondary to pembrolizumab, a finding not described in previous literature. The remarkably high amplitude of these triphasic waves can be mistaken for epileptiform discharges and thus warrant clinical suspicion when there is a history of pembrolizumab use.
DISCLOSURES: *Nothing to disclose.*
KEYWORDS: Comprehensive Care and MS, Monoclonal Antibodies

(CRS16) A Patient With Tumefactive Multiple Sclerosis and Enlarged Choroid Plexus: Could There Be a Connection?

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BACKGROUND: Tumefactive multiple sclerosis (TMS) is a rare radiological multiple sclerosis phenotype that presents with tumorlike lesions. Choroid plexus (CP) is vital for cerebrospinal fluid (CSF) production, immune regulation, and immune cell trafficking into the central nervous system (CNS). CP enlargement has been shown to be associated with an increased MS lesion load and inflammatory CNS activity.
OBJECTIVES: To report the unique co-occurrence of TMS and enlarged CP.
METHODS: Case report.
RESULTS: A 29-year-old White woman developed headache and right visual field deficit that resolved after steroid treatment. Fifteen years later, she presented with right tongue numbness, speech difficulty, and 1 focal seizure. Brain MRI revealed 2 new enhancing tumefactive brain lesions in the left frontal lobe and right parietal lobes; periventricular, deep white matter, cortical and juxtacortical regions; a previously seen left occipital nonenhancing lesion; and CP enlargement. Cervical spine MRI showed a lesion at C1-C2 with patchy enhancement. MRI volumetric analysis is currently being performed. CSF analysis did not reveal pleocytosis or oligoclonal immunoglobulin (IgG) bands. Myelin oligodendrocyte glycoprotein IgG, neuromyelitis optica IgG, antinuclear antibody, extractable nuclear antigen screen, antineutrophil cytoplasmic antibody, rheumatoid factor, angiotensin-converting enzyme, and soluble IL-2 receptor in serum were negative or normal. The patient was diagnosed with TMS and received intravenous methylprednisolone (1g/day for 3 days) followed by oral steroid taper. While on oral steroids, the patient had another relapse, which required an additional course of high-dose steroids (methylprednisolone,1g/day for 5 days). Disease-modifying treatment (DMT) with ofatumumab was initiated. Re-baseline MRI brain, cervical, and thoracic spine imaging performed 6 months after starting ofatumumab treatment demonstrated resolution of contrast enhancement, an interval reduction in MS lesion volume, and persistent CP enlargement. The patient had not relapsed and had no MRI signs of MS activity 3 years after starting DMT.
CONCLUSIONS: This case highlights the potential role of CP enlargement in the pathogenesis of TMS. Further studies are warranted to explore CP enlargement as a biomarker for MS activity and its implications in TMS.
DISCLOSURES: *Nothing to disclose.*
KEYWORDS: Imaging and MS

(CRS17) When Glioblastoma Multiforme Imitates Progressive Multifocal Leukoencephalopathy: A Case Study of a Patient Treated With Natalizumab

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BACKGROUND: The co-occurrence of glioblastoma multiforme (GBM) is rare in patients with multiple sclerosis (MS). Population-based cancer registries have reported a higher proportion of brain tumors in MS patients compared with the general population. Although this may partly reflect surveillance bias, gliosis has been speculated to play a role in tumorigenesis. Existing studies do not account for the influence of disease-modifying therapies (DMTs) or the oncogenic potential of the John Cunningham virus (JCV) in this context.
OBJECTIVES: To describe a case of GBM in a patient with MS treated with natalizumab who was initially misdiagnosed with progressive multifocal leukoencephalopathy (PML).
METHODS: Case report.
RESULTS: A woman in her 40s with a 5-year history of MS, previously treated with interferon β-1a and ocrelizumab, presented with seizures. She had been receiving natalizumab and dalfampridine for the past year. Brain MRI revealed a diffusion-weighted imaging signal change in the mesial temporal lobe, prompting concerns about PML. Serum JCV antibody testing was positive, leading to natalizumab discontinuation and teriflunomide initiation. Follow-up MRI 2 months later revealed T2/FLAIR hyperintensity in the mesial left temporal lobe. The cerebrospinal fluid analysis did not detect JCV by polymerase chain reaction. A subsequent MRI showed a hemorrhagic left temporal lobe mass with thick peripheral nodular enhancement, surrounding edema, and abnormal enhancement along the subependymal surface of the left lateral ventricle. Biopsy confirmed GBM IDH-wildtype with MET amplification and negative MGMT promoter methylation. The patient underwent gross total resection followed by radiation, temozolomide, and bevacizumab. Despite receiving aggressive treatment, she died 8 months later.
CONCLUSIONS: This case underscores the rare concurrence of GBM and MS, initially misattributed to PML due to JCV antibody positivity in a natalizumab-treated patient. Although this case appears to represent primary GBM, given the IDH-wildtype and other molecular markers, the potential contribution of DMTs and JCV in oncogenesis warrants further exploration. More extensive population studies are necessary to investigate the relationship among MS, DMT exposure, JCV status, and the development of GBM. These findings could inform better diagnostic and therapeutic strategies for this challenging and almost universally fatal combination of pathologies.
DISCLOSURES: *Elise Johnson: Genentech, Sanofi Genzyme (consulting fee). Julie L. Penneau, Michelle K. Harms: Nothing to disclose. Sam I. Hooshmand: Amgen, Sanofi Genzyme (consulting fee, contracted research); EMD Serono (contracted research, speakers bureau); Genentech (consulting fee); Novartis (contracted research); TG Therapeutics (consulting fee, speakers bureau).*
KEYWORDS: Disease-Modifying Treatments in MS, Immunology and MS, Oncogenesis and MS

(CRS18) Refractory Anti-NMDAR Encephalitis With Severe Psychiatric Symptoms: Two Cases

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BACKGROUND: A significant proportion of patients with autoimmune encephalitis require second-line treatment. A study dedicated to N-methyl-D-aspartate receptor (NMDAR) encephalitis found the number to be 37% of patients, 74% of whom were tumor-negative. Delays in diagnosis are common for those with a prior psychiatric history, as symptoms are often misattributed to psychiatric disorders. In contrast, those with acute-onset psychosis and no psychiatric history are more likely to receive prompt neurological evaluation. Early second-line therapy, commonly rituximab, especially in tumor-negative and refractory cases, improves outcomes and reduces recurrence risk.
OBJECTIVES: This study emphasized the importance of evaluating patients with prior psychiatric diagnoses who present with psychiatric symptoms unresponsive to antipsychotics or exhibit atypical features such as seizures, autonomic dysfunction, or focal neurological signs. The study also explored treatment strategies for refractory cases, focusing on second-line therapies such as rituximab.
METHODS: A retrospective chart review of patients was conducted.
RESULTS: Case 1 was a 31-year-old woman with a history of depression, bipolar disorder, schizophrenia, and alcohol use disorder who was admitted for acute psychosis and catatonia. Despite treatment with antipsychotics and benzodiazepines, her condition deteriorated rapidly, requiring restraints and continuous monitoring. She

also developed intermittent autonomic dysfunction and focal nonconvulsive status epilepticus (left temporal seizures). Case 2 was a 31-year-old previously healthy woman who presented with 2 weeks of dissociative amnesia and severe cognitive changes and later developed seizures. A diagnostic workup revealed pleocytosis on lumbar puncture; however, neuraxial imaging and a full-body scan showed no abnormalities or malignancy. Continuous electroencephalogram monitoring detected extreme delta brush activity. Infectious disease testing was negative, and anti-NMDAR antibodies were present in her cerebrospinal fluid and serum. Initial treatments, including 5 to 7 sessions of plasmapheresis, methylprednisolone, and intravenous immunoglobulin, did not result in clinical improvement. As a result, second-line therapy with 2 doses of intravenous rituximab, administered 2 weeks apart, was initiated. The patient showed slight improvement, including the ability to follow basic commands and transition to a soft diet, before being discharged to rehabilitation after a prolonged hospital course.

CONCLUSIONS: Autoimmune encephalitis should be considered in patients with prior psychiatric diagnoses who are unresponsive to antipsychotics. Despite available treatments, many patients experience severe long-term disabilities or fatal outcomes caused by delayed diagnosis. Management requires a multidisciplinary approach, individualized treatment plans, and timely escalation of therapy in refractory cases.

DISCLOSURES: *Pakinam Aboutaleb, Shima Zargar: Nothing to disclose. Tania Reyna: Alexion, Biogen, EMD Serono, TG Therapeutics (consulting fee); Biogen, EMD Serono, Novartis, TG Therapeutics, UCB (research support).*

KEYWORDS: Autoimmune Encephalitis

(CRS19) Atypical Presentation of Myelin Oligodendrocyte Glycoprotein Antibody Disease in Patient With Well-Controlled HIV: A Case Report

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BACKGROUND: Myelin oligodendrocyte glycoprotein antibody disease (MOGAD) is an autoimmune disorder that presents as a central nervous system demyelinating disease. Although it has overlapping clinical features with multiple sclerosis (MS) and neuromyelitis optica spectrum disorders, MOGAD is now recognized as a distinct entity. A diagnostic criterion for MOGAD was recently proposed, although the disease spectrum continues to evolve.

OBJECTIVES: To contribute to the list of atypical cases of MOGAD because there is a dearth of data about rapid cognitive decline as the initial presentation of MOGAD.

METHODS: Information was gathered through a review of the patient's medical chart.

RESULTS: A 29-year-old man with a history of treated HIV (currently undetectable viral load) and recently treated ocular syphilis presented with a 2-week history of word-finding difficulties and slow cognition. He also reported intermittent headaches for several weeks. On examination, he demonstrated decreased speech output, irritability, hyperreflexia, a positive Hoffman sign on the left, and mild appendicular ataxia. His Montreal Cognitive Assessment score was 6. MRI of the brain revealed multiple nonenhancing T2/FLAIR hyperintensities in the bilateral optic nerves, periventricular white matter, left cerebellar peduncle, right superior cerebellar peduncle, and right posterior medulla. Notably, the lesion in the left cerebellar peduncle was hyperintense on diffusion-weighted imaging. Spine MRI showed enhancing lesions at C1, C2, C3, and T4 levels. Cerebrospinal fluid analysis revealed 9 cells (96% lymphocytes), normal glucose and protein, and negative results for oligoclonal bands, cytology, cultures, VDRL, John Cunningham virus, PCR, and meningitis, encephalitis, and paraneoplastic panels. Serum MOG immunoglobulin G (cell-based assay) was positive at a titer of 1:1000. The patient was treated with a course of intravenous methylprednisolone, resulting in both subjective and objective improvement. He was to receive a 3-month taper of oral prednisone.

CONCLUSIONS: A patient presenting with cognitive decline, speech difficulties, headache, and multifocal demyelinating lesions in both the brain and spinal cord, along with positive serum MOG.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: MOGAD, Myelin Oligodendrocyte Glycoprotein Antibody Disease, Cognitive Decline

(CSR20) Case Report on Acute Disseminated Encephalomyelitis Following COVID-19 Vaccine

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BACKGROUND: Acute disseminated encephalomyelitis (ADEM) is a rare autoimmune disease that has rarely been reported following COVID-19 vaccination.

OBJECTIVES: We report a case of ADEM following COVID-19 vaccination to help better understand the potential association between the disease and the vaccination.

METHODS: Case report.

RESULTS: A 74-year-old man presented with acute onset of generalized weakness and numbness in all 4 extremities. He reported difficulty walking, frequent falls, double vision, slurred speech, and urinary incontinence. He also had episodes of what he described as "wicked," a blank stare with no loss of consciousness. His symptoms started about 2 weeks after his COVID-19 vaccination. He had no prior viral infection before his symptom onset, and initially, he went to a local hospital due to frequent falls, where he had testing, including cervical and thoracic spine MRIs, which were unremarkable with no cord lesions. He was discharged to a rehabilitation facility. His condition continued to decline, and he was urgently admitted to the hospital for further workup after he was seen in our clinic. His neurological examination results were remarkable for diffuse muscle weakness at 4/5 in his arms and 3/5 in his legs, diminished sensation to light touch and pinprick from his left knee up to T_4 level, brisk reflexes in his arms with positive Hoffman sign, and upgoing toes with no clonus. He had extensive blood work, with results that were all negative or within normal. His cerebrospinal fluid test results showed white blood cell count of 76 with 85% lymphocytes, protein level of 70 mg/dL, and glucose level of 123 mg/dL with negative autoimmune panel. Repeat brain CT and spine MRI with and without contrast showed multiple abnormal foci of enhancement identified in the brain parenchyma, lower pons, cervical spinal cord, and thoracic spinal cord up to T9 level, suggesting inflammatory or infectious process. Results from electromyography and a nerve conduction study of his left upper and lower extremities showed no evidence of generalized polyneuropathy or myopathy. He was diagnosed with ADEM and was treated with intravenous methylprednisolone sodium succinate 1 g daily for 3 days. He responded very well, and his strength significantly improved. He was discharged to inpatient rehabilitation for 2 weeks, where he continued to improve. In his last office follow-up 6 months after his symptom onset, he has almost returned to his baseline condition. Repeat brain CT and spine MRI with and without contrast showed interval improvement of prior enhancement.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Immunology and MS

(CSR21) Measuring Outcomes and Value: An Integrated, Novel Solution for Generating Insights in Multiple Sclerosis Study: Case Trajectories Supported By Multimodal Insights

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BACKGROUND: Multimodal data from the Octave platform were collected from participants enrolled in the Measuring Outcomes and Value: An Integrated, Novel Solution for Generating Insights in Multiple Sclerosis study. This included a multiprotein serum assay, the Multiple Sclerosis Disease Activity (MSDA) test, quantitative MS-specific MRI reports, and clinical insights reports generated by MS-certified nurse care partners using data collected by the Octave Care mobile application.

OBJECTIVES: To examine MSDA scores in the context of common MS management scenarios in a case series of persons with MS (PwMS).

METHODS: All participant cases from the parent trial were reviewed (n = 86), and a subset of cases were identified based on data completeness and availability of MSDA scores plus or minus 30 days around common MS scenarios, which included disease-modifying therapy (DMT) switch; pseudorelapse, defined by increasing MS symptoms in the presence of a stressor (eg, infections or heat); symptom fluctuation, defined by the presence of increasing and decreasing symptoms throughout study participation; and stability, defined by no gadolinium-enhancing or T2 new or enlarging lesions, clinical relapses, or Expanded Disability Status Scale score progression. We calculated descriptive statistics of these case series scenarios in this population and will present detailed case timelines for representative participants from these categories.

RESULTS: Out of 86 cases, 36 cases met our inclusion criteria. Of the 36 participants, 30 were female and 6 were male, with a mean age of 42 (SD, 11) years; 6% (n = 2) had DMT switches, 19% (n = 7) had pseudorelapses, 3% (n = 1) had both a DMT switch and pseudorelapse, 33% (n = 12) had symptom fluctuations, and 39% (n = 14) had stability. Most participants exhibited low to moderate MSDA scores throughout follow-up, con-

sistent with imaging and physical examination scores and lack of confirmed relapses. We observed a decrease in MSDA scores post DMT transition in both participants with DMT switches. Both participants with symptom fluctuation without confirmed relapse had consistently low or moderate MSDA scores over follow-up time.

CONCLUSIONS: MSDA scores coincide with common MS scenarios: Repeated low scores are present during periods of MS stability, even in the presence of other stressors such as infections or heat, and low/moderate scores are present during periods of symptom fluctuation. Utilization of the MSDA test for clinical management of PwMS between standard visits may create opportunities to ensure stable disease status or to intervene for better clinical outcomes.

DISCLOSURES: *Tamara Shabi, Emily M. Schorr, Revere P. Kinkel, Jennifer Graves: Octave Bioscience (contracted research). Annalise Miner: Nothing to disclose. Heather Hua, Rachel Angel, Kelly Leyden, Franklin X. Faust, Lynden Bajus, Ferhan Qureshi, James Eubanks, Sarah Eagleman: Octave Bioscience (salary, employee).*

KEYWORDS: Complementary/Alternative Therapies in MS, Comprehensive Care and MS, Imaging and MS

DISEASE-MODIFYING THERAPY

(DMT01) Disease-Modifying Therapy Selection By Treatment-Naive Patients

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BACKGROUND: The introduction of over 20 disease-modifying therapies (DMTs) for multiple sclerosis (MS) presents patients with complex decisions balancing safety, efficacy, adverse effects, and usability. Among these considerations, efficacy and safety are the 2 primary factors that influence treatment decisions. Shared decision-making (SDM) between patients and providers has been shown to positively affect treatment adherence and outcomes. SDM ensures that treatment aligns with patient priorities and lifestyle.

OBJECTIVES: This study examines how age, sex, and ethnicity influence patient preferences during DMT selection.

METHODS: A survey was administered to 42 DMT-naive patients with MS undergoing therapy selection. Patients ranked factors such as efficacy, safety, adverse effects, ease of use, monitoring, vaccination compatibility, and pregnancy compatibility in order of preference.

RESULTS: As their first priority, 86% of patients ranked efficacy or safety. Patients aged 18 to 35 years prioritized efficacy (63% for efficacy and 23% for safety), whereas those 36 years or older favored safety (30% for efficacy and 55% for safety). Women ranked efficacy higher than safety, whereas men were evenly split. Black participants prioritized safety (25% efficacy and 50% safety), whereas White participants leaned toward efficacy rather than safety (efficacy 45%, safety 29%). Hispanic and Asian populations showed mixed preferences.

CONCLUSIONS: Younger patients and women tend to prioritize high-efficacy treatments over safety, highlighting the need for tailored discussions in SDM. These findings can guide clinicians in aligning treatment strategies with patient demographics and preferences.

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DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Disease-Modifying Treatments in MS, Economic Issues and MS

(DMT02) Outpatient Ocrevus Zunovo Subcutaneous Infusion: Real-World Experience

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BACKGROUND: Ocrevus Zunovo (OZ) is a recent US Food and Drug Administration–approved combination of hyaluronidase, an enzyme that increases the absorption of drugs into tissue, and ocrelizumab, a widely used disease-modifying therapy (DMT) for multiple sclerosis (MS). OZ (ocrelizumab/hyaluronidase) is a 10-minute subcutaneous infusion that can be administered in the clinic as an alternative to intravenous administration in an infusion center, allowing for increased patient convenience, decreased visit times, and reduced infusion center capacity constraints.

OBJECTIVES: To evaluate real-world patient experiences with outpatient administration of subcutaneous OZ, assessing comfort with treatment initiation, tolerability, and treatment-related adverse effects (AEs).

METHODS: Thirty-five consecutive patients completed preinfusion, immediate postinfusion, and 72-hour postinfusion questionnaires before and after OZ treatment. Each patient received a standardized pretreatment protocol with oral premedications to mitigate infusion-related reactions and enhance patient experience. The surveys were designed to assess ease of transition to a subcutaneous infusion from prior treatment (if relevant), tolerability, AEs, and patient satisfaction with OZ.

RESULTS: Twenty-one patients transitioned to OZ from intravenous ocrelizumab. Eight patients received OZ as their first MS DMT, and 6 patients transitioned from other treatments. Thirty-four patients reported high satisfaction with OZ and minimal AEs. One patient presented to the emergency department for evaluation of generalized body aches following the infusion. Overall, infusion-related AEs, such as redness or tenderness at the infusion site, occurred in most patients and were usually very mild or mild (73%). No patients reported more than moderate discomfort, and 100% of patients preferred subcutaneous administration over intravenous infusion. Patients with prior experience with intravenous ocrelizumab rated subcutaneous infusion of OZ as more convenient than intravenous infusion.

CONCLUSIONS: OZ subcutaneous infusion administered in the clinic setting is a convenient and efficient treatment option for patients with MS, increasing patient convenience, providing decreased patient discomfort, and reducing time burdens and infusion center scheduling challenges. These patient-reported outcomes support the integration of subcutaneous OZ into routine clinical care by improving the patient experience and increasing access to treatment.

DISCLOSURES: *Angela Holian: Genentech, TG Therapeutics (consulting fee). Monica W. Buckley, Leann Dixon, Linda Morris, Alexandra Simpson, Mini Singh: Nothing to disclose. Brian G. Weinshenker: Alexion, MedImmune, UCB Biosciences, Viela Bio/Horizon Therapeutics (chair of committees for clinical trials in neuromyelitis optica spectrum disorders); Genentech (consulting fee, speakers' bureau). Robert K. Shin: EMD Serono, Novartis, TG Therapeutics (consulting fee, speakers' bureau).*

KEYWORDS: Disease-Modifying Treatments in MS, Ocrevus Zunovo

(DMT03) Meningioma Formation Highly Associated With Dimethyl Fumarate Use in Patients With Multiple Sclerosis

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BACKGROUND: Dimethyl fumarate (DMF) was approved by the Food and Drug Administration for multiple sclerosis (MS) in April 2013. At the MS Center at Ochsner Health in New Orleans, Louisiana, we have observed a higher rate of meningioma formation in patients who have taken DMF. Biologically, DMF activates the nuclear factor erythroid 2-related factor (Nrf2) pathway, which has been associated with an increase in neoplastic cellular proliferation (Wu S, Lu H, Bai Y. Nrf2 in cancers: a double-edged sword. *Cancer Med*. 2019;8(5):2252-2267. doi:10.1002/cam4.2101).

OBJECTIVES: To investigate the odds of developing meningioma in people with MS (PwMS) who have ever taken DMF compared with PwMS who have never taken DMF. Our hypothesis is that those with DMF exposure have significantly higher odds of future meningioma formation than those with no DMF exposure.

METHODS: We conducted a retrospective case-control study of PwMS seen at Ochsner Health between April 30, 2013, and November 1, 2024. Participants were PwMS who have developed a meningioma. Control participants were PwMS who had not developed a meningioma. The original data set contained 23 participants and 3495 potential control participants. Participants were matched to control participants on age (within 1 year) and sex, using a 1:9 matching ratio (23-229). The exposure was defined as DMF use for 6 months or more prior to meningioma development (cases) or no meningioma development (controls). A conditional logistic regression

model was used to determine the association between DMF and meningioma development.

RESULTS: The conditional OR of meningioma development in those exposed to DMF (yes vs no) was 3.01 (95% CI, 1.15-7.85; *P*=.021).

CONCLUSIONS: The odds of developing meningiomas are significantly higher in PwMS exposed to DMF than in PwMS not exposed to DMF. The observation reveals a significant potential health risk associated with DMF use. We plan to explore whether this observation can be replicated in a larger data set.

DISCLOSURES: *Bridget A. Bagert: Amgen, Bristol Myers Squibb (consulting fee); Atara, Genentech, Sanofi (consulting fee, contracted research); EMD Serono, TG Therapeutics (consulting fee, speakers' bureau). Amber E. Peskin: Sanofi (consulting fee). Leonardo Seoane, Emma Hillis: Nothing to disclose.*

KEYWORDS: Disease-Modifying Treatments in MS, Epidemiology of MS, Pharmacovigilance

(DMT04) Long-Term Follow-Up on Discontinuation of Disease-Modifying Therapy in Patients With Multiple Sclerosis Older Than 60 Years

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BACKGROUND: Multiple sclerosis (MS) is an immune-mediated disorder that commonly manifests with relapses resulting from inflammation in the central nervous system. The mainstay of relapse prevention is disease-modifying therapy (DMT). As persons with MS (PwMS) age, relapse rates tend to decrease and DMT-associated risks likely increase, making the optimal strategy for DMT use among older PwMS unclear.

OBJECTIVES: To guide clinical decisions by evaluating relapse risk, MRI changes, and patient-reported outcomes among older PwMS who discontinue DMT.

METHODS: Inclusion criteria included age greater than or equal to 60 years, MS diagnosis prior to 60 years, a visit to a Cleveland Clinic MS center from 2010 to 2016, and data collected in the Cleveland Clinic Knowledge Program—later replaced by the Multiple Sclerosis Performance Test (MSPT). Clinical data were collected from chart review and MSPT data, with a follow-up time frame of February 2018 to April 2024. Patients were grouped into DMT continuers and DMT discontinuers, with outcomes of interest being number of clinical relapses, new T2 lesions, gadolinium-enhancing lesions, Quality of Life in Neurological Disorders (Neuro-QoL) scores, and MSPT scores. Mixed-effects regression and survival models were used to assess outcomes.

RESULTS: A total of 600 PwMS were included in the original study. As of the updated investigation, 101 (16.8%) patients have died. The median follow-up time after 60 years was 10.5 years (IQR, 7.7-13.4), and 396 (66.0%) patients discontinued DMT. For 62.8% of discontinuers, the discontinued DMT was glatiramer acetate or an interferon. In the overall cohort, 20 (3.3%) patients had at least 1 relapse recorded after 60 years. Risk of relapse was not significantly different between DMT discontinuers and continuers (HR, 1.80; 95% CI, 0.51-6.39; *P* = .365). Incidence of new T2 and gadolinium-enhancing lesions and degree of parenchymal volume loss did not differ significantly between groups. Neuro-QoL Fatigue *t* scores slightly worsened for DMT discontinuers over time (both before and after discontinuation) and improved over time for the DMT continuers. No other significant differences were noted in MSPT or Neuro-QoL scores.

CONCLUSIONS: These data provide valuable insights into relapse risk among PwMS older than 60 years; specifically, relapse risk is low overall and does not differ significantly between those who continue a DMT vs those who discontinue a DMT. These findings support DMT discontinuation as a strategy for managing MS among older patients.

DISCLOSURES: *Daniel R. Orme, Eric Matesen: Nothing to disclose. Devon S. Conway: Alexion, TG Therapeutics (consulting fee); Amgen, Department of Defense, EMD Serono (research support); Biogen (research support, speaking fees); Bristol Myers Squibb, Novartis (consulting fee, research support). Nicolas Thompson: EMD Serono (research support). Le H. Hua: Alexion, Bristol Myers Squibb, EMD Serono, Genzyme, Horizon, Novartis, TG Therapeutics (fees for speaking, consulting, advisory board activities); Genentech (fees for speaking, consulting, advisory board activities, research salary support).*

KEYWORDS: Discontinuation, Disease-Modifying Treatments in MS, Natural History of MS, Age and MS

(DMT05) Real-World Experience of Ozanimod in Adults With Multiple Sclerosis at 12-Month Follow-Up

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BACKGROUND: Ozanimod is a second-generation sphingosine-1-phosphate receptor modulator approved for treatment of relapsing multiple sclerosis (MS). However, real-world data are lacking on ozanimod effectiveness in clinical practice.

OBJECTIVES: To determine the characteristics of people with MS (PwMS) treated with ozanimod, treatment persistence, tolerance, and effectiveness over 1 year.

METHODS: Data were retrospectively collected for PwMS receiving ozanimod at 2 tertiary MS centers who had a diagnosis of MS or clinically isolated syndrome, had received 1 or more dose(s) of ozanimod outside of a clinical trial, and were 18 years or older at ozanimod initiation. We evaluated data up to 1 year after ozanimod start, and a paired *t* test or the McNemar test was used to compare differences between times.

RESULTS: We identified 206 PwMS for inclusion, of whom 186 (90%) had relapsing-remitting MS. Most (n = 146; 71%) had prior disease-modifying therapy (DMT) experience, switching most often from fingolimod (n = 56; 38%) or dimethyl fumarate (n = 22; 15%) to ozanimod. The most common reason for switching to ozanimod was insurance requirements (n = 48; 33%), followed by poor tolerance of prior DMT (n = 29; 20%). Most PwMS (n = 149; 72%) remained on ozanimod at last data collection. The most frequent reasons for discontinuation were adverse effects (n = 21; 37%) and MRI activity (n = 9; 16%). Few PwMS reported tolerability concerns (19%, 9%, and 5% at 3, 6, and 12 months, respectively), with no adverse events for 89% of PwMS at 3, 6, and 12 months. There were no cases of serotonin syndrome. By 12 months, 94% of PwMS did not have a clinical relapse compared with 83% at baseline before starting ozanimod. At 12 months, fewer PwMS had new or enlarging brain T2 lesions (26% vs 6%; *P* = .03) or enhancing lesions (24% vs 7%; *P* = .02) compared with baseline before ozanimod.

CONCLUSIONS: Ozanimod was well tolerated, with good treatment persistence, minimal relapse activity, and reductions in radiographic disease activity compared with baseline.

DISCLOSURES: *Jessica Cooperrider, Jeffrey T. Lambe, Michelle Chu, Du Mengke: Nothing to disclose. Jennifer Reardon: Bristol Myers Squibb (salary, shareholder). Burhan Chaudhry: Bristol Myers Squibb (salary). Paul Damemarie, Andrew Thorpe: Bristol Myers Squibb (salary, employee, shareholder). Carrie M. Hersh: Alexion, EMD Serono, Genentech, Genzyme, Horizon, TG Therapeutics (consulting fee); Biogen, Bristol Myers Squibb, Novartis (consulting fee, contracted research). Devon S. Conway: Alexion, TG Therapeutics (consulting fee); Amgen, EMD Serono (contracted research); Biogen (contracted research, speakers' bureau); Bristol Myers Squibb, Novartis (consulting fee, contracted research).*

KEYWORDS: Disease-Modifying Treatments in MS, Real-World Data

(DMT06) Treatment Outcomes in People With Multiple Sclerosis Who Switched From Teriflunomide to Fumarates vs Initiating Fumarates as a First-Line Therapy

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BACKGROUND: Optimization of multiple sclerosis (MS) long-term outcomes requires early intervention using effective disease-modifying therapies (DMTs). There is limited understanding of real-world clinical outcomes among people with MS (PwMS) who switch between teriflunomide (TERI) and fumarate (FUM) therapies vs those treated with FUM in the first line (FUM-1L).

OBJECTIVES: To compare the annualized relapse rate (ARR) in PwMS who started on TERI and then switched to FUM vs those who started on FUM-1L.

METHODS: This retrospective analysis of the Komodo Health claims database included patients newly diagnosed with MS who initiated either TERI or FUM as first-line therapy for 90 days or more between January 1, 2017, and July 31, 2023. Those who switched from TERI to FUM were propensity score (PS) matched 1:2 with patients on FUM-1L. For each patient switching from TERI to FUM, a cohort of patients on FUM-1L were evaluated as potential matches by having at least as many days between (1) initial MS diagnosis and DMT initiation and (2) initiation of first-line

DMT and end of follow-up in the study. Patients switching from TERI to FUM were then matched without replacement to the control patients on FUM-1L on baseline demographic and comorbidities measured during the 12 months prior to first-line DMT initiation. ARR rates were computed using generalized linear models, adjusting for matched-pair correlation.

RESULTS: In PS-matched patients switching from TERI to FUM (n = 172) and patients on FUM-1L (n = 344) starting from first DMT to end of follow-up, the overall mean ARR was 0.42 (95% CI, 0.33-0.53) and 0.18 (95% CI, 0.14-0.23), respectively, with a rate ratio of 2.34 (95% CI, 1.64-3.36; $P < .0001$). In TERI to FUM and FUM-1L, when ARR was analyzed starting from first DMT to FUM index date, the mean ARR was 0.49 (95% CI, 0.37-0.64) and 0.19 (95% CI, 0.15-0.26), respectively, with a rate ratio of 2.50 (95% CI, 1.65-3.78; $P < .0001$). When ARRs of TERI to FUM and FUM-1L were compared starting from FUM index date to end of follow-up, the mean ARR was 0.35 (95% CI, 0.25-0.47) and 0.16 (95% CI, 0.11-0.23), respectively, with a rate ratio of 2.17 (95% CI, 1.36-3.48; $P = .0012$).

CONCLUSIONS: Patients demonstrated improved outcomes after they switched from TERI to FUM, but optimal outcomes were achieved when FUM was initiated in the first line. These findings highlight the clinical benefits of early initiation of FUM for PwMS.

STUDY SUPPORT: *Biogen*

DISCLOSURES: *Devon S. Conway: Alexion, TG Therapeutics (consulting fee); Biogen (contracted research, speakers' bureau); Bristol Myers Squibb, Novartis (consulting fee, contracted research); Department of Defense, EMD Serono, Horizon Therapeutics (contracted research). Ashmanie Mahatoo, Shailee Shah, Lori H. Travis, Jemima Akinsanya: Nothing to disclose. Alexander Szewczyk: Biogen (salary). James B. Lewin, Nicholas Belviso, Sai L. Shankar: Biogen (ownership interest, salary).*

KEYWORDS: Disease-Modifying Treatments in MS

(DMT07) Key Drivers of Health-Related Quality of Life Among Patients With Neuromyelitis Optica Spectrum Disorder: Findings From a Global Systematic Literature Review

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BACKGROUND: Neuromyelitis optica spectrum disorder (NMOSD) is a chronic autoimmune condition defined by damage to the central nervous system, which can present as longitudinally extensive transverse myelitis, optic neuritis, area postrema, or other diencephalic, cerebral, and pain syndromes. Subsequent NMOSD attacks often lead to cumulative, persistent disability, which affects health-related quality of life (HRQOL).

OBJECTIVES: To perform a systematic literature review (SLR) to characterize HRQOL for people with NMOSD.

METHODS: An SLR was conducted following Cochrane guidelines to identify studies with findings reporting HRQOL in NMOSD published before May 2023 in MEDLINE and Embase. Abstracts from relevant conferences published in the past 3 years were manually searched.

RESULTS: A total of 62 original studies were included in the SLR; 87% were observational studies, and 71% were from Asia. HRQOL among patients with NMOSD as measured by EuroQol-5D (16 studies) and Short Form Health Survey (SF-36; 32 studies) ranged widely, from 0.41 to 0.82 (scale, 0-1) and 34.2 to 79.1 (scale, 0-100), respectively. Of the 32 studies that used the SF-36, 18 had baseline measurements for the SF-36 physical component score, ranging from 27.1 to 42.5, and for the mental component score, ranging from 37.6 to 55.0. Findings from several studies characterized the substantial impact to HRQOL among patients with NMOSD: A total of 83% to 84% of patients reported pain, 71% were fatigued, 68% reported sleep disturbances, 64% experienced sexual dysfunction, and 45% to 52% had depression. The most frequently assessed patient-reported outcomes in NMOSD were related to depression and anxiety, as measured by Beck Depression Inventory (15 studies), followed by pain as measured by Brief Pain Inventory (9 studies) and McGill Pain Questionnaire (7 studies). Despite using pain medication, 70% of patients had a mean pain intensity of 4.3 (scale, 0-10). Patients with neuropathic pain were characterized by higher pain scores and had a significantly higher OR for depression compared with patients with other types of pain.

CONCLUSIONS: Patients with NMOSD are characterized by substantial impact to HRQOL; pain, fatigue, sleep disturbances, sexual dysfunction, and depression greatly affected patients. This review highlights the critical need for comprehensive management of NMOSD to effectively improve physical and mental well-being and enhance QOL for patients with NMOSD.

DISCLOSURES: *Jodie M. Burton: Canadian Agency for Drugs and Technologies in Health (consulting fee); Alexion, Biogen, Novartis, Roche (consulting fee, advisory boards, honoraria); University of Calgary, MS Canada (contracted research). Dustin Cavida, Kristina R. Patterson, Haridarshan Patel, Jenny Y. Park: Amgen (employee, stockholder). Liu Zhang: Amgen (contracted research).*

KEYWORDS: Comprehensive Care and MS, Disease-Modifying Treatments in MS, Management of Activities of Daily Living in MS

(DMT08) Retrospective Evaluation of Infusion Tolerability: Ublituximab Real-World Observational Survey

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BACKGROUND: Ublituximab is a novel monoclonal antibody targeting CD20 and is glycoengineered for enhanced antibody-dependent cellular cytolysis. In the ULTIMATE phase 3 studies, the incidence of infusion-related reactions (IRRs) was highest with the first infusion (43%) and markedly decreased with subsequent infusions (10% with the second, 8% with the third infusion, and 7% with the fourth infusion). Premedications prior to each infusion in the studies included an antihistamine and corticosteroid. Acetaminophen was not permitted at the first infusion to not confound day 2 laboratory results but could be utilized for subsequent infusions at the investigator's discretion.

OBJECTIVES: To describe the tolerability profile of ublituximab infusions in the real-world clinical practice setting.

METHODS: ENAMOR is a retrospective, blinded survey to assess the tolerability profile in people with MS (PwMS) treated with ublituximab in a real-world setting. Clinics completed a single survey to collect data on 10 to 20 PwMS who received up to 4 ublituximab infusions for analyses related to the infusion experience, including premedications, incidence of IRRs, and infusion time.

RESULTS: A total of 21 clinics participated in the ENAMOR survey, collecting data on 401 PwMS. Prior to initiating ublituximab, 127 (31.7%) PwMS were previously on an infusible anti-CD20 therapy. Clinics reported that all infusions were completed in the specified time (median time for the first infusion was 240 minutes, with 60 minutes as the median time for infusions 2-4). IRRs occurred in 19.2% of PwMS with the first infusion, 6.9% with the second infusion, 7.7% with the third infusion, and 5.1% with the fourth infusion. All clinics indicated use of a standardized protocol for premedications and, notably, all utilized an antipyretic with the first infusion, which may have contributed to the lower observed first infusion IRR rate compared with findings from the phase 3 studies.

CONCLUSIONS: Data from the ENAMOR survey support the conclusion that ublituximab infusions are well tolerated in the real-world clinical practice setting. Additional data are to be presented at the meeting.

DISCLOSURES: *Edward J. Fox, Peter Sportelli, Hari Miskin, Christopher A. Garner: TG Therapeutics (salary).*

KEYWORDS: Disease-Modifying Treatments in MS, Immunology and MS

(DMT09) Efficacy and Safety of Subcutaneous Ofatumumab in Patients With Relapsing Multiple Sclerosis Switching From Intravenous Anti-CD20 Therapy by Racial/Ethnic Minority Subgroup

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BACKGROUND: Race/ethnicity may affect disease course in patients with relapsing multiple sclerosis (PwRMS); however, ethnically diverse groups are often underrepresented in clinical trials. It is important to understand the potential impact of race/ethnicity on response to multiple sclerosis (MS) therapies.

OBJECTIVES: This post hoc analysis from the OLIKOS study (NCT04486716) assessed by race/ethnicity subgroup the maintenance of efficacy/safety of ofatumumab (OMB) in PwRMS switching from intravenous (IV) anti-CD20 therapy.

METHODS: OLIKOS enrolled PwRMS (aged 18-60 years) who had received 2 or more courses of ocrelizumab/rituximab, were stable on previous therapy, and switched for reasons other than safety/lack of efficacy. Patients received OMB 20 mg subcutaneously (SC) via autoinjector pen, with standard loading/monthly maintenance doses,

over 12 months. Primary end point was proportion of patients with no change or reduction in the number of gadolinium-enhancing (Gd+) T1 lesions observed by MRI from baseline (BL) to month (M) 12 (only patients with evaluable MRI at BL/M12 were included in the analysis [n = 84]). Secondary end points included immune biomarker changes and treatment-emergent adverse events (TEAEs).

RESULTS: Of 102 patients in the OLIKOS full analysis set, 20 (19.6%) identified as non-Hispanic Black (NHB), 30 (29.4%) as Hispanic/Latino (Hispanic), 48 (47.1%) as non-Hispanic White (NHW), and 4 (3.9%) as other. The mean (SD) age was 43.8 years (8.9) for NHB patients, 41.4 years (7.8) for Hispanic patients, and 44.6 years (8.4) for NHW patients. NHB and Hispanic patients tended to have slightly higher median [min-max] Expanded Disability Status Scale scores at BL (3.0 [0.0-5.5] and 3.25 [0.0-5.5], respectively) than NHW patients (2.5 [0.0-5.5]). At M12, 100% of the 81 patients with evaluable MRI assessments met the primary end point across all race/ethnicity subgroups, with no Gd+T1 lesions identified. Mean immunoglobulin G (IgG) and immunoglobulin M (IgM) levels (g/L) remained within normal reference levels (IgG, 7-16; IgM, 0.4-2.3) across all subgroups from BL to M12. A total of 84.3% (86/102) experienced TEAEs during the study, with 90% (18/20), 70% (21/30), and 91.7% (44/48) of NHB, Hispanic, and NHW patients reporting AEs, respectively. The most common TEAEs across all subgroups were COVID-19 (30.4%), headache (13.7%), and fatigue (11.8%).

CONCLUSIONS: OMB 20 mg SC maintained efficacy and safety in PwRMS switching from IV anti-CD20 therapies regardless of race/ethnicity, as demonstrated by no new Gd+T1 lesions across all subgroups.

DISCLOSURES: *Enrique Alvarez: Atara, Biogen, Bristol Myers Squibb, Genentech/Roche, National Institutes of Health, National Multiple Sclerosis Society, Novartis, Patient-Centered Outcomes Research Institute, Rocky Mountain MS Center, Sanofi, TG Therapeutics (research support); Biogen, Celgene/Bristol Myers Squibb, Cionic, EMD Serono/Merck, Genentech/Roche, Horizon/Amgen, Novartis, Sanofi, TG Therapeutics (consulting fee). Le H. Hua: Alexion, EMD Serono, Genentech, Genzyme, Horizon, Novartis, TG Therapeutics (speaking, consulting, advisory board activities); Genentech (research support). Benjamin M. Greenberg: Alexion, Arialys, Bayer, Clene, Cycle, EMD Serono, Genentech/Roche, Genzyme, Horizon, Immunovant, InterVenn Biosciences, IQVIA, Janssen, Novartis, PHAR, PRIME Education, Sandoz, Signant Health, Syneos Health, TG Therapeutics (consulting fee); Anokion, National Institutes of Health, Regeneron (grant funding); board of Siegel Rare Neuroimmune Association (unpaid member); Clene, GenrAb (equity); UpToDate (royalty). Roland G. Henry: Atara, Boston, Celgene, Genentech/Roche, MedDay Pharmaceuticals, Neurona Therapeutics, Novartis, QIA Consulting, Sanofi Genzyme (consulting fee and/or research funding). Brandon Brown, Rebecca Piccolo: Novartis Pharmaceuticals (salary, stockholder). Angel R. Chinea: Allergan, Biogen, EMD Serono, Genentech, Novartis, Sanofi Genzyme, Teva (speaker).*

KEYWORDS: Disease-Modifying Treatments in MS

(DMT10) MRI-Supported Relapses as Potential Relapsing Multiple Sclerosis Trial Outcome Measure: Use in the Opera I and II Trials With Ocrelizumab

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BACKGROUND: Trials involving patients with relapsing multiple sclerosis (RMS) have a reduction of the annualized relapse rate (ARR) as the primary end point. However, ARR reductions are much lower than reductions in new/enlarging (n/e) T2 lesions. In the OPERA I and II trials comparing ocrelizumab (OCR) with interferon β-1a (IFN), the ARR reductions of 46% and 47%, respectively, were lower than the n/e T2 lesion reductions of 77% and 83%. Possible confounders include pseudoexacerbations, symptom recrudescence events meeting relapse criteria without focal inflammation.

OBJECTIVES: To evaluate MRI-supported relapse as an outcome measure in the OPERA RMS trials, including the effect on disability accumulation vs MRI-unsupported or MRI-indeterminate relapses.

METHODS: Protocol defined relapses (PDR) in the OPERA trials were categorized as MRI-supported (n/e T2 lesion developed in the subsequent MRI), MRI-unsupported (no n/e T2 lesion in the subsequent MRI), or MRI-indeterminate (no subsequent MRI was obtained). Twelve-week confirmed disability progression (12wCDP) and progression independent of relapses (PIRA) were evaluated in patients with MRI-supported and MRI-unsupported relapses.

RESULTS: There were 35 MRI-supported relapses in the OCR arm (annualized rate [AR], 0.025 [95% CI, 0.018-0.035]) and 189 in the IFN arm (AR, 0.145 [95% CI, 0.120-0.174]), resulting in an 83% ARR reduction (rate ratio [RR], 0.17 [95% CI, 0.12-0.20]; $P < .0001$). However, MRI-unsupported relapses were not reduced in 158 in the OCR cohort (AR, 0.112 [95% CI, 0.093-0.135]) and 146 in the IFN cohort (AR, 0.111 [95% CI, 0.091-0.134]) (RR, 1.01 [95% CI, 0.77-1.33], $P = .93$). Few MRI-indeterminate relapses occurred (2 with OCR and 6 with IFN). More patients with MRI-unsupported relapses (14.4% with OCR, 27.4% with IFN) than MRI-supported relapses (8.0% with OCR, 21.0% with IFN) experienced 12wCDP. Few patients experienced PIRA, although this was also more common with MRI-unsupported relapses (1.0% with OCR, 7.4% with IFN) than MRI-supported relapses (0.0% with OCR, 4.2% with IFN). Patients at baseline with MRI-supported relapses tended to be younger and less disabled, have more enhancing lesions, and have higher neurofilament light levels.

CONCLUSIONS: OCR demonstrated greater ARR reduction when using MRI-supported relapses than traditional PDR, suggesting a contribution of pseudoexacerbations to PDR that may contribute noise in the primary outcome of RMS trials. This may have implications for RMS study design. MRI-unsupported relapses were associated with greater disability accumulation, warranting further exploration.

DISCLOSURES: *Enrique Alvarez: Atara, Biogen, Bristol Myers Squibb, Genentech/Roche, National Institutes of Health, National Multiple Sclerosis Society, Novartis, Patient-Centered Outcomes Research Institute, Rocky Mountain MS Center, Sanofi, TG Therapeutics (research support); Biogen, Celgene/Bristol Myers Squibb, Cionic, EMD Serono/Merck, Genentech/Roche, Horizon/Amgen, Novartis, Sanofi, TG Therapeutics (consulting fee). Jessica Priest, Sierra Hennon, David E. Jones: F. Hoffmann-La Roche (shareholder); Genentech (employee). Fabien Bakdache, Qing Wang, Licinio Craveiro: F. Hoffmann-La Roche (employee, shareholder). Stephen Krieger: Baim Institute, Cleveland Clinic, MedRX, Octave (consulting fee); Biogen (consulting fee, contracted research, speakers' bureau); Bristol Myers Squibb (contracted research); EMD Serono, Genentech, TG Therapeutics (consulting fee, speakers' bureau); Novartis, Sanofi/Genzyme (consulting fee, contracted research).*

KEYWORDS: Comprehensive Care and MS, Disease-Modifying Treatments in MS, Imaging and MS

(DMT11) Long-Term Outcomes of the Ozanimod Open-Label Extension Study in Patients With Relapsing Multiple Sclerosis Stratified by Sex

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BACKGROUND: Ozanimod, an oral sphingosine 1-phosphate receptor 1 and 5 modulator, is approved in multiple countries for the treatment of adults with relapsing forms of multiple sclerosis (RMS) or moderately to severely active ulcerative colitis.

OBJECTIVES: Report the safety and efficacy of extended ozanimod exposure stratified by sex.

METHODS: Participants with RMS completing phases 1 to 3 of the ozanimod parent trials were eligible for the DAYBREAK open-label extension trial (NCT02576717) of ozanimod 0.92 mg/d. The primary objective was to evaluate safety; treatment-emergent adverse events (TEAEs) were monitored. The annualized relapse rate (ARR) was calculated via a negative binomial regression pool for all parent trial treatment groups. New/enlarging T2 lesions and the number of gadolinium-enhancing (GdE) lesions were reported for participants who entered DAYBREAK from active-controlled phase 3 trials (database lock: April 7, 2023).

RESULTS: Of 2494 DAYBREAK participants receiving 1 or more doses of ozanimod 0.92 mg, 1668 (66.9%) and 826 (33.1%) were female and male, respectively. The mean of ozanimod exposure in DAYBREAK was 60.5 months (range, 0.03-81.5; 8405.2 total patient-years [PY]) for female participants and 61.9 months (range, 0.7-80.7; 4259.6 total PY) for male participants. In DAYBREAK, 1516 (90.9%) female participants

had any TEAE, 269 (16.1%) had a serious TEAE (SAE), and 64 (3.8%) discontinued due to a TEAE; relatively similar rates occurred in male participants. In female participants, the most common TEAEs were nasopharyngitis (22.0%), headache (19.2%), COVID-19 (17.4%), and upper respiratory tract infection (13.6%), which occurred at relatively similar rates in male participants. In female and male participants, adjusted ARR in DAYBREAK was 0.098 (95% CI, 0.083-0.116) and 0.099 (95%CI, 0.077-0.127), respectively. At DAYBREAK completion, 69.2% and 68.9% of female and male participants were relapse-free, respectively. In DAYBREAK, 3- and 6-month confirmed disability progression occurred in 16.4% and 14.3% of female participants, respectively, and in 18.8% and 17.1% of male participants, respectively. At month 60, adjusted mean number of new/enlarging T2 lesions per scan relative to DAYBREAK baseline (range, 0.753-0.958) and adjusted mean number of GdE lesions (0-0.102) were relatively similar, regardless of parent trial treatment and sex.

CONCLUSIONS: Long-term ozanimod treatment had a favorable safety profile and sustained efficacy for measures of disease activity and progression, with similar results regardless of sex.

FUNDING: Bristol Myers Squibb

DISCLOSURES: *Eva K. Havrdová: Actelion, Celgene, Sanofi Genzyme (advisory boards); Biogen, Merck Serono, Novartis (advisory boards; honoraria/research support); Czech Ministry of Education, National Institute for Neurological Research, European Union-Next Generation EU (research support); Roche, Teva (honoraria/research support). Matilde Inglese: Alexion, Amgen, Biogen, Bristol Myers Squibb, Genzyme, Merck, Novartis, Roche (consulting fee). Italian Multiple Sclerosis Society Foundation, National Institutes of Health, National Multiple Sclerosis Society (grants); Multiple Sclerosis Journal (coeditor). Maria Pia Sormani: Alexion, Biogen, Immunic Therapeutics, Merck, Novartis, Roche, Sanofi (consulting fee). Ieffrey A. Cohen: Astoria, Atara, Biogen, Bristol Myers Squibb, Convelo, Viatris (consulting fee). Krysztof W. Selmaj: Biogen, Celgene, Genzyme, Merck, Novartis, Ono Pharma, Roche, Synthon, Teva (consulting fee). Lawrence Steinman: 180 Life Sciences, AbbVie, Atreca, EMD Serono, Novartis, Pasithea, Teva, TG Therapeutics (consulting fee); Atara (contracted research); Bristol Myers Squibb (consulting fee, contracted research). Douglas L. Arnold: Biogen, Biohaven, Bristol Myers Squibb, Eli Lilly, EMD Serono, Find Therapeutics, Frequency Therapeutics, GlaxoSmithKline, Idorsia Pharmaceuticals, Kiniksa Pharmaceuticals, Merck, Novartis, Race to Erase MS, Roche, Sanofi-Aventis, Shionogi, Xfacto Communications (consulting fee); NeuroRx (equity interest). Xavier Montalban: AbbVie, Actelion, Alexion, BIAL, Biogen, Bristol Myers Squibb/Celgene, EMD Serono, European Committee for Treatment and Research in Multiple Sclerosis, Excemed, Genzyme, Hoffmann-La Roche, Immunic Therapeutics, Janssen Pharmaceuticals, MedDay Pharmaceuticals, Medscape, Merck, Multiple Sclerosis International Federation, Mylan, National Multiple Sclerosis Society, NervGen Pharma, Neuraxpharm, Novartis, Peervoice, Samsung-Biosys, Sandoz, Sanofi Genzyme, Teva Pharmaceutical, TG Therapeutics, and or any of their affiliates (lecture honoraria, travel expenses, participation in scientific meetings, clinical trial steering committee membership, clinical advisory board participation to institution). Daniela Rau: Bayer, Biogen, Celgene, Eli Lilly, Merck, Roche, Sanofi, Teva (consulting fee, speakers' bureau); Novartis (consulting fee, contracted research, speakers' bureau). Kerstin Hellwig: Almirall, Hexal, TG Therapeutics (honoraria); Bayer (research grants); Biogen, Bristol Myers Squibb, Genzyme, Merck Serono, Novartis, Roche, Teva (honoraria, research grants). Corey Cusack, Shafeeq Dugger, Jon V. Riolo, Erik DeBoer: Bristol Myers Squibb (employee and/or shareholder). Sara Eichau: Bayer, Biogen, Bristol Myers Squibb, Janssen, Merck, Novartis, Roche, Sanofi Genzyme, Teva (consulting fee, speakers' bureau).*

KEYWORDS: Disease-Modifying Treatments in MS, Immunology and MS, Women With MS

(DMT12) Subgroup Analysis of Ozanimod Efficacy and Safety During the DAYBREAK Open-Label Extension Trial by Sex and Prior Exposure to Disease-Modifying Treatment

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BACKGROUND: An open-label extension (OLE) trial (DAYBREAK) of ozanimod in patients with relapsing multiple sclerosis (RMS) was recently completed; primary results have been reported.

OBJECTIVES: This post hoc exploratory analysis evaluated the efficacy and safety of ozanimod 0.92 mg during DAYBREAK by sex and exposure to disease-modifying therapy (DMT) prior to ozanimod initiation.

METHODS: Participants with RMS completing phases 1 to 3 of the ozanimod parent trials were eligible for the DAYBREAK OLE trial (NCT02576717) of ozanimod 0.92 mg/d. This subgroup analysis assessed adjusted annualized relapse rate (ARR) during the OLE using negative binomial regression, 3- and 6-month confirmed disability progression (CDP) in the parent and OLE trials, and treatment-emergent adverse events (TEAEs) in women and men who were DMT-naive and DMT-exposed prior to parent-trial enrollment (database lock: April 7, 2023).

RESULTS: The 2494 DAYBREAK participants included 1180 DMT-naive women, 488 DMT-exposed women, 602 DMT-naive men, and 224 DMT-exposed men. Baseline characteristics were similar across subgroups except that DMT-exposed women and men had a lower mean age at MS symptom onset than their DMT-naive counterparts, and DMT-exposed women had higher baseline Expanded Disability Status Scale scores than DMT-naive women. Ozanimod exposure in the OLE trial (mean 60, 61, 62, and 62 months) and overall (mean 74, 75, 76, and 75 months) was similar in DMT-naive women, DMT-exposed women, DMT-naive men, and DMT-exposed men, respectively. ARR was higher in DMT-exposed women (0.13; 95% CI, 0.10-0.16) and men (0.13; 95% CI, 0.08-0.19) than in DMT-naive women (0.07; 95% CI, 0.06-0.10) and men (0.08; 95% CI, 0.06-0.11). A smaller proportion of women—DMT-naive (16%) or -exposed (16%)—had 3-month CDP in the parent trials and the OLE than did men (naive: 19%, exposed: 21%); the same was true for 6-month CDP (women: 14% and 14%; men: 17% and 19%, respectively). Men had lower overall exposure-adjusted incidence rates (IR) per 1000 person-years for any TEAE (naive: 521.8; exposed: 473.2) than women (naive: 750.9; exposed: 742.7); treatment-naive men had the lowest IR of serious TEAEs (men: 24.4 [naive], 38.5 [exposed]; women: 35.5 [naive], 32.7 [exposed]).

CONCLUSIONS: Lower ARRs in DMT-naive vs DMT-exposed men and women support an increased benefit of early initiation of ozanimod as first-line therapy. The higher CDP rates in men than women are consistent with previous reports that men with MS have more rapid disease progression than women. Men had a lower incidence rate of TEAEs than women.

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DISCLOSURES: *Eva K. Havrdová: Actelion, Celgene, Sanofi Genzyme (advisory boards); Biogen, Merck Serono, Novartis (advisory boards; honoraria/research support); Czech Ministry of Education, National Institute for Neurological Research, European Union-Next Generation EU (research support); Roche, Teva (honoraria/research support). Matilde Inglese: Alexion, Amgen, Biogen, Bristol Myers Squibb, Genzyme, Merck, Novartis, Roche (consulting fee). Italian Multiple Sclerosis Society Foundation, National Institutes of Health, National Multiple Sclerosis Society (grants). Multiple Sclerosis Journal (co-editor). Maria Pia Sormani: Alexion, Biogen, Immunic Therapeutics, Merck, Novartis, Roche, Sanofi (consulting fee). Ieffrey A. Cohen: Astoria, Atara, Biogen, Bristol Myers Squibb, Convelo, Viatris (consulting fee). Krysztof W. Selmaj: Biogen, Celgene, Genzyme, Merck, Novartis, Ono Pharma, Roche, Synthon, Teva (consulting fee). Lawrence Steinman: 180 Life Sciences, AbbVie, Atreca, EMD Serono, Novartis, Pasithea, Teva, TG Therapeutics (consulting fee); Atara (contracted research); Bristol Myers Squibb (consulting fee, contracted research). Douglas L. Arnold: Biogen, Biohaven, Bristol Myers Squibb, Eli Lilly, EMD Serono, Find Therapeutics, Frequency Therapeutics, GlaxoSmithKline, Idorsia Pharmaceuticals, Kiniksa Pharmaceuticals, Merck, Novartis, Race to Erase MS, Roche, Sanofi-Aventis, Shionogi, Xfacto Communications (consulting fee); NeuroRx (equity interest). Xavier Montalban: AbbVie, Actelion, Alexion, BIAL, Biogen, Bristol Myers Squibb/Celgene, EMD Serono, European Committee for Treatment and Research in Multiple Sclerosis, Excemed, Genzyme, Hoffmann-La Roche, Immunic Therapeutics, Janssen Pharmaceuticals, MedDay Pharmaceuticals, Medscape, Merck, Multiple Sclerosis International Federation, Mylan, National Multiple Sclerosis Society, NervGen Pharma, Neuraxpharm, Novartis, Peervoice, Samsung-Biosys, Sandoz, Sanofi Genzyme, Teva Pharmaceutical, TG Therapeutics, and or any of their affiliates (lecture honoraria, travel expenses, participation in scientific meetings, clinical trial steering committee membership, clinical advisory board participation to institution). Daniela Rau: Bayer, Biogen, Celgene, Eli Lilly, Merck, Roche, Sanofi, Teva (consulting fee, speakers' bureau); Novartis (consulting fee, contracted research, speakers' bureau). Kerstin Hellwig:*

Almirall, Hexal, TG Therapeutics (honoraria); Bayer (research grants); Biogen, Bristol Myers Squibb, Genzyme, Merck Serono, Novartis, Roche, Teva (honoraria, research grants). Corey Cusack, Shafeeq Dugger, Jon V. Riolo, Erik DeBoer: Bristol Myers Squibb (employee and/or shareholder). Sara Eichau: Bayer, Biogen, Bristol Myers Squibb, Janssen, Merck, Novartis, Roche, Sanofi Genzyme, Teva (consulting fee, speakers' bureau).

KEYWORDS: Disease-Modifying Treatments in MS, Subgroup Analysis

(DMT13) Impact of Ofatumumab on Patient Satisfaction and Quality of Life in Multiple Sclerosis: A Single-Center, Cross-Sectional Study

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BACKGROUND: Monoclonal antibodies have significantly improved the management and course of multiple sclerosis (MS). Among these, ofatumumab stands out for its convenience, allowing self-administration at home via monthly subcutaneous injections. However, limited evidence exists on its impact on patient satisfaction, treatment efficacy, disease burden, and the occurrence of adverse events (AEs). Expert MS nurses play a crucial role in patient education, treatment adherence, and the management of AEs, further enhancing the therapeutic experience.

OBJECTIVES: To evaluate the impact of ofatumumab on patient satisfaction, treatment efficacy, disease burden, and the occurrence of AEs at baseline and after 6 months of treatment.

METHODS: A single-center, cross-sectional experimental study was conducted at the MS Center of the University of Bari. Data were collected at baseline and after 6 months using a structured questionnaire with 4 sections: sociodemographic information, the Treatment Satisfaction Questionnaire for Medication (TSQM) to assess drug satisfaction, the Multiple Sclerosis Impact Scale (MSIS-29) to measure disease burden, and an assessment of AEs. Expert MS nurses provided guidance on self-administration, monitored patient progress, and offered support throughout the study period. Descriptive and inferential statistics were performed using IBM SPSS version 14.

RESULTS: The study cohort included 93 patients, 61.3% of whom were women, with a mean age of 37.3 ± 10.6 years. Over time, a significant reduction in AEs was observed, with no differences between sexes (mean for women, 4.33 vs mean for men, 3.44; $P > .05$). A significant increase in global satisfaction was noted (women: 15.00; men: 15.83; $P < .05$). Treatment efficacy was inversely related to adverse effects ($r = -0.34$; $P < .01$) and convenience ($r = -0.27$; $P < .01$) but positively associated with global satisfaction ($r = 0.10$; $P > 0.05$). MSIS-29 scores revealed correlations between perceived efficacy ($r = 0.25$; $P < .05$) and AEs ($r = -0.38$; $P < .01$). TSQM scores showed strong relationships with convenience ($r = 0.82$; $P < .01$) and global satisfaction ($r = 0.91$; $P < .01$), underscoring the importance of the drug's user-friendly administration.

CONCLUSIONS: The perceived efficacy of ofatumumab is influenced by adverse effects but significantly enhances the impact of the disease on patients' daily lives. Home administration reduces hospital visits, contributing to higher patient satisfaction and improved quality of life. In addition, the role of expert MS nurses in guiding patients through treatment and managing AEs was instrumental in achieving these positive outcomes.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Disease-Modifying Treatments in MS, Employment in MS, Nursing Management in MS

(DMT14) Continuous Ofatumumab Treatment Up to 7 Years Shows a Consistent Safety Profile and Delays Disability Progression in People With Relapsing Multiple Sclerosis

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BACKGROUND: Ofatumumab, a fully human anti-CD20 monoclonal antibody, demonstrated superior efficacy vs teriflunomide in the phase 3 ASCLEPIOS I/II trials in people with relapsing multiple sclerosis (PwRMS). Previously reported data of up to 6 years of ofatumumab treatment demonstrated a favorable safety profile and sustained efficacy.

OBJECTIVES: To describe long-term safety of ofatumumab and assess disability outcomes (up to 7 years) of early initiation of ofatumumab treatment vs delayed treatment (after switching from teriflunomide) in PwRMS, including those recently diagnosed (≤ 3 years) and treatment naive (RDTN).

METHODS: Safety analyses included all participants who received 1 or more dose(s) of ofatumumab in ASCLEPIOS I/II, APOLITOS, APLIOS, or ALITHIOS. Efficacy analyses evaluated cumulative data up to 7 years (cutoff of September 25, 2024) from PwRMS randomly assigned to ofatumumab or teriflunomide in ASCLEPIOS I/II, regardless of whether they entered the ALITHIOS open-label extension phase. Event rates at 3-month and 6-month confirmed disability worsening (3m/6mCDW), progression independent of relapse activity (PIRA; CDW events without prior confirmed relapses), and relapse-associated disability worsening (RAW; disability onset< 90 days from relapse) were assessed.

RESULTS: Exposure-adjusted incidence rates of adverse events (AEs), serious AEs, serious infections, and malignancies remained low and consistent, with no increased risk over 6 years. Previously reported 6-year data (cutoff of September 25, 2023) showed that Kaplan-Meier cumulative event rates were numerically lower in PwRMS receiving continuous ofatumumab in ASCLEPIOS I/II and ALITHIOS (ofatumumab-ofatumumab) vs delayed treatment with teriflunomide-ofatumumab for 6mCDW (21.1% vs 24.8%; $P = .063$), 6mPIRA (15.5% vs 16.6%), and 6mRAW (5.2% vs 5.8%). In RDTN participants, the effect size for PwRMS receiving ofatumumab-ofatumumab vs teriflunomide-ofatumumab was larger (6mCDW: 16.6% vs 23.7%; $P = .033$; 6mPIRA: 11.1% vs 16.8%; 6mRAW: 4.3% vs 4.8%). Updated 7year safety and efficacy data will be presented at the annual meeting.

CONCLUSIONS: These analyses further support long-term safety and efficacy data for ofatumumab in PwRMS, including RDTN PwRMS, informing clinical decision-making.

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KEYWORDS: Disease-Modifying Treatments in MS, Immunology and MS

(DMT15) Changes in Cognitive Fatigue and Brain Activation After 12 Months of Treatment With Ocrelizumab

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BACKGROUND: Cognitive fatigue (CF) is one of the most prevalent and persistent symptoms associated with multiple sclerosis (MS). In previous work, we have developed a fatigue induction paradigm to coincidently study brain activation and behavior as CF develops in MS. This paradigm has consistently shown fatigue-related changes in brain activation in a network of areas, including the caudate nucleus of the basal ganglia, the thalamus, the insula, and the ventromedial prefrontal cortex. We used this paradigm at 2 time points: before individuals with MS had started a course of treatment with ocrelizumab and 12 months into their treatment.

OBJECTIVES: Our hypothesis was that after 12 months on ocrelizumab, individuals with MS would show a normalization of self-reported CF and increased CF-related brain activation.

METHODS: Six women with MS (mean age, 41) and 8 age-matched female controls (mean age, 40) participated. The participants with MS participated in 2 sessions, a baseline session (Time1) and a follow-up session 12 months later (Time2). For controls, only Time1 data were available. In each session, participants worked through 8 blocks of a modified version of the Symbol Digit Modalities Test while functional neuroimaging data were acquired. Each block consisted of 35 stimuli and took 4 minutes to complete. Participants rated their level of CF at baseline and after each task block using a visual analogue scale of fatigue (VAS-F).

RESULTS: To test the idea that self-reported CF would normalize in the MS group, we compared the VAS-F scores from the MS group at Time1 and Time2. Baseline CF decreased after 12 months ($t[5] = 0.49$; $P = .32$; $d = 0.45$), and although the difference was not significant, the effect size was moderate. Moreover, at Time1, the MS group reported more CF than the control group, a difference that was not significant but had a large effect size ($t[6] = 0.90$; $P = .20$; $d = 0.74$). Conversely, after 12 months on ocrelizumab, the difference between the MS and control groups was small ($t[7] = 0.39$; $P = .30$; $d = 0.30$), with a weak effect size. These differences were accompanied by the predicted increase in activation in the fatigue network in the MS group from baseline to 12 months later.

CONCLUSIONS: After 12 months on ocrelizumab, preliminary results in individuals with MS showed a normalization of self-reported CF and an associated increase in baseline CF-related brain activation. This suggests that ocrelizumab may help decrease baseline levels of CF in individuals with MS.

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KEYWORDS: Disease-Modifying Treatments in MS, Fatigue, Imaging and MS

(DMT16) Immune Cell and Inflammatory Marker Dynamics in Cerebrospinal Fluid After Cladribine Tablet Treatment in Patients With Multiple Sclerosis

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BACKGROUND: The effect of cladribine tablet (CladT) therapy on intrathecal inflammation in people with relapsing multiple sclerosis (PwRMS) remains unclear. CLOCK-MS (NCT03963375) is an ongoing, open-label, phase 4, randomized, multicenter study exploring the mechanism of action of CladT in RMS.

OBJECTIVES: To assess longitudinal changes in lymphocytes and soluble markers of intrathecal inflammation in PwRMS following CladT treatment.

METHODS: PwRMS (N = 47) were randomly assigned 1:2:2:1 to a lumbar puncture at baseline (BL) and at either 5 weeks (w), 10w, 1 year, or 2 years post CladT treatment initiation. Cerebrospinal fluid (CSF) from patients completing testing at w5 (n = 7), w10 (n = 10), and year 1 (n = 12) post treatment and blood samples from all 47 patients were analyzed. Single-cell RNA sequencing was performed on a subset of CSF and blood samples.

RESULTS: At BL, participants were 42.9 ± 12.3 years old and 59.6% women, with a median Expanded Disability Status Scale (EDSS) score of 2.3. One year after CladT therapy, EDSS was unchanged ($P = 1.0$) whereas gadolinium-enhancing lesions were significantly reduced vs BL ($P = .004$). Blood B-cell count was reduced at w5 and w10 vs BL ($P < .0001$) and remained lower at year 1 ($P = .023$). A significant reduction in CSF B-cells was observed at w10 ($P = .001$); however, the reduction was not significant at year 1 ($P = .051$). Reduced memory B cells in the CSF were seen at w5 ($P = .023$) and w10 ($P = .005$) and persisted to year 1 ($P = .023$) vs BL. Blood T-cells were significantly reduced at w5 ($P < .0001$), w10 ($P = .001$), and year 1 ($P = .010$) vs BL. CSF T-cells were significantly reduced at w10 ($P = .002$) and year 1 ($P = .016$) vs BL. Various immune cell subsets in the CSF were affected by CladT therapy, including reduced $CD4^+$ T-cells ($P = .002$), an increased proportion ($P = .049$) of $CD4^+$ T regulatory (Treg) cells, and reduced monocytes ($P = .010$) at w10 vs BL. No significant change in CSF neurofilament light chain (NfL) was observed at w5 or w10 post CladT vs BL, but serum NfL was reduced at year 1 ($P = .002$). Transcriptomic analyses of immune cells supported the emergence of populations of $CD4^+$ Treg cells early after CladT therapy, which remained elevated 1 year later in the CSF. Further, T-cell clonal diversity was observed within CSF and altered by CladT treatment.

CONCLUSIONS: Early and sustained effects of CladT therapy can be detected in the CSF, including reductions in B and T cells and an increase in proportion of $CD4^+$ Treg cells, which may be associated with its therapeutic benefit in RMS.

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KEYWORDS: Disease-Modifying Treatments in MS, Immunology and MS

(DMT17) Relationship Between Cognitive Performance and Brain Volume Outcomes in Patients With Early Relapsing Multiple Sclerosis in the ENLIGHTEN Ozanimod Open-Label Study

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BACKGROUND: Low Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) scores are associated with small brain volumes (BVs) in relapsing multiple sclerosis (RMS). The ongoing ENLIGHTEN study is primarily evaluating Symbol Digit Modalities Test (SDMT) scores, a BICAMS component, over 3 years in patients with early RMS on ozanimod. Secondary and exploratory end points include other BICAMS measures (Brief Visuospatial Memory Test–Revised [BVMT-R] and California Verbal Learning Test, Second Edition [CVLT-II]) and BV outcomes.
OBJECTIVES: To determine the percentage of patients with unimpaired cognitive performance (CP) and explore relationships between CP and whole and regional BV after 1 year of ozanimod.
METHODS: ENLIGHTEN (NCT04140305) is an open-label study of ozanimod 0.92 mg daily. This ad hoc interim analysis (cutoff of February 7, 2024) evaluated the percentage of patients with unimpaired CP at 1 year in those with baseline and 1-year data. Unimpaired CP was defined as SDMT score greater than 44, BVMT-R score greater than 17, or CVLT-II score greater than 39 (Beier M, Gromisch ES, Hughes AJ, et al. Proposed cut scores for tests of the Brief International Cognitive Assessment of Multiple Sclerosis (BICAMS). *J Neurol Sci.* 2017;381:110-116. doi:10.1016/j.jns.2017.08.019). Percentages (Wald 95% CIs) and odds of having unimpaired CP by tertiles of whole BV (WBV), cortical grey matter volume (CGMV), and thalamic volume (TV) at 1 year were assessed.
RESULTS: Mean (SD) baseline SDMT, BVMT-R, and CVLT-II scores were 53.2 (11.6; n = 168), 24.4 (7.2; n = 157), and 53.5 (10.8; n = 166), respectively. At baseline and 1 year of ozanimod, 80.4% and 85.1%, 85.0% and 85.6%, and 86.3% and 90.1% of patients had unimpaired CP per the SDMT, BVMT-R, and CVLT-II, respectively. SDMT was unimpaired in 87.8% (95% CI, 78.6%-96.9%) of patients in the high-WBV tertile vs 76.0% (95% CI, 64.2%-87.8%) in the low tertile (OR, 2.3; 95% CI, 0.7-8.0; nominal $P = .1932$) at 1 year. A similar trend was seen for the CGMV tertiles (high: 95.9%; 95% CI, 90.4%-100.0%; low: 82.4%; 95% CI, 71.9%-92.8%; OR, 5.0; 95% CI, 1.0-49.8; $P = .0517$), and the TV tertile comparison reached nominal significance (high: 93.9%; 95% CI, 87.2%-100.0%; low: 75.5%; 95% CI, 63.5%-87.6%; OR, 5.0; 95% CI, 1.2-29.0; $P = .0224$). Similarly, the largest BV tertiles had the largest numerical percentages of patients with unimpaired CP per the CVLT-II at 1 year; this observation was true only for TV based on the BVMT-R. **CONCLUSIONS:** After 1 year of ozanimod, CP was unimpaired in 85.1% to 90.1% of patients. Patients with higher BV generally had less cognitive impairment, suggesting an association between BV and cognition in RMS and warranting further exploration of early ozanimod for preserving BV and cognitive function.

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KEYWORDS: Cognition and MS, Disease-Modifying Treatments in MS, Imaging and MS

(DMT18) Safety and Tolerability of 30-Minute Ublituximab Infusions: Updates From the ENHANCE Study

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BACKGROUND: Ublituximab is an anti-CD20 monoclonal antibody glycoengineered for enhanced antibody-dependent cellular cytotoxicity. Ublituximab is approved for relapsing forms of multiple sclerosis (RMS), with an administration schedule of a 150-mg dose on day 1 followed by 450-mg doses on day 15, week 24, and subsequently every 24 weeks. Conventional 450-mg infusions are administered over 1 hour; however, preliminary data from the ongoing ENHANCE study demonstrated that 450 mg of ublituximab could be safely infused in 30 minutes at week 24.
OBJECTIVES: To provide data on the safety and tolerability of 30-minute, 450-mg infusions at week 24 in participants from the ongoing ENHANCE study.
METHODS: ENHANCE (TG1101-RMS401) is a 48-week trial evaluating the efficacy of a modified ublituximab regimen. The study is actively enrolling people with RMS who are treatment naive or transitioning from other disease-modifying therapies. Participants transitioning from prior anti-CD20 therapy with a B-cell depleted state (< 10 cells/μL) received a 450-mg ublituximab infusion in 1 hour on day 1. Participants with a nondepleted state (B-cells ≥ 10 cells/μL) received 150 mg of ublituximab on day 1 followed by 450 mg of ublituximab administered in 1 hour on day 15. At week 24, all participants received 30-minute, 450-mg ublituximab infusions.
RESULTS: As of October 9, 2024, 44 participants from 16 centers have received 30-minute, 450-mg ublituximab infusions at week 24. Of these participants, 31 had depleted state and 13 had nondepleted state at study entry. Twenty-nine participants transitioned from ocrelizumab, of which 51.7% (15 of 29) reported a wearing-off effect. At day 1, the rates of infusion-related reactions (IRRs) were 15% (2 of 13) and 26% (8 of 31) for participants who received 150 mg and 450 mg of ublituximab, respectively. At week 24, the rate of IRRs for 30-minute infusions was 18% (8 of 44) and all were grade 1 or 2. All 30-minute infusions were completed, with 89% (39 of 44) completed without interruption or slowing. In addition to infusion modification, IRRs were managed with supportive antihistamine and all resolved.
CONCLUSIONS: Administration of a full 450-mg dose in 1 hour on day 1 was well tolerated in patients with B-cell depletion transitioning from prior anti-CD20 therapy. In addition, the frequency of IRRs observed during the 30-minute infusion at week 24 was low and establishes feasibility of rapid infusions that may offer improved convenience. Enrollment in ENHANCE is ongoing, and additional data will be presented.

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KEYWORDS: Disease-Modifying Treatments in MS, Immunology and MS

(DMT19) Real-World Effectiveness and Safety of Cladribine Tablets in Patients With Relapsing Multiple Sclerosis After Suboptimal Response to Prior Injectable Therapy

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BACKGROUND: Cladribine tablets (CladT) are approved in the United States for the treatment of relapsing multiple sclerosis (RMS). Real-world data on the effectiveness, treatment adherence, satisfaction, and safety of CladT in people with RMS (PwRMS) switching from injectable disease-modifying therapies (iDMTs) are limited.

OBJECTIVES: To evaluate the real-world effectiveness, patient-reported treatment adherence and satisfaction, and safety of CladT in PwRMS after a suboptimal response to an iDMT.

METHODS: CLICK-MS (NCT03933215) was a 24-month (m), observational, single-arm, phase 4 study in PwRMS 18 years or older who switched to CladT after a suboptimal response to a platform iDMT. The primary end point was 24m annualized relapse rate (ARR) after initiating CladT. Key secondary end points included adherence and satisfaction as assessed by the Multiple Sclerosis Treatment Adherence Questionnaire (MS-TAQ) and safety.

RESULTS: The study included 62 PwRMS who switched from an iDMT to CladT (mean age, 49 years; 79% women; 83.9% White). Of these, 34 (55%) completed the study. Mean (SD) 24m prior ARR was 0.2 (0.32). Absolute lymphocyte count was within normal range for 83.9% of PwRMS. The most common prior iDMTs were glatiramer acetate (56.5%) and interferon beta-1a (25.8%). The 24m ARR post initiation of CladT was 0.02 (95% CI, 0.000-0.059). Among MS-TAQ respondents, the self-reported adherence rate (≥ 97.4%; n = 37 of 38) and satisfaction ("very satisfied" mean score > 3.9) for CladT across all 4 treatment weeks during a 2-year course was high. Of the participants, 41.9% (26 of 62) experienced treatment-emergent adverse events (TEAEs), and most were mild to moderate in severity. During the 24m observation period, 42 (68%) completed the CladT treatment. Of the 20 (32.3%) who discontinued CladT treatment (mainly due to COVID-19 pandemic–related logistic issues), 3 discontinued due to TEAEs. The most reported TEAEs were lymphopenia (9 of 62; 14.5%), COVID-19 (4 of 62; 6.5%), and herpes zoster (4 of 62; 6.5%). Two (3.2%) PwRMS experienced serious TEAEs. At the 24m visit, grade 3 lymphopenia was reported in 1 participant. No participants experienced grade 4 lymphopenia.

CONCLUSIONS: In this study, PwRMS who were previously treated with an iDMT in the real world and switched to CladT had a low ARR (0.02). Patient-reported treatment adherence and satisfaction with CladT were high among respondents. Most TEAEs were consistent with previous findings with CladT. The CLICK-MS study provides support for switching PwRMS to CladT after experiencing a suboptimal response to an iDMT.

DISCLOSURES: *Joshua Katz: Biogen, EMD Serono, Genentech, Novartis, Sanofi-Genzyme (speakers' bureau). Robert Pace: Alexion, Amgen/Horizon, Biogen, EMD Serono, Genentech, Novartis, Sanofi, TG Therapeutics (consulting fee, speakers' bureau). Augusto Miravalle: Alexion, Celgene, EMD Serono, Genentech, Genzyme, Novartis (consulting fee, speakers' bureau). Julie Aldridge, Angela Chandler: EMD Serono (salary).*

KEYWORDS: Cladribine Tablets, Real-World Evidence, Disease-Modifying Treatments in MS

(DMT20) Secondary Immunodeficiencies in People With Relapsing Multiple Sclerosis Treated With Ocrelizumab vs Rituximab

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BACKGROUND: Anti-CD20 monoclonal antibodies have revolutionized relapsing multiple sclerosis (RMS) treatment due to their high efficacy and tolerability. Ocrelizumab (OCR) is the standard of care, whereas rituximab (RTX) is a commonly used off-label alternative. At our center, the choice between OCR and RTX often depends on insurance coverage, with only RTX funded by public health care. The impact of anti-CD20 therapies on lymphocyte, neutrophil, and immunoglobulin levels remains understudied, although deficiencies are frequently observed and have been associated with increased risk of infection. Therefore, investigating the comparative risk of biochemical immunodeficiency in people with RMS treated with OCR and RTX is critical to optimizing patient safety.

OBJECTIVES: To characterize and compare lymphocyte, neutrophil, and immunoglobulin levels over time in people with RMS treated with OCR vs RTX.

METHODS: This was an observational retrospective chart review of patients with confirmed RMS who were started on OCR or RTX between January 2017 and June 2023. Lymphocyte, neutrophil, and immunoglobulin levels (eg, IgG, IgA, IgM) from before and after treatment initiation were collected, and deficiencies were defined as values below the lower limit of normal per local laboratory guidelines. Survival analysis comprised Kaplan-Meier curves with log-rank tests and Cox proportional hazards models.

RESULTS: A total of 350 people with RMS treated with OCR (n = 175) or RTX (n = 175) were included. Patients treated with OCR had a mean (SD) age of 48.3 (8.2) years, were 78.7% female, and had been on treatment for a mean of 60.9 (19.1) months; patients treated with RTX had a mean age of 44.5 (10.5) years, were 69.6% female, and had been on treatment for a mean of 42.7 (19.5) months. A significantly shorter time to IgM deficiency was observed with RTX compared with OCR (29.6 vs 40.0 months; $P = .02$). No significant differences in time to secondary immunodeficiency between treatment groups were seen for lymphocytes, neutrophils, IgG, or IgA levels. Cox proportional hazards analysis revealed treatment with RTX was the only variable associated with a higher risk of IgM deficiency (HR, 1.54; 95% CI, 1.06-2.23; $P = .02$).

CONCLUSIONS: RTX was associated with a shorter time to and increased risk of IgM hypogammaglobulinemia compared with OCR, highlighting the importance of long-term monitoring. Further investigation is needed to understand the clinical implications of these findings to optimize treatment decisions.

DISCLOSURES: *Julia Handra, David J. Hunt, Jomana Morkous, Kyra West, Wakeel Kasali, Son Luu, Robert L. Carruthers, Virginia Devonshire, Nathan Y. Chu, Alice Schabas: Nothing to disclose. Donna Kuipers: Apotec, Biogen, EMD Serono, Novartis, Roche, Sentrex (consulting fee).*

KEYWORDS: Comprehensive Care and MS, Disease-Modifying Treatments in MS, Immunology and MS

(DMT21) Efficacy and Safety of Inebilizumab Among Non-White Demographic Groups With Neuromyelitis Optica Spectrum Disorder: N-Momentum Study Subgroup Analysis

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BACKGROUND: There is a need for efficacy and safety information on disease-modifying therapies for neuromyelitis optica spectrum disorder (NMOSD) in non-White demographic groups. Inebilizumab (INEB), an anti-CD19 B-cell depleting antibody, is approved for the treatment of NMOSD in adults seropositive for

aquaporin-4 antibody (AQP4+).

OBJECTIVES: To evaluate the efficacy of inebilizumab in Asian, Hispanic/Latino (H/L), and Black/African American (B/AA) patients with NMOSD.

METHODS: N-MOmentum (NCT02200770) was a double-blind, phase 2/3 trial that assessed the efficacy and safety of INEB in adults with NMOSD, with a 28-week randomized controlled period (RCP) (intravenous INEB 300 mg or placebo [PBO] on days 1 and 15) and an open-label period (OLP) of 2 years or more.

RESULTS: Participants receiving INEB in the RCP were less likely to have an attack compared with those receiving PBO: Asian (HR, 0.20; 95% CI, 0.06-0.66; *P*=.01), H/L (HR, 0.25; 95% CI, 0.06-1.01; *P*=.05), B/AA (HR, 0.33; 95% CI, 0.02-5.31; *P*=.44), White (HR, 0.27; 95%CI, 0.11-0.66; *P*=.004). Expanded Disability Status Scale (EDSS) scores worsening from baseline to last RCP visit for participants receiving INEB vs PBO were: Asian (OR, 0.58; 95% CI, 0.09-3.63; *P*=.56), H/L (OR, 0.50; 95% CI, 0.09-2.70; *P*=.4), White (OR, 0.37; 95% CI, 0.14-0.95; *P*=.04). B/AA participants receiving INEB (0/15) did not experience EDSS worsening compared with 20% of PBO (1/5) participants. For participants who received any INEB during the study (combined RCP/OLP), the annualized attack rates were: Asian 0.10 (95% CI, 0.05-0.18), H/L 0.07 (95% CI, 0.04-0.15), B/AA 0.05 (95% CI, 0.01-0.33), White 0.08 (95% CI, 0.05-0.13). Among INEB participants, 1 or more investigational product-related treatment-emergent adverse events were reported: Asian (16/46), H/L (12/40), B/AA (12/19), White (48/120).

CONCLUSIONS: Non-White NMOSD participants receiving inebilizumab had improved outcomes compared with those receiving placebo, and results were similar to those seen in White participants. However, evaluation of larger populations is needed to confirm these results.

DISCLOSURES: *Friedemann Paul: Bayer, Biogen Idec, Merck Serono, Novartis, Sanofi Genzyme, Teva (contracted research, speakers' bureau, travel reimbursement); German Research Council, German Competence Network for Multiple Sclerosis (contracted research); Guthy-Jackson Charitable Foundation (travel reimbursement); Novartis (study steering committee). Kazuo Fujihara: AbbVie, Alexion, Asahi Kasei Kuraray Medical, Biogen, Chugai/Roche, Eisai, Japan Tobacco, MedImmune/Viela Bio, Merck, Merck Biopharma, Mitsubishi-Tanabe, Novartis, Teijin, Takeda Pharmaceutical Company, UCB (consulting fee, speakers' bureau, steering committees); Ministry of Health, Welfare, and Labor of Japan (contracted research). Mirla Avila: Amgen, EMD Serono, Biogen, Bristol Myers Squibb (consulting fee). Yanping Wu, Kristina R. Patterson, Dan Cimbora: Amgen (salary, employee, stockholder). Bruce A.C. Cree: Alexion, Atara, Autobahn, Avotres, Biogen, Boston Pharma, EMD Serono, Gossamer Bio, Horizon, Immunic Therapeutics, Neuron 23, Novartis, Sandoz, Sanofi, Siemens, TG Therapeutics, Therini Bio (consulting fee); Genentech (research).*

KEYWORDS: Disease-Modifying Treatments in MS, Immunology and MS, Management of Activities of Daily Living in MS

(DMT22) Improvements in Pain and Disability Contribute to Improved Quality of Life After Inebilizumab Treatment in Attack-Free Neuromyelitis Optica Spectrum Disorder Participants

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BACKGROUND: Chronic pain and disability are enduring effects of NMOSD and contribute to decreased quality of life (QOL). We evaluated pain and QOL improvement in attack-free, inebilizumab-treated participants over 3 years to determine improvements in non–attack-related pain and QOL.

METHODS: N-MOmentum (NCT02200770) was a phase 2/3 trial with 230 participants (randomly assigned 3:1, 300-mg inebilizumab:placebo), with an open-label extension of 2 or more years. Year-over-year changes in pain (SF-36 bodily pain score [BPS]), QOL (SF-36 physical component summary [PCS]), and disability (Expanded Disability Status Scale [EDSS]) were assessed for significance using mixed linear models in participants who were attack-free with 3 or more years of inebilizumab. Sensitivity analysis was conducted in participants who were attack-free for 6 or more months prior to inebilizumab treatment to control for acute attack-related recovery.

RESULTS: At baseline, 36 of 95 participants reported an abnormal QOL score (SF36 PCS< 40); 32 of these 36 reported increased pain (SF36-BPS< 40), and 18 of 36 reported significant disability (EDSS≥ 5). After 3 years of inebilizumab, QOL scores improved in 32 of 36 attack-free participants with an abnormal baseline QOL score; 37 of 95 participants had abnormal pain scores (SF36 BPS< 40) at baseline, and improvements were reported in 29 of 37 (*P*< .001) after 3 years of inebilizumab. SF36 PCS and BPS scores improved in participants with normal (≥ 40) baseline scores after 3 years of inebilizumab. Improvements in EDSS from baseline to 3 years of inebilizumab were observed in 40 of 91 participants, including 25 of 69 with less disability (<5 EDSS) and 15 of 22 with greater disability (≥ 5 EDSS) at baseline. Results were consistent with the sensitivity analysis.

CONCLUSIONS: Year-over-year improvements in pain, QOL, EDSS, and FSS were observed in attack-free participants on inebilizumab and independent of acute attack-related recovery.

DISCLOSURES: *Orhan Aktas: Alexion, Almirall, Bayer, Biogen, Amgen, Merck Serono, Novartis, Roche, Sanofi, Teva (contracted research, personal fees). German Research Foundation, German Ministry of Education and Research (contracted research); Guthy-Jackson Charitable Foundation (travel reimbursement. Friedemann Paul: Bayer, Biogen, Merck Serono, Novartis, Sanofi Genzyme, Teva (contracted research, speakers' bureau, travel reimbursement). German Research Council, German Competence Network for Multiple Sclerosis (contracted research); Guthy-Jackson Charitable Foundation (travel reimbursement); Novartis (study steering committee). Douglas Sato: Conselho Nacional de Desenvolvimento Científico e Tecnológico (grants); Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (contracted research). Alexion, Amgen, Merck, Roche (consulting fee). Biogen, Merck, Teva (grants). Jodie M. Burton: Canadian Agency for Drugs and Technologies in Health (consulting fee); Alexion, Biogen, Novartis, Roche (consulting fee, advisory boards, honoraria); University of Calgary, MS Canada (contracted research). Kristina R. Patterson: Amgen (salary, employee, stockholder). Bruce A.C. Cree: Alexion, Atara, Autobahn, Avotres, Biogen, Boston Pharma, EMD Serono, Gossamer Bio, Horizon, Immunic Therapeutics, Neuron 23, Novartis, Sandoz, Sanofi, Siemens, TG Therapeutics, Therini Bio (consulting fee); Genentech (research).*

KEYWORDS: Disease-Modifying Treatments in MS, Immunology and MS, Management of Activities of Daily Living in MS

(DMT23) Adherence to Biologic Therapies Among Patients With Neuromyelitis Optica Spectrum Disorder in the United States

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BACKGROUND: Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune demyelinating disease characterized by relapses and risk of disability accumulation. Adherence to therapy among patients with NMOSD on approved biologics remains to be extensively characterized.

OBJECTIVES: To assess adherence to approved biologics among patients with NMOSD in the United States.

METHODS: A retrospective cohort study among adult patients with NMOSD treated with approved biologics (inebilizumab, eculizumab, or satralizumab) was conducted using the Komodo Research Database (August 2020-September 2023). Adherence to treatment was assessed as percentage of days covered (PDC) from treatment initiation to data availability measured as a continuous and binary variable (PDC≥80%= adherent). Difference in continuous PDC (ΔPDC) was assessed using fractional regression adjusting for demographic characteristics (age, sex, race, region, health plan) and NMOSD-associated conditions (neuropathic pain, bladder dysfunction, hemiplegia/paraplegia) at baseline.

RESULTS: In total, 111 patients were included in analyses: 45% taking inebilizumab, 28% taking eculizumab, 27% taking satralizumab. Patients were, on average, 43.0 years old, 85.6% were female, and 34.2% were Black/African American. Common baseline NMOSD-associated conditions included neuropathic pain (43.2%), bladder dysfunction (18.0%), and hemiplegia/paraplegia (17.1%). Prevalent comorbidities during the study period included hypertension (36.9%), obesity (30.6%), and depression (29.7%). Mean duration (SD) of follow-up was 17.3 ± 6.9 months and varied by treatment: inebilizumab (16.4 ± 6.3 months), eculizumab (20.6 ± 7.4 months), and satralizumab (15.5 ± 6.6 months). Adherence was substantially higher among patients taking inebilizumab (mean PDC, 85.2% ± 19.0; adherent, 72.0%) than on eculizumab (mean PDC,73.2% ± 21.5; adherent, 45.2%) and satralizumab (mean PDC, 66.5% ± 30.0; adherent, 53.3%). Fractional regression adjusting for covariates revealed patients on inebilizumab had significantly higher adherence compared with satralizumab (ΔPDC, 20.8%; *P*=.005) and higher compared with eculizumab (ΔPDC,10.2%; *P*=.090).

CONCLUSIONS: Among patients with NMOSD treated with approved biologics, patients on inebilizumab had substantially higher adherence to treatment com-

pared with those on eculizumab and satralizumab. Further research assessing the impact of adherence on patient outcomes, including relapses and treatment persistence, can further elucidate important evidence to guide effective clinical decision-making.

DISCLOSURES: *Bruce A.C. Cree: Alexion, Atara, Autobahn, Avotres, Biogen, Boston Pharma, EMD Serono, Gossamer Bio, Horizon, Immunic Therapeutics, Neuron 23, Novartis, Sandoz, Sanofi, Siemens, TG Therapeutics, Therini Bio (consulting fee); Genentech (research). Kristina R. Patterson: Amgen (salary, employee, stockholder). Andrea Meyers, Jenny Y. Park: Amgen (employee, stockholder). Patrick Gagnon-Sanschagrin, Jessica Maitland: Amgen (paid consulting services).*

KEYWORDS: Disease-Modifying Treatments in MS, Immunology and MS, Management of Activities of Daily Living in MS

(DMT24) Baseline Characteristics and Initial 6 Months in De-escalating Treatment From B-Cell Depletion to Fumarates

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Background: Early initiation of high-efficacy therapies is becoming increasingly common in the treatment of patients with multiple sclerosis (MS). As patients age, however, the occurrence of relapses decreases and the risk of infections increases due to immunosenescence, suggesting that de-escalation may be able to maintain efficacy and improve safety. Switching to fumarates from B-cell–depleting therapies is an attractive option in stable patients who are starting to develop infections or are getting older.

OBJECTIVES: To prospectively evaluate the transition from B-cell depletion to fumarates in patients with MS.

METHODS: Patients with MS 18 years or older who decide to de-escalate from B-cell depletion to fumarates will be prospectively followed for 2 years. Patients need to have been clinically and radiographically stable for 2 years, been on B-cell depletion for 1 year prior to the switch, and have an Expanded Disability Status Scale (EDSS) score of less than 7. The transition period between treatments is 6 to 12 months. The primary end point is a composite that includes relapses, new T2 or enhancing lesions, and 6-month confirmed disability progression.

RESULTS: The 10 patients in this pilot study were enrolled as of July 2024. An additional patient screened was declined due to their EDSS being greater than 6.5. The mean age at enrollment was 51.7 years (SD ± 8.4), 90% were female, and all self-identified as White (10% Hispanic). Half were taking ocrelizumab, 40% taking rituximab, and 10% taking ofatumumab. Eight patients transitioned to diroximel fumarate (DRF) and 2 to dimethyl fumarate (DMF). Three patients have discontinued fumarate treatment due to tolerability (2 on DRF and 1 on DMF) and are continuing to be followed. None of the patients experienced a relapse, a new T2 or enhancing lesion, or serious infection.

CONCLUSIONS: De-escalating from B-cell–depleting therapies to fumarates appears to maintain efficacy early in this transition. This is a 2-year study that is ongoing to better evaluate efficacy and safety of this treatment switch.

DISCLOSURES: *Lillian Farrell: Nothing to disclose. Evan Riddle, Jim Lewin, Jason P. Mendoza: Biogen (salary). Enrique Alvarez: Atara, Biogen, Bristol Myers Squibb, Genentech/Roche, National Institutes of Health, National Multiple Sclerosis Society, Novartis, Patient-Centered Outcomes Research Institute, Rocky Mountain MS Center, Sanofi, TG Therapeutics (research support); Biogen, Celgene/Bristol Myers Squibb, Cionic, EMD Serono/Merck, Genentech/Roche, Horizon/Amgen, Novartis, Sanofi, TG Therapeutics (consulting fee).*

KEYWORDS: Disease-Modifying Treatments in MS

(DMT25) Clinical and Radiological Outcomes of Directed Treatment Transitions From Gilenya to Generic Fingolimod

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BACKGROUND: Gilenya (fingolimod), a sphingosine-1-phosphate (S1P) receptor agonist, is an effective treatment for multiple sclerosis (MS). However, increased relapse activity has been observed after transitioning to generic fingolimod despite prior prolonged disease stability.

OBJECTIVES: To quantify the clinical and radiological impact of treatment transitions from Gilenya to generic fingolimod in people with MS.

METHODS: People receiving care at a single tertiary MS center from January 2023 to November 2024 were retrospectively studied. Inclusion criteria included (1) men and women 18 years and older who were (2) treated with Gilenya for at least 1 year before beginning treatment with generic fingolimod for at least 6 months with (3) clinical data including absolute lymphocyte count (ALC) values while taking Gilenya and 8 weeks after transitioning to generic fingolimod. A linear mixed effects model was estimated to measure differences in adverse effects by treatment group. A zero-inflated Poisson mixed model was estimated for ALC differences, a serological metric indicative of S1P receptor modulation, by treatment group. Kaplan-Meier curves were estimated for the time to MRI advancement and clinical relapse, and a log-rank test was used for quantifying differences between Gilenya and generic fingolimod while accounting for right censoring.

RESULTS: The cohort included 88 people with MS (71 were women; 76 were White; mean age when starting Gilenya was 39.6 years (SD, 10.6); mean age when starting generic fingolimod was 46.9 years (SD, 11.2); mean disease duration from time of first symptom was 17.2 years (SD, 7.9). A 6.6-fold increase in adverse effects was observed with generic fingolimod relative to Gilenya (95% CI, 4.19-10.27, $P<.0001$). The ALC increased by 8.7% while on generic fingolimod relative to Gilenya (95% CI, 1.86%-15.96%; $P=.02$), with intersubject variability estimated to be 2.0%. MS relapse activity was observed in 2 people (2.3%) while taking Gilenya (average treatment duration on Gilenya was 3.3 years [SD, 3.6]) and in 10 people (11.4%) while taking generic fingolimod (average treatment duration on generic fingolimod was 1.3 years [SD, 0.8]). Relapse types included MRI advancement only (Gilenya, 2; generic fingolimod, 5) and MRI advancement with clinical worsening (generic fingolimod, 5). The time to MRI advancement ($P=.0021$) and time to clinical relapse ($P=.0022$) while on generic fingolimod were significantly lower than on Gilenya.

CONCLUSIONS: Based on serological, clinical, and radiological measures, measures of disease stability appear to be less optimal with generic fingolimod. Evidence of medication intolerance and worsening outcomes suggests a need for increased awareness among clinicians and patients, findings that may be related to potency and bioequivalence with generic alternatives.

DISCLOSURES: *Mahi A. Patel, Tom G. Punnen, Kevin Shan, Morgan McCreary, Paula Hardeman: Nothing to disclose. Crystal M. Wright: Cycle Pharmaceuticals, EMD Serono, Sanofi (consulting fee). Shanan B. Munoz: Genentech (research support); Bristol Myers Squibb, Horizon Therapeutics, Novartis, TG Therapeutics (consulting fee). Katy W. Burgess: Bristol Myers Squibb (consulting fee). Benjamin M. Greenberg: Alexion, Arialys Therapeutics, Clene Nanomedicine, Cycle Pharmaceuticals, EMD Serono, Genentech/Roche, Horizon Therapeutics/Amgen, IQVIA, Novartis, PRIME Education, Sandoz, Sanofi/Genzyme, Signant, Syneos, TG Therapeutics (consulting fee); Clene Nanomedicine, GenrAb (ownership interest); Anokion, National Institutes of Health, Regeneron (grants); Siegel Rare Neuroimmune Association (unpaid board member); UpToDate (royalty). Lindsay A. Horton: Biogen, EMD Serono (consulting fee). Peter V. Sguigna: Bristol Myers Squibb, EMD Serono, Genentech, Horizon Therapeutics (consulting fee); Clene Nanomedicine, Congressionally Directed Medical Research Programs, Genentech, National Institute on Aging, Patient-Centered Outcomes Research Institute, Zenas BioPharma (research support). Lauren M. Tardo: EMD Serono (consulting fee); MJH Life Sciences, NeurologyLive (paid support); the MOG Project (nonpaid medical adviser). Olaf Stuve: Current Treatment Options in Neurology (section editor). EMD Serono, National Multiple Sclerosis Society, United States Department of Veterans Affairs, Biomedical Laboratory Research and Development (grants); EMD Serono, Novartis, Octave Bioscience (adviser); Genentech-Roche, Novartis (data monitoring committees); Therapeutic Advances in Neurological Disorders, Expert Review of Clinical Immunology (editorial boards). Darin T. Okuda: Alexion, Novartis (contracted research); Biogen, Cortechs.AI, Eisai, Genentech, Genzyme/Sanofi, Immunic Therapeutics, Moderna, Pfizer, RVL Pharmaceuticals., Zenas BioPharma (consulting fee); EMD Serono/Merck (consulting fee, contracted research); Revert Health (founder); Board of Regents of The University of Texas System (royalty).*

KEYWORDS: Comprehensive Care and MS, Disease-Modifying Treatments in MS, Economic Issues and MS

(DMT26) Optimal Dosing of Anti-CD20 Therapies in Patients With Multiple Sclerosis: Accounting for Immunological and Patient-Reported Factors

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BACKGROUND: Anti-CD20 therapies are a mainstay of the treatment for relapsing and

progressive multiple sclerosis (MS). These drugs include ocrelizumab and ublituximab, recently approved by the US Food and Drug Administration, and are administered as infusions every 6 months. However, a few studies examined extended dosing intervals and found those regimens to have comparable efficacy to the standard. The biannual infusion schedule, although convenient compared with more frequent dosing, can still impose a significant financial and logistical burden on patients. There are additional concerns over immunosuppression and vaccine efficacy. With this in mind, examining whether the dosing interval can be extended would be beneficial. On the other hand, there have been some reports of a wearing-off phenomenon, or "crap gap," in the days and weeks preceding an infusion. It will be important to ascertain this as patients who experience it may not be ideal candidates for extended interval dosing.

OBJECTIVES: (1) Evaluate whether extending the interval based on B-cell repletion is comparable in efficacy to standard dosing. (2) Evaluate whether there are any predisposing characteristics or clinical or immunological correlates for patients who experience the wearing-off phenomenon. (3) Make recommendations for optimal dosing for B-cell therapies.

METHODS: We will examine extended interval dosing and the wearing-off phenomenon in our database cohort of about 500 patients receiving ocrelizumab infusions. In our practice, many patients are on extended interval dosing, and we collect patient-reported outcomes at regular visits. We will analyze various factors, including patient demographics, disease and treatment duration, B-cell repletion, lymphocyte profile including T cells, and patient-reported experience. We then hope to propose recommendations for optimal dosing of these therapies.

RESULTS: Currently undergoing data analysis.

CONCLUSIONS: Currently undergoing data analysis.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Disease-Modifying Treatments in MS, Immunology and MS

(DMT27) Fatigue and Cognition Burden Among Black/African American and Hispanic and Latino People With Relapsing Multiple Sclerosis Receiving Ocrelizumab for 2 Years

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BACKGROUND: Fatigue and cognitive impairment are common symptoms of multiple sclerosis (MS), which may have major impacts on daily life. CHIMES (NCT04377555) aimed to evaluate clinical and radiological outcomes with ocrelizumab (OCR) in Black and African American and Hispanic and Latino people with relapsing MS (BPwRMS; HPwRMS), who are historically understudied but may now have higher MS incidence and increased risks of disease and disability progression vs their White counterparts.

OBJECTIVES: To evaluate patient-reported cognition and fatigue measures among BPwRMS and HPwRMS over 2 years of OCR treatment. METHODS: This prospective, open-label, single-arm, phase 4 study included BPwRMS and HPwRMS in the United States and Kenya aged 18 to 65 years with baseline Expanded Disability Status Scale scores of 0 to 5.5. Participants received 2 300-mg OCR infusions 14 days apart and 600 mg every 24 weeks for 1 year, with an optional 3-year extension. CHIMES participants completed the Brief Illness Perception Questionnaire (IPQ), MS Impact Scale (MSIS-29), Modified Fatigue Impact Scale (MFIS), SymptoMScreen, and Symbol Digit Modalities Test (SDMT) at baseline and through 96 weeks of OCR treatment. Mean (SD) change from baseline is reported for each instrument.

RESULTS: Of 182 participants, mean (SD) age was 35.5 (10.5) years and body mass index was 31.0 (7.4) kg/m^2. Most (72.5%) were women; 62% were BPwRMS and 38% were HPwRMS. During OCR treatment, improved patient perceptions were observed on the Brief IPQ (−4.8 [10.7]; range, 0-80) and MSIS-29 physical (−4.8 [17.4]; range, 0-100) and psychological (−5.4 [21.7]) scores. Fatigue improved during OCR treatment (total MFIS score, −2.5 [15.3]; possible range, 0-84), with greater change observed for HPwRMS (−4.3 [14.6]) vs BPwRMS (−1.2 [15.7]). SymptoMScreen fatigue scores also improved in BPwRMS and HPwRMS (−0.3 [1.6] for all CHIMES participants; possible range, 0-10). Cognitive scores improved in HPwRMS (MFIS, −2.0 [7.2]; SymptoMScreen, −0.3 [1.3]), whereas BPwRMS did not show improvement (0.5 [7.6]; −0.01 [1.4]). Similarly, scores improved in BPwRMS (5.7 [11.5]) and HPwRMS (6.2 [10.5]). SDMT scores declined by 4 points in only 16 participants (11%).

CONCLUSIONS: OCR may improve patient-reported outcomes on perceived symptoms, fatigue, and cognition. Characterizing effects of MS disease-modifying therapies on quality of life, fatigue, and cognition may guide development and use of comprehensive efficacy profiles to support decisions on MS treatments.

DISCLOSURES: *Mitzi J. Williams: Alexion, Biogen, Bristol Myers Squibb, Novartis (consulting fee); Amgen, EMD Serono, Genentech, Sanofi, TG Therapeutics (consulting fee, speakers' bureau). Angel R. Chinea, Gregory F. Wu: Biogen (contracted research). Lilyana Amezcua: Bristol Myers Squibb Foundation, Genentech, National Institute of Neurological Disorders and Stroke, National Multiple Sclerosis Society, Sanofi-Genzyme (contracted research). Lilyana Amezcua, Nancy L. Monson: EMD Serono, Genentech (consulting fee). Krupa Pandey, Juzar Hooker: Nothing to disclose. Fernando X. Cuascut: Biogen, EMD Serono, Genentech, Novartis (consulting fee). Lawrence P. Goldstick: Biogen, Eli Lilly, EMD Serono, Moderna, Roche-Genentech, Sanofi-Genzyme, TGA Therapeutics (consulting fee, contracted research); Bristol Myers Squibb (consulting fee). Nancy L. Monson: GenrAb (ownership interest); MSPrecise (receipt of intellectual property rights/patent holder). Evanthia Bernitsas: Biogen, Bristol Myers Squibb, Horizon, Janssen Pharmaceuticals (consulting fee); Brain Sciences (section editor-in-chief); Chugai, F. Hoffmann-La Roche, Mallinckrodt, MedImmune, Novartis, Sanofi-Genzyme, TG Therapeutics (grant support); EMD Serono, Genentech (consulting fee, grant support). Anthony T. Reder: Bayer, Biogen, EMD Serono, F. Hoffmann-La Roche, Genentech (consulting fee, unrestricted research grant); Mallinckrodt (unrestricted research grant support); MedLink (editor); Novartis, TG Therapeutics (consulting fee). Gregory F. Wu: EMD Serono, Roche (consulting fee, contracted research); Novartis, Sage, Sangamo (consulting fee). Jinglan Pei, Ibraheem Abioye: F. Hoffmann-La Roche (ownership interest); Genentech (salary). Timothy Vartanian: Biogen, EMD Serono, Genentech, Novartis, National Institutes of Health, National Multiple Sclerosis Society (consulting fee).*

KEYWORDS: Disease-Modifying Treatments in MS

(DMT28) Medication-Related Osteonecrosis of the Jaw as a Consequence of Anti-CD20 Monoclonal Antibodies in an Individual With Multiple Sclerosis

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BACKGROUND: Medication-related osteonecrosis of the jaw (MRONJ) is a serious condition typically caused by antiresorptive or antiangiogenic drugs. However, MRONJ can also be induced by medications that do not directly affect bones or blood vessels.

OBJECTIVES: This report presents a case of MRONJ in a female patient following the administration of ocrelizumab as treatment for multiple sclerosis (MS).

METHODS: In August 2022, a woman aged 49 years was referred to the Oral Medicine and Special Care Dentistry Clinic due to severe gum pain. Clinical examination revealed that the socket of an extracted left mandibular second molar had not healed even after 5 months. The patient experienced severe pain upon touch, exudative secretions, and incomplete mucosal recovery, marked by a depression at the extraction site. Although the pain lessened with antibiotics, it recurred and worsened upon discontinuation. The patient's medical history indicated a diagnosis of MS in 2007. Notably, she had received the first injection of ocrelizumab 6 months prior to the examination.

RESULTS: Based on clinical and radiographic evidence of a nonhealing socket and the patient's medical and dental history, the lesion was diagnosed as MRONJ. The patient was prescribed broad-spectrum antibiotics and chlorhexidine mouthwash. In her first follow-up 2 weeks later, she reported decreased pain and resolution of other symptoms. Given that no other known factors and drug history could account for the MRONJ in this patient and previous reports suggest a relationship between rituximab and MRONJ, there may also be an association between ocrelizumab and MRONJ.

CONCLUSIONS: To establish MRONJ as a complication of ocrelizumab, further clinical studies involving a larger patient population receiving this medication are recommended.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Adverse Event, Disease-Modifying Treatments in MS

(DMT29) Comparative Analysis of Hypogammaglobulinemia and Infections in Patients with Multiple Sclerosis Treated With B-Cell Depletion Therapy and Cladribine: A Literature Review

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BACKGROUND: Multiple sclerosis (MS) is a chronic autoimmune disorder affecting the central nervous system and involves demyelination and impairment of nerve function. To date, there has not been a comprehensive overview to assess the involvement of different isotypes of immunoglobulins associated with hypogammaglobulinemia in individuals with MS receiving anti-CD20 therapy and the associated serious infections in comparison with cladribine. Cladribine is a newer synthetic purine analogue used primarily in hairy cell leukemia and has shown efficacy against MS.
OBJECTIVES: (1) Assess the severity of hypogammaglobulinemia. (2) Assess the associated risk of serious infections in patients with MS on B-cell therapies vs those on cladribine.
METHODS: A literature review of studies published between 2008 and 2024 was conducted on PubMed and Google Scholar. Of 448 articles screened, 43 were analyzed, capturing demography, baseline Expanded Disability Status Scale score, baseline immunoglobulin (Ig) levels, posttreatment with rituximab, ocrelizumab, ofatumumab, and cladribine, and the type of serious infections associated with each therapy. We defined hypogammaglobulinemia as serum IgG level less than 700 mg/dL stratified into mild (400-699 mg/dL), moderate (200-399 mg/dL), and severe (0-199 mg/dL). An IgM level less than 50 mg/dL was considered less than the lower limit of normal.
RESULTS: The analysis revealed a posttreatment mean IgG level of 973 mg/dL for ofatumumab, 959 mg/dL for rituximab, and 902 mg/dL for ocrelizumab. Patients had an initial reduction in IgM followed by a subsequent reduction in IgG levels as the studies progressed in ocrelizumab and rituximab, with the degree of hypogammaglobulinemia ranging from mild to moderate. Ofatumumab showed a greater reduction in IgM compared with IgG. Posttreatment IgG levels with cladribine showed remarkable stability, with minimal reductions observed. With respect to associated infections, ocrelizumab showed a high occurrence of respiratory infections, followed by urinary tract infections (UTIs) and appendicitis. Ofatumumab showed occurrence of pneumonia, upper respiratory tract infections (URTIs), and appendicitis. A high occurrence of lower RTIs followed by UTI and URTI was observed in patients on rituximab. Infection rates were notably low across all studies in cladribine.
CONCLUSIONS: Compared with B-cell therapies, findings suggest that cladribine has a more favorable Ig profile, with minimal impact on both IgG and IgM levels and correspondingly low infection rates. This opens a foundation for physicians to consider the importance of formulating and optimizing strategies while treating patients with MS with B-cell therapies and the need for further studies on cladribine.
DISCLOSURES: *Nothing to disclose.*
KEYWORDS: Disease-Modifying Treatments in MS

(DMT30) Real-World Experience With Ocrelizumab: 8-Year Data

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BACKGROUND: Ocrelizumab (OCR) is a humanized, monoclonal antibody targeting CD20+B cells approved for relapsing multiple sclerosis (RRMS) and primary progressive multiple sclerosis. This trial is a prospective study in a real-world MS population with the primary objective of assessing OCR-associated adverse events (AEs).
OBJECTIVES: To document the frequency of infections, incidence of cancer, and other AEs in patients treated with OCR in a real-world population. We sought to compare the frequency of AEs in patients similar to those in the pivotal trials with those who would have been excluded based on being 55 years or older, higher Expanded Disability Status Scale (EDSS) scores, and/or preexisting medical conditions.
METHODS: The study includes all patients at the Elliot Lewis Center treated with OCR since its commercial release in March 2017. Initial assessments include EDSS, brain MRI, and medical history (including infection history, history of malignancy, and exposure to immunosuppressive treatment).
RESULTS: As of November 1, 2024, 482 people were enrolled and followed for 1 to 15 cycles. The patient population was 25% male and 75% female, with an age range of 18 to 73 years and an EDSS range of 0 to 7.5 (median 2.5). Of these, 31% were 55 years or older; 20% had a baseline EDSS greater than or equal to 6; 68% had RRMS; and 32% had progressive forms of MS (primary-progressive or secondary-progressive). The overall infection rate, including COVID-19, was 79.0 cases per 100 patient-years (PY) compared with 76.2 cases per 100 PY in the 5-year clinical trial data. Although patients 55 years or older and/or with an EDSS score of 6 or above did not have a higher rate of overall infection, they did have a higher rate of serious infections, with 4.6 cases per 100 PY (3.7 cases per 100 PY in patients age ≥ 55; 4.9 cases per 100 PY in patients with EDSS ≥ 6 compared with 1.9 cases per 100 PY in patients age <55 and 1.8 cases per 100 PY in patients with EDSS <6.0). Patients with an EDSS of 6 or more had a higher rate of urinary tract infections (UTIs; 32.7 cases per 100 PY) compared with patients with EDSS scores less than 6 (13.1 cases per 100 PY). Malignancies occurred at a rate of 0.8 cases per 100 PY, similar to that observed in the general MS population.
CONCLUSIONS: Older patients (age ≥ 55) and/or patients with more disability (EDSS ≥ 6) did not have a higher risk of infections compared with younger patients (age <55) and/or patients with less disability (EDSS <6), but infections tended to be more serious, with a 2.5 times greater risk of requiring hospitalization. There was also a higher rate of UTIs in patients with more disability (EDSS ≥ 6), as would be expected in this population.
DISCLOSURES: *Paige E. Greenawalt, Sam M. Stine, Paola Castro Mendoza, Ellen S. Lathi: Nothing to disclose. Andrew J. Bouley: Biogen, EMD Serono, Genentech (speakers' bureau); Sanofi (advisory council); TG Therapeutics (ad board, speakers bureau). Joshua Katz: EMD Serono, Genentech, Sanofi, TG Therapeutics (advisory committee, speakers' bureau).*
KEYWORDS: Disease-Modifying Treatments in MS, Ocrelizumab

(DMT31) Introducing Ublituximab at the University of Cincinnati Waddell Center for Multiple Sclerosis: Our Early Experience

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BACKGROUND: Ublituximab, an FDA-approved anti-CD20 monoclonal antibody, is a new therapy for relapsing-remitting multiple sclerosis (RRMS). Although findings from clinical trials have shown its safety and efficacy, real-world data remain limited.
OBJECTIVES: To evaluate the early safety and efficacy of ublituximab.
METHODS: A retrospective cohort study was conducted at the University of Cincinnati Waddell Center for Multiple Sclerosis in Ohio. Data were collected from patients treated with ublituximab between April 2023 and July 2024. Patients were required to be 18 years or older, diagnosed with RRMS, and to have completed at least the initial 2 loading doses. The collected variables included demographics, clinical data, and MRI activity (new T2 lesions or contrast-enhancing lesions). $CD19^+$ B-cell repopulation was recorded as any $CD19^+$ count greater than 0. Octave Bioscience's Multiple Sclerosis Disease Activity (MSDA) scores, derived from serum biomarkers, were also recorded. Statistical analyses included descriptive statistics and the Wilcoxon signed-rank test for nonnormally distributed data.
RESULTS: A total of 44 patients were included, with a mean age of 45.9 ± 10.3 years; 70% were women, and 64% identified as White. Seventeen patients (38.6%) had been on other anti-CD20 therapies prior to initiating ublituximab. The mean duration of ublituximab therapy was 5.40 ± 3.92 months. Before starting any anti-CD20 therapy, 68.2% of patients experienced clinical relapses requiring high-dose steroid treatment. This rate decreased to 11.7% during prior anti-CD20 therapies and dropped to 0% after initiating ublituximab. No MRI activity was observed following ublituximab initiation compared with 3 patients (17.6%) who experienced MRI activity during prior anti-CD20 therapies (mean onset, 31 months). Two patients (4.5%) reported subjective progression while on ublituximab. During prior anti-CD20 therapies, 71% of patients (12 of 17) experienced B-cell repopulation events, with 41.2% (7 of 17) showing persistent repopulation. After switching to ublituximab, B-cell repopulation events decreased to 27.2% (12 of 44). The mean MSDA score decreased from 4.73 ± 0.57 before anti-CD20 therapy to 1.7 ± 0.72 after ublituximab therapy (P>.05). No adverse events were reported.
CONCLUSIONS: Ublituximab shows promising efficacy and safety, with potential for depleting B cells. Due to the low study power from the small sample size and short follow-up, results should be interpreted with caution and larger studies are needed.
DISCLOSURES: *Sara Esmaeili, Blake Cox, Alexander Mirzoev, Joseph LaPorta: Nothing to disclose. Kiranpal S. Sangha: TG Therapeutics (advisory board). W. Daniel Chapman: Amgen, EMD Serono/Merck (consulting fee); Biogen (consulting fee, speakers' bureau); Novartis (contracted research). Lawrence Goldstick: Biogen, Roche/Genentech, Sanofi-Genzyme (consulting fee, contracted research); Bristol Myers Squibb, EMD Serono (consulting fee); TG Therapeutics (speakers' bureau, consulting fee). Aram Zabeti: Alexion/AstraZeneca, Bristol Myers Squibb, Sanofi, TG Therapeutics (speakers' bureau); Horizon/Amgen (speakers' bureau, consulting fee).*
KEYWORDS: Disease-Modifying Treatments in MS, Ublituximab, Safety, Efficacy, Real World

(DMT32) Hypogammaglobulinemia in Patients With Multiple Sclerosis Treated With Ocrelizumab: Year 8 Data

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BACKGROUND: Ocrelizumab (OCR) is a humanized anti-CD20 monoclonal antibody approved for the treatment of relapsing multiple sclerosis (MS) and primary progressive MS. Long-term exposure to other B-cell depleting agents has been associated with low IgG level. After 2 to 3 years of OCR treatment, a small proportion of patients developed low IgG level (1.5% in OPERA I and OPERA II and 1.1% in ORATORIO), but this was not associated with a higher rate of infection. Patients with preexisting low IgG level were excluded from the phase 3 trials for OCR and may be at additional risk for infection.

OBJECTIVES: To evaluate the impact of OCR on IgG levels and frequency of infections in a real-world population.

METHODS: As of November 1, 2024, 454 patients who had baseline IgG levels received commercial OCR at The Elliot Lewis Center. Normal IgG level was defined as 600 to 1640 mg/dL. Individuals were monitored for the occurrence of adverse events and had biannual assessments of serum IgG. Cycle 1 was two 300-mg doses of OCR; cycle 2 was the first full 600-mg dose. We defined 2 groups for the purpose of identifying the risk of infection after the development of low IgG level: Group A included infections that occurred in patients with normal IgG values or until the development of the first low IgG value, and group B included all infections that occurred after the first measurement of a low IgG value regardless of later normal values.

RESULTS: Over the course of 15 OCR treatment cycles, mean IgG level declined by 15.4% and 10% of patients (n = 47) had at least 1 low IgG value. Patients with normal IgG at baseline (n = 439) had an infection rate of 78.8 cases per 100 patient-years (PY) compared with 93.4 cases per 100 PY in patients who had low IgG values at baseline (n = 15; 3%). The severe infection rates of these groups were 2.4 cases per 100 PY and 7.0 cases per 100 PY, respectively. The infection rate for group A was 81.7 cases per 100 PY, whereas that for group B was 119.2 cases per 100 PY. The rate of severe infections for group A was 2.4 cases per 100 PY, whereas that for group B was 4.9 cases per 100 PY.

CONCLUSIONS: Over the course of 15 OCR treatment cycles, mean IgG level decreased and 10% of patients developed IgG values below 600 mg/dL. Patients with low IgG level at baseline and those who developed low IgG values post baseline had an increased risk of infection.

DISCLOSURES: *Paola Castro Mendoza, Sam M. Stine, Paige E. Greenawalt, Ellen S. Lathi: Nothing to disclose. Andrew J. Bouley: Biogen, EMD Serono, Genentech (speakers' bureau); Sanofi (advisory council); TG Therapeutics (advisory board, speakers' bureau). Joshua Katz: EMD Serono, Genentech, Sanofi, TG Therapeutics (advisory board, speakers' bureau).*

KEYWORDS: Disease-Modifying Treatments in MS, Immunology and MS, Ocrelizumab

(DMT33) Age and Liver Function Analysis of Ozanimod Therapy Outcomes in Multiple Sclerosis: Real-World Evidence From a Large Integrated Health Care System Retrospective Case Series

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BACKGROUND: Ozanimod is approved in multiple countries for the treatment of adults with relapsing forms of multiple sclerosis (MS) based on findings from 2 randomized clinical trials and a long-term, open-label extension study demonstrating clinical effectiveness and safety.

OBJECTIVES: To present real-world evidence of age-related medication persistence and liver function test outcomes of people with MS (PwMS) who are adults treated with ozanimod using retrospective data from a large health care system.

METHODS: A manual chart review of electronic health records from Providence Health & Services and affiliates identified PwMS 18 years or older initiating ozanimod treatment on or before September 15, 2023, with an observation period of 1 year after ozanimod initiation. Treatment persistence overall and by age group (18-49 and ≥ 50 years) was assessed using Kaplan-Meier analysis. Maximum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) IU/L levels, normalized to the upper limit of reference range (ULRR), were assessed (1) before ozanimod (BO; ie, 365-day period prior to initiating ozanimod) and (2) on ozanimod (OO; ie, ozanimod start to earliest of 365 days or discontinuation).

RESULTS: Data were extracted for 143 PwMS. Median age was 48.6 (IQR, 39.2-57.8) years. Of the total, 77 (53.8%) were aged 18 to 49 years and 66 (46.2%) were 50 years or older. Restricted mean treatment continuation time was 351 and 327 days for the 2 age groups, respectively, over the 365-day period (340 days overall, previously reported). The predicted probability of PwMS remaining on ozanimod on day 365 (81.2% overall) was 87.4% and 74.2% for the 2 age subgroups, respectively (P=.04; log-rank test). BO data were available for 125 PwMS and OO data for 108 PwMS. For the BO group, maximum ALT/AST level was less than or equal to ULRR in 103 (82.4%) PwMS, greater than ULRR and less than or equal to 3 times ULRR in 19 (15.2%) PwMS, and greater than 3 times and equal to or less than 5 times ULRR in 3 (2.4%) PwMS. In the OO group, maximum ALT/AST level was less than or equal to ULRR in 79 (73.1%) PwMS, greater than ULRR and less than or equal to 3 times ULRR in 23 (21.3%) PwMS, greater than 3 times and equal to or less than 5 times ULRR in 4 (3.7%) PwMS, greater than 5 times and equal to or less than 10 times ULRR in 1 PwMS (0.9%), and greater than 10 times ULRR in 1 PwMS (0.9%).

CONCLUSIONS: These real-world data indicate a high rate of treatment persistence and a relatively low risk of substantial ALT/AST elevation within 1 year of ozanimod initiation. Although patients 50 years or older were more likely to discontinue, treatment persistence remained high among these PwMS.

DISCLOSURES: *Lawrence Huang, Sevda Molani, Raul A. Ocasio, Andria Chada: Nothing to disclose. Pavle Repovic: Alexion, Banner, Biogen, Bristol Myers Squibb, EMD Serono, Genentech, Genzyme, Horizon, Novartis, TG Therapeutics (consulting fee, honoraria). Michael Chiorean: AbbVie, Arena, Bristol Myers Squibb, Eli Lilly, Janssen, Medtronic, Pfizer (consulting fee); AbbVie, Bristol Myers Squibb, Janssen, Medtronic, Pfizer (speakers' bureau); Fuji, Gilead, Janssen, Novartis, Pfizer, Takeda (contracted research). Damemarie Paul, Jennifer Reardon, Andrew Thorpe: Bristol Myers Squibb (salary, shareholder). Jennifer Hadlock: Bristol Myers Squibb, Gilead, Janssen, Novartis, Pfizer (research funding).*

KEYWORDS: Real-World Evidence, Ozanimod, Age

(DMT34) Two-Year Findings on the Safety and Efficacy of Cladribine Tablets After Treatment With Natalizumab

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BACKGROUND: Natalizumab (NTZ) is associated with an increased risk of developing progressive multifocal leukoencephalopathy (PML) and disease reactivation upon cessation in people with relapsing multiple sclerosis (PwRMS). In such patients, switching rapidly from NTZ to cladribine tablets (CladT; 3.5-mg/kg cumulative dose over 2 years), a high-efficacy therapy, may be particularly advantageous to maintain control of disease progression and prevent disease reactivation while minimizing PML risk without continuous immune suppression.

OBJECTIVES: To report safety and efficacy over 24 months (M) after switching PwRMS from NTZ to CladT.

METHODS: CLADRINA (NCT04178005) is an open-label, phase 4 study in PwRMS who switched to CladT within 4 weeks of their last infusion with NTZ. The primary outcome measure is the change in $CD3^+$ T lymphocytes, $CD19^+$ B lymphocytes, and dendritic cells from baseline (BL) to M12 and M24. Annualized relapse rates (ARRs); Expanded Disability Status Scale (EDSS) scores; MRI outcomes over 24M; Multiple Sclerosis Disease Activity (MSDA) scores at 6M, 9M, 12M, and 24M; and the safety profile of CladT over 24M were also evaluated.

RESULTS: Overall, 40 PwRMS were included (age [mean ± SD], 41.3 ± 10.2 years; 70% female). The mean time between NTZ discontinuation and CladT initiation was 12.2 days (range, 3.0-27.0), with most PwRMS switching due to positive John Cunningham virus titer results. Lymphocyte dynamics from BL to M12 and M24 will be reported. A reduction in ARR was observed between BL (0.10; 95% CI, 0.00-0.22) and 12M (0.03; 95% CI, 0.00-0.08) after switching from NTZ to CladT, which persisted over 24M. The median EDSS score remained stable at 2.0 (range, 0.0-6.0) 24M after switching (BL, 2.3; range, 0.0-5.5). At 24M after switching, 100% of PwRMS remained free from T1 gadolinium-enhancing lesions (vs 97.5% at BL) and 89.2% (vs 97.5% at BL) were free from new T2 lesions. The MSDA score was not inferior (ie, either unchanged or lower on average) after switching at each time point (6M, 9M, 12M, and 24M) vs BL. The most common study drug-related adverse events were upper respiratory tract infection (12.5%), nausea (10.0%), and headache (7.5%). No

cases of PML or rebound disease activity were reported. Overall, CladT was well tolerated in PwRMS after switching from NTZ.

CONCLUSIONS: Results of the 2-year CLADRINA study show that switching rapidly from NTZ to CladT maintains disease stability. CladT is a safe and effective treatment sequencing option, with no cases of PML or rebound disease activity.

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KEYWORDS: Cladribine, Treatment Switch, Disease-Modifying Treatments in MS

(DMT35) Exploratory MRI Outcomes and Plasma Neurofilament Light Chain Levels in Frexalimab-Treated Participants With Relapsing Multiple Sclerosis: Week 48 Results From the Phase 2 Open-Label Extension

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BACKGROUND: Frexalimab, a second-generation monoclonal antibody targeting CD40 ligand (CD40L), inhibits the costimulatory CD40/CD40L pathway, which is important for the activation and function of adaptive and innate immunity. Through this upstream mechanism of action, frexalimab has the potential to address both acute and chronic neuroinflammation. In a phase 2 trial in participants with relapsing multiple sclerosis (RMS; NCT04879628), frexalimab rapidly reduced new gadolinium-enhancing T1-lesions, but less is known about its effects on biomarkers of chronic neuroinflammation and neurodegeneration.

OBJECTIVES: To report exploratory MRI outcomes and changes in plasma neurofilament light chain (NfL) levels at week (W) 48 in the phase 2 open-label extension (OLE).

METHODS: In the double-blind period (DBP), 129 participants were randomly distributed to frexalimab$_{1200/\text{intravenous (IV)}}$ (n=52), frexalimab$_{300/\text{subcutaneous (SC)}}$ (n=51), or matching placebo arms (placebo$_{IV}$: n=12; placebo$_{SC}$: n=14). Participants initially receiving placebo switched to respective frexalimab arms at W12 and entered the OLE. Exploratory assessments include measures of paramagnetic rim lesions (PRLs), new T1-hypointense lesions, and NfL levels.

RESULTS: Of 129 participants, 125 completed the DBP and entered the OLE; 112 (87%) remained in the study as of September 19, 2023 (W48 cutoff). The mean baseline age (± SD) was 36.6 (± 9.4) years; 66% were women. At baseline, 19 of 46 (41%) participants at sites with sufficient imaging capability had 1 or more PRLs. New PRLs were detected in each of the frexalimab$_{300/SC}$ arms between W8 and W20, whereas no new PRLs were detected from baseline to W48 in the frexalimab$_{1200/IV}$ arms. The numbers of new T1-hypointense lesions (mean ± SD) were low at W48: 0.1 ± 0.4 in frexalimab$_{1200/IV}$, 0.8 ± 1.6 in frexalimab$_{300/SC}$, 0.0 ± 0.0 in placebo$_{IV}$/frexalimab$_{1200/IV}$, and 0.6 ± 1.0 in placebo$_{SC}$/frexalimab$_{300/SC}$ arms. Also, at W48, NfL levels (geometric mean ± SD) were 6.7 ± 2.0 in frexalimab$_{1200/IV}$, 8.1 ± 1.7 in frexalimab$_{300/SC}$, 9.6 ± 1.7 in placebo$_{IV}$/frexalimab$_{1200/IV}$, and 7.8 ± 2.1 pg/mL in placebo$_{SC}$/frexalimab$_{300/SC}$ arms, corresponding to a 41%, 35%, 24%, and 33% reduction from baseline, respectively.

CONCLUSIONS: These exploratory MRI and NfL data contribute to understanding the effect of frexalimab on chronic neuroinflammation and neurodegeneration and support further investigations in both RMS and nonrelapsing secondary progressive MS.

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KEYWORDS: Disease-Modifying Treatments in MS

(DMT36) Ocrelizumab Treatment in Multiple Sclerosis: 11-Year Efficacy and Safety Clinical Trial Data

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BACKGROUND: Ocrelizumab (OCR), an anti-CD20 monoclonal antibody, is approved for treating adult patients with relapsing multiple sclerosis (PwRMS) and primary progressive MS (PPMS). Understanding the long-term impact of OCR on patients is now possible in the context of 11 years of OCR experience.

OBJECTIVES: To investigate the consistency of the efficacy and safety profiles of OCR by examining long-term efficacy and safety data from OCR clinical trials (CTs) and open-label extension (OLE) periods over a follow-up of up to 11 years (up to November 2023).

METHODS: Efficacy and safety outcomes were reported for PwMS treated with OCR in ongoing or completed CTs and their OLE follow-ups. Disability progression was assessed through 48-week (W) confirmed disability progression (CDP) on the Expanded Disability Status Scale (EDSS) and composite CDP. Rates per 100 patient-years (PY) were recorded for adverse events (AEs), serious AEs, and nonserious and serious infections (NSIs, SIs).

RESULTS: After 11 years, 74.9% of PwRMS on OCR were free from 48W-CDP–EDSS events and 91.7% did not need a walking aid. In PwPPMS, 33.5% remained free from 48W-CDP–EDSS eventa and 17.8% from composite CDP; 79.5% did not require a wheelchair. Early OCR treatment significantly reduced the risk of disability milestones compared with delayed treatment. In clinical trials with more than an 11-year follow-up period (with>60% of patients who received ≥ 8 doses of OCR), no new safety concerns were observed. In PwRMS and progressive multiple sclerosis (PMS), respectively, reported rates (excluding COVID-19 AEs) per 100 PY (95% CI) were: AE, 223 (221-225) and 213 (210-216); serious AE, 5.9 (5.6-6.2) and 10.8 (10.1-11.5); and SIs, 1.7 (1.5-1.8) and 3.7 (3.3-4.1). Infections were the most common AE, primarily of a urinary or respiratory nature in both PwRMS and PwPMS. NSI rates (95% CI) were 63.8 (62.8-64.9) per 100 PY in PwRMS and 57.1 (55.4-58.8) per 100 PY in PwPMS. Most patients with at least 1 recurrent (nonserious and serious) infection had 1 recurrence.

CONCLUSIONS: OCR demonstrated a stable and favorable long-term risk-benefit profile over 11 years. Disability progression and rates of AEs remained stable, supporting its continued use in treating MS.

DISCLOSURES: *Robert Bermel: AstraZeneca, Eli Lilly, EMD Serono/Merck, Genzyme/Sanofi, Labcorp, TG Therapeutics, Viela Bio/Horizon (consulting fee); Biogen, Novartis,*

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KEYWORDS: Disease-Modifying Treatments in MS

(DMT37) Baseline Characteristics in the Tolebrutinib Phase 3 Primary Progressive Multiple Sclerosis PERSEUS Clinical Trial

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BACKGROUND: Treatment options remain limited for people with primary progressive multiple sclerosis (PPMS) with only 1 approved therapy, which has had modest effects on disability accumulation. Tolebrutinib is an oral, brain-penetrant, and bioactive Bruton tyrosine kinase inhibitor that modulates persistent immune activation within the central nervous system, including disease-associated microglia and B cells. Tolebrutinib demonstrated a significant benefit on disability accumulation versus placebo in a nonrelapsing secondary progressive MS population. PERSEUS (NCT04458051) is a phase 3 trial evaluating the efficacy, safety, and tolerability of tolebrutinib in participants with PPMS.

OBJECTIVES: To present baseline characteristics of participants in the PERSEUS trial.

METHODS: PERSEUS is a randomized, double-blind, placebo-controlled, parallel-group, multicenter, event-driven trial. Enrollment criteria included being 18 to 55 years of age, diagnosis of PPMS according to the 2017 McDonald criteria, Expanded Disability Status Scale (EDSS) score of 2.0 to 6.5 at screening, positive cerebrospinal fluid findings (oligoclonal bands and/or elevated immunoglobulin G index), and, in some countries early in study enrollment with subsequent global implementation, either no access to ocrelizumab (eg, due to being unavailable nationally or not being reimbursed for the approved indication) or intolerance (due to adverse effects or safety reasons) or ocrelizumab treatment failure. Participants were randomly distributed 2:1 to receive tolebrutinib, 60 mg, or placebo once daily.

RESULTS: A total of 767 participants were enrolled, with a mean age of 45.3 years. Approximately 54% of participants were male and 83% were White. At baseline, mean EDSS was 4.9 (median, 5.0; n=766), mean time since symptom onset was 7.7 years, and mean time since PPMS diagnosis was 4.2 years. Most participants (59%) were treatment-naive. On MRI, 89% of participants had no gadolinium-enhancing lesions, and median T2 lesion volume was 10.8 cm^3.

CONCLUSIONS: This trial will provide a comprehensive assessment of tolebrutinib efficacy and safety in the PPMS population, for which limited approved treatment options exist.

RESULTS: Trial results are anticipated in 2025.

DISCLOSURES: *Robert J. Fox: AB Science, Bristol Myers Squibb, Eli Lily, EMD Serono, Genentech, Greenwich Biosciences, Immunic, INmune Bio, Janssen, Siemens, TG Therapeutics (consulting fee); Biogen, Novartis, Sanofi (consulting fee, research support). Daniel S. Reich: Abata, Intramural Research Program of National Institute of Neurological Disorders and Stroke, National Institutes of Health, Sanofi (grant/research support). Anthony Traboulsee: Biogen, EMD Serono, Roche, Sanofi (consulting and/or speaking and grant/research support). Celia Oreja-Guevara: Bayer, Biogen, Merck Serono, Novartis, Roche, Sanofi, Teva (speaking and/or consultancy). Gavin Giovannoni: Astoria Biologica, Aurinia Pharmaceuticals, Biogen, Bristol Myers Squibb-Celgene, GSK, Janssen/J&J, Japanese Tobacco, Merck KGaA/EMD Serono, Moderna, Novartis, Roche/Genentech, Sandoz, Sanofi, Vir Biotechnology, Viracta (consulting/speaking and/or research support). Patrick Vermersch: AB Science, Ad Scientiam, Celgene-Bristol Myers Squibb, Imcyse, Roche (honoraria or consulting); Biogen, Merck, Novartis, Sanofi (honoraria, consulting, or research support); F. Hoffmann-La Roche (research support). Sana Syed, Furong Sun, Naji Salloum, Timothy J. Turner, Erik Wallstroem: Sanofi (employee). Amit Bar-Or: Accure, Atara, Biogen, Biotherapeutics, Bristol Myers Squibb, Gossamer, GSK, Janssen, MedImmune, Sanofi (speaking and/or consulting); Biogen Idec (grant support to institution); EMD Serono, Novartis, Roche Genentech (grant support to institution; speaking and/or consulting).*

KEYWORDS: Clinical Trial, Primary Progressive MS, Tolebrutinib, Disease-Modifying Treatments in MS

(DMT38) Incidence of Relapses After Meningococcal Vaccination in Clinical Trials and Real-World Evidence of Eculizumab and Ravulizumab in Anti–Aquaporin-4 Antibody-Positive Neuromyelitis Optica Spectrum Disorder

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BACKGROUND: Ravulizumab and eculizumab are complement component 5 inhibitor therapies (C5ITs) approved for anti–aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4-Ab+NMOSD). Because C5ITs are associated with increased *Neisseria meningitidis* infection risk, patients are generally advised to be vaccinated for 2 or more weeks before receiving C5ITs; however, any vaccination may further activate the complement pathway. Because of this, patients with complement-mediated diseases, including NMOSD, may experience increased signs and symptoms of their underlying disease when vaccinated before C5IT initiation.

OBJECTIVES: To report on relapses occurring within 4 weeks of meningococcal vaccination before initiating (1) ravulizumab in patients screened in CHAMPION-NMOSD (NCT04201262), (2) either eculizumab or placebo in patients enrolled in PREVENT (NCT01892345), and (3) eculizumab in a regulatory-mandated postmarketing surveillance (PMS) study of patients with AQP4-Ab+NMOSD in Japan.

METHODS: Analysis included patients with vaccination data in (1) those screened in CHAMPION-NMOSD, irrespective of screening outcome, (2) those randomly assigned to receive placebo or eculizumab in PREVENT, and (3) those included in the Japanese PMS study from approval (November 2019) to data cutoff (October 2023). Outcomes were physician-reported relapses occurring within 4 weeks of last meningococcal vaccination and before ravulizumab, eculizumab, or placebo initiation.

RESULTS: This analysis included 70 patients from CHAMPION-NMOSD (57 enrolled; 13 screen failures), 2.9% (2/70) of whom experienced a relapse per analysis criteria; both were screen failures. In PREVENT, 3.1% (3/96) of eculizumab-treated and 10.6% (5/47) of placebo-treated patients had a relapse. In the Japanese PMS study, 0.7% (1/151) of patients experienced a relapse.

CONCLUSIONS: This retrospective analysis of both clinical trial and real-world data indicates a low relapse incidence (0.7%-3.1%) within 4 weeks of meningococcal vaccinations before C5IT initiation and 10.6% for those randomly assigned to placebo. Available information precludes determination as to whether relapses observed are attributable to meningococcal vaccination or inherent relapse risk among patients with AQP4-Ab+NMOSD.

DISCLOSURES: *Sami Fam, Kerstin Allen, Becky Parks: Alexion, AstraZeneca Rare Disease (salary, employee).*

KEYWORDS: Complement C5 Inhibitors, NMOSD, Meningococcal Vaccination

(DMT39) Ocrelizumab Subcutaneous Administration: Further Characterization of the Benefit-Risk Profile From the Ocarina II Study and Patient Preferences

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BACKGROUND: The OCARINA II study (NCT05232825) showed that ocrelizumab (OCR) subcutaneous (SC), 920 mg, (coformulated with recombinant human hyaluronidase PH20 [rHuPH20]) has a similar benefit-risk profile to OCR intravenous (IV), 600 mg, in

people with relapsing and primary progressive multiple sclerosis (PwRMS/PwPPMS).

OBJECTIVES: To further characterize the benefit-risk profile of OCR SC based on updated efficacy and safety data and new patient-reported outcomes (PROs) from the OCARINA II study at the clinical cut-off date (CCOD; up to September 2024).

METHODS: OCR-naive PwRMS/PwPPMS (18-65 years; Expanded Disability Status Scale score [EDSS]: 0-6.5) were randomly distributed 1:1 to receive OCR IV, 600 mg, or OCR SC, 920 mg, during the controlled period. At week (W) 24, all patients (OCR IV/SC and OCR SC/SC arms) could enter the treatment phase with OCR SC up to W96. End points included EDSS, relapses, safety, and PROs (Multiple Sclerosis Treatment Preference Questionnaire [MSTPQ] and Patient Preference Questionnaire [PPQ]).

RESULTS: OCR SC resulted in nearly complete suppression of relapse activity up to W48, with 97.2% (OCR SC/SC) and 98.1% (OCR IV/SC) of patients being relapse-free. Safety data in the OCR SC all-exposure group (December 2023, CCOD): adverse event (AE), 75.1%; serious AE, 2.6%; injection reaction (IR), 51.5% (local IR, 50.2% and systemic IR, 11.6%). All IRs were nonserious and mild/moderate in intensity; 74.1% of IRs resolved (mostly ≤ 3 days). No treatment-emergent antidrug antibodies to OCR were reported; the incidence of treatment-emergent anti-rHuPH20 antibodies was 0.4%. Small decreases in mean immunoglobulin G and M levels were observed in both arms. At W48, the MSTPQ showed that among participants previously treated for MS, 81.6% preferred OCR; 98.1% were satisfied/very satisfied with OCR as an MS treatment. According to the PPQ, where patients experienced both OCR IV and SC administration, 80.4% preferred SC administration. W72 efficacy/safety data will be presented.

CONCLUSIONS: SC OCR continues to show efficacy and safety that is similar to the well-established intravenous route of administration at the CCOD. Patients preferred and expressed a high level of satisfaction with the subcutaneous route of administration.

DISCLOSURES: *Scott D. Newsome: Biogen, Genentech (consulting fee, contracted research); Bristol Myers Squibb, Novartis, TG Therapeutics (consulting fee); Department of Defense, Patient-Centered Outcomes Research Institute, Lundbeck, National Multiple Sclerosis Society, Sanofi, Stiff Person Syndrome Research Foundation (contracted research); F. Hoffmann-La Roche (contracted research, study lead). Lawrence Goldstick: Biogen, Roche/Genentech, Sanofi-Genzyme (consulting fee, contracted research); Bristol Myers Squibb, EMD Serono (consulting fee); TG Therapeutics (consulting fee, speakers' bureau). Krzysztof Selmaj: Biogen, Bristol Myers Squibb, Celgene, F. Hoffmann-La Roche, Merck, Novartis, TG Therapeutics (consulting fee, speakers' bureau). Ewa Krzystanek: Bayer, Merck-Serono, Novartis (consulting fee, speakers' bureau); Biogen (consulting fee, speakers' bureau, study lead); F. Hoffmann-La Roche (speakers' bureau, study lead, consulting fee); Polish Multiple Sclerosis Society (consulting fee); Janssen, Merck, TG Therapeutics (study lead); Lundbeck (speakers' bureau, study lead); Pfizer, Sandoz, Sanofi-Genzyme, Teva, UCB (speakers' bureau). Dusanka Zecevic, Catarina Figueiredo, Susanne Clinch, Caroline Giacobino, Jay Azmi: F. Hoffmann-La Roche (ownership interest, salary). Diego Centonze: Actelion, Mitsubishi (clinical trials); Alexion, Almirall, Amicus, Bayer, Chiesi, GW Pharmaceuticals, Horizon, Janssen, Sandoz, Viatris (consulting fee, speakers' bureau); Bayer Schering, Lundbeck (contracted research); Biogen, Bristol Myers Squibb, F. Hoffmann-La Roche, Merck-Serono, Novartis, Sanofi-Genzyme (consulting fee, speakers' bureau, contracted research, clinical trials); Celgene, Teva (consulting fee, speakers' bureau, contracted research).*

KEYWORDS: Comprehensive Care and MS, Disease-Modifying Treatments in MS

(DMT40) Incidence and Outcome of Meningococcal Infection With Eculizumab or Ravulizumab in Patients With Generalized Myasthenia Gravis or Neuromyelitis Optica Spectrum Disorder: An Analysis of Clinical Practice in the United States

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BACKGROUND: Eculizumab and ravulizumab are effective treatments for generalized myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD). Safety mitigations, including vaccinations, are used to reduce the risk of *Neisseria meningitidis* (*Nm*) infection associated with these treatments.

OBJECTIVES: To evaluate exposure-adjusted *Nm* infection and mortality in eculizumab- or ravulizumab-treated patients with gMG and NMOSD in the United States using postmarketing pharmacovigilance data (*Nm* case counts) and commercial data (exposure).

METHODS: The US Alexion safety database was searched for eculizumab (data cutoff: October 2023) and ravulizumab (data cutoff: December 2023) across approved indications (gMG, NMOSD, paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome) using the MedDRA High-Level Term *Neisseria infection*. Only *Nm*-associated cases were included. Reporting rates were calculated cumulatively per 100 patient-years.

RESULTS: US *Nm* infection and mortality annual reporting rates in eculizumab-treated patients remained stable over 16 years across approved indications (2023: 0.12 and 0.01, respectively; exposure: 34,484 patient-years). In 2023, US postmarketing *Nm* infection reporting rates in eculizumab-treated patients with gMG and NMOSD were 0.04 (exposure: 9181 patient-years) and 0.10 (exposure: 1988 patient-years), respectively. At data cutoff, there were no *Nm* infections among ravulizumab-treated patients with gMG. No *Nm* fatalities were noted for eculizumab- or ravulizumab-treated patients with gMG and NMOSD.

CONCLUSIONS: *Nm* infection and mortality reporting rates for patients with gMG and NMOSD remained stable despite increasing eculizumab and ravulizumab exposure over time. These results suggest US *Nm*-related risk mitigation strategies are effective in patients receiving eculizumab or ravulizumab.

DISCLOSURES: *Shirali Pandya, Lokesh Jha, Imad Al-Dakkak, Feifei Yang, Hua Zhang, Arshad Mujeebuddin: Alexion, AstraZeneca Rare Disease (salary, employee).*

KEYWORDS: Eculizumab, Ravulizumab, Meningococcal Infection

(DMT41) Neuroimmune Modulation As a Pro-Remyelination Therapy for Relapsing-Remitting Multiple Sclerosis: Rationale, Objective, and Study Design

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BACKGROUND: Multiple sclerosis (MS) is characterized by pathological loss of myelin, resulting in axonal vulnerability, degeneration, and significant accumulation of disability. While current disease-modifying therapies (DMTs) may reduce focal inflammatory activity and disease progression, there are no approved treatments to promote remyelination and restore neurological function. Neuroimmune modulation by electrical stimulation of the vagus nerve has been shown to accelerate remyelination in validated preclinical models of MS, with improvement of blood-brain barrier function, increased clearance of myelin debris, and induction of gene transcription related to remyelination. Based on these findings, a clinical study has been designed to evaluate this approach and its potential treatment effect in people with elapsing-remitting MS (RRMS).

OBJECTIVES: To determine the safety and treatment effect of neuroimmune modulation on remyelination and functional outcomes in adults with RRMS.

METHODS: This will be a multicenter, randomized, sham-controlled, and double-blinded pilot study that includes 1-way crossover to open-label after completion of the 6-month assessments. Up to 60 people with functional deficits but without focal inflammatory activity while on a stable regimen of DMT will be implanted with a proprietary integrated neurostimulator on the left cervical vagus nerve through a single incision during an outpatient procedure. Participants will be randomly distributed (1:1) to either active stimulation (treatment) or nonactive stimulation (control) with primary outcome measures assessed at 12 and 24 weeks. After 24 weeks, all devices will be activated in a long-term, open-label study extension.

RESULTS: Effectiveness of treatment will be evaluated by measuring the change from baseline in electrophysiology and imaging outcomes suggestive of remyelination including, but not limited to, visual evoked potential latency and magnetization transfer ratio. We will also assess clinical end points, including change from baseline in low-contrast letter acuity, high-contrast visual acuity, National Eye Institute Visual Function Questionnaire, Expanded Disability Status Scale scores, and Multiple Sclerosis Functional Composite scores at 12 and 24 weeks.

CONCLUSIONS: Neuroimmune modulation via vagus nerve stimulation will be evaluated as a remyelination therapy in patients with RRMS on stable DMTs with functional deficits in visual acuity.

DISCLOSURES: *Shiv Saidha: Amgen, Horizon Therapeutics, ImmPACT Bio, Rewind Therapeutics (advisory board); Biogen, Genentech, Novartis, SetPoint Medical (consulting fee, contracted research); Clene (contracted research, advisory board); InnoCare Pharma, Kiniksa, Medical Logix (consulting fee); JuneBrain (consulting fee, ownership interest); LAPIX Therapeutics (consulting fee, contracted research, ownership interest); MedDay (contracted research). Kathryn C. Fitzgerald: SetPoint Medical (consulting fee). David Chernoff: Aqtual, Dextera (advisor). David Chernoff, Yaakov Levine: SetPoint Medical (ownership interest, salary).*

KEYWORDS: Disease-Modifying Treatments in MS

(DMT42) Postapproval Safety of Cladribine Tablets in the Treatment of Patients With Multiple Sclerosis: 2024 Update

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BACKGROUND: Cladribine tablets, 3.5mg/kg, over 2 years is an established disease-modifying therapy for patients with relapsing multiple sclerosis. In line with the label for cladribine tablets, no further treatment is given in years 3 and 4.

OBJECTIVES: To provide the most recent information on new postapproval safety data concerning cladribine tablets as they become available.

METHODS: Adverse events (AEs) from postapproval sources (including spontaneous individual case safety reports, noninterventional postmarketing studies, and reports from other solicited sources) are presented up to July 2024. AE rates are shown as reporting rate expressed per estimated 100 person-years (95% CI) for an estimated 251,900 person-years of exposure (PYE) in more than 100,000 patients since the approval of cladribine tablets in 2017. PYE are estimated cumulatively (by quarter) from sales data.

RESULTS: Exposure-adjusted reporting rates were: hypersensitivity, 1.13 (1.09-1.18) (2858 reports); serious infections, 0.50 (0.48-0.53) (1270 reports); herpes zoster, 0.33 (0.31-0.35) (830 reports); liver injury, 0.25 (0.23-0.27) (623 reports); malignancies, 0.16 (0.14-0.17) (397 reports); serious lymphopenia, 0.10 (0.09-0.12) (259 reports); seizures, 0.06 (0.05-0.07) (160 reports); tuberculosis, 0.01 (0.01-0.02) (35 reports); and opportunistic infections other than progressive multifocal leukoencephalopathy (PML) and tuberculosis, 0.02 (0.01-0.02) (39 reports). No confirmed cases of PML were reported. Cumulatively, 474 pregnancies have been identified. Among 200 pregnancies with known outcomes, there were 127 live births without congenital anomalies, 36 spontaneous abortions, 30 elective terminations, 2 reports of ectopic pregnancy, 1 report of stillbirth with fetal defects, and 4 pregnancies resulting in live births with congenital anomalies (1 major [atrial septal defect] and 3 minor). Data for year 5 and beyond after initial exposure to cladribine tablets were in line with the known safety profile and did not show any new or unexpected AEs or risks.

CONCLUSIONS: Cumulative to July 2024, the safety profile of cladribine tablets is consistent with findings from the clinical development program and previous safety updates. The currently available data, while limited, does not show an increased risk of adverse pregnancy outcomes in patients receiving cladribine tablets.

DISCLOSURES: *Thomas P. Leist: Acorda, Bayer, Biogen, Daiichi Sankyo, EMD Serono, Novartis, ONO, Pfizer, Teva (clinical research grants and/or consulting fee). Bassem Yamout: Bayer, Biogen, Novartis (research grants, honoraria for lectures, advisory board); Genpharm, Roche, Sanofi, The healthcare business of Merck KGaA, Darmstadt, Germany (honoraria for lectures, advisory board; Pfizer (research grants). Danielle E. Harlow: EMD Serono (salary). Andrija Javor: Ares Trading S.A. (affiliate of Merck KGaA, Darmstadt, Germany), Lausanne, Switzerland (salary). Andrew Galazka: Ares Trading S.A. (affiliate of Merck KGaA, Darmstadt, Germany; former employee); the healthcare business of Merck KGaA, Darmstadt, Germany (consultant, salary). Joerg Seebeck: The healthcare business of Merck KGaA, Darmstadt, Germany (salary).*

KEYWORDS: Cladribine, Safety, Disease-Modifying Treatments in MS

(DMT43) Comparative Assessment of Switching Outcomes for Cladribine Tablets Versus Fingolimod, Dimethyl Fumarate, and Teriflunomide in Patients With Multiple Sclerosis at 4 Years

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BACKGROUND: Data on long-term treatment persistence of cladribine tablets (CladT) in real-world settings are limited in the United States.

OBJECTIVES: To evaluate long-term (up to 4 years) treatment switching in patients with multiple sclerosis (PwMS) in the US treated with CladT vs fingolimod (FTY), dimethyl fumarate (DMF), and teriflunomide (TER).

METHODS: This retrospective study used the Komodo health care map database and included patients 18 years of age or older with 2 or more MS diagnoses 30 days or more apart between April 1, 2018, and March 31, 2024; ≥1 claim for CladT, FTY, DMF, or TER between April 1, 2019, and March 31, 2022 (initiation date=index); and no index disease-modifying therapy (DMT) within 1 year before the index date (baseline). A minimum of 12 months of continuous medical and pharmacy eligibility were required before the index date and 24 months after the index date. In each of the comparisons, standardized mortality ratio weights were generated based on propensity scores to balance baseline demographic and clinical covariates. The proportion of time spent switching to another DMT and the time spent switching during the follow-up period were evaluated across DMT groups. ORs and HRs for switching were estimated, along with bootstrapped 95% CIs, using double robust logistic and Cox regression models.

RESULTS: A total of 10,372 people with multiple sclerosis met the study inclusion criteria (CladT n=706; FTY n=1435; DMF n=5164; TER n=3067) and had a median follow-up of 2.9 to 3.3 years. The overall mean age was 47 years, and 75% were women. In the weighted population, only 12% of patients receiving CladT switched to another DMT within 4 years, compared with 34% for FTY, 53% for DMF, and 37% for TER. The ORs (95% CI) for switching treatment over 4 years compared with CladT were 3.69 (2.81-4.87) for FTY, 7.98 (6.13-10.48) for DMF, and 4.16 (3.19-5.47) for TER. The HRs (95% CI) for time to switch over a 4-year period were significantly higher for FTY 3.11 (2.39-4.03), DMF 5.93 (4.73-7.42), and TER 3.63 (2.88-4.58) compared to CladT.

CONCLUSIONS: In this real-world study, 12% of patients treated with CladT switched to another DMT during the follow-up period (up to 4 years), which was significantly lower than treatment switches observed in those treated with FTY, DMF, or TER.

DISCLOSURES: *Ajay Gupta: EMD Serono (consulting fee, speakers' bureau). Joanna P. MacEwan, Jeffrey Anderson, Xin Zhao, Sonia Kim, Andy Surinach, Yu Hong: EMD Serono (employer-granted funding from EMD Serono to conduct the study). Amy L. Phillips, Xiaoxue Chen: EMD Serono (salary).*

KEYWORDS: Cladribine Tablets, Treatment Persistence, Switching Between DMTs, Real-World Evidence, Disease-Modifying Treatments in MS

(DMT44) Evaluation of Ofatumumab Use at the University of Cincinnati Waddell Center for Multiple Sclerosis Clinic: A Real-World Study

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BACKGROUND: Ofatumumab (OFB) is an anti-CD20 monoclonal antibody approved by the United States Food and Drug Administration for relapsing-remitting multiple sclerosis (RRMS), clinically isolated syndrome (CIS), and active secondary progressive multiple sclerosis (aSPMS) with subcutaneous dosing. There are limited studies that have looked at the safety and efficacy of OFB use in a real-world setting.

OBJECTIVES: This study aims to evaluate the safety and efficacy of OFB.

METHODS: A retrospective cohort study was conducted with data collected from the University of Cincinnati Waddell Center for Multiple Sclerosis clinic in Cincinnati, Ohio, for all patients with RRMS or aSPMS treated with OFB between January 2021 and November 2024. Patients were included if they had received at least 3 doses of OFB. Collected variables were demographics, prior disease-modifying therapy (DMT), clinical relapses, MRI activity, adverse events, and laboratory data. Clinical relapses were defined as events requiring high-dose steroids. MRI activity included any new T2 or contrast-enhancing lesions. Hypogammaglobulinemia (HGG) was defined as serum immunoglobulin G (IgG) or IgM less than 600 or 40 mg/dL, respectively.

RESULTS: A total of 166 patients on OFB were included with a mean (SD) duration of therapy of 585 (± 337) days. The mean (SD) age was 43.92 (± 11.3) years; 80.7% were women, and 68% identified as White. OFB was the first DMT for 45 patients (27%); 59 (35.5%) switched from other anti-CD20 therapies. There were no clinical relapses in 96.8%, and there was no MRI activity in 90.4% of patients after treatment with OFB. The mean (SD) number of clinical relapses was 0.03 (± 0.17), and the mean (SD) number of MRI active lesions was 0.12 (± 0.38) on OFB. MRI activity appeared after 11.6 months, and clinical relapse after 7 months, on average, following OFB. Patients who switched from prior DMTs to OFB did not experience significant differences in clinical relapses or MRI activity. Subjective symptom progression was reported in 11.49% of patients. HGG occurred in 10.8% (IgG) and 26.4% (IgM) of patients. Neutropenia (absolute neutrophil count<1500) and lymphopenia (absolute lymphocyte count<1000) occurred in 4.4% and 13.1% of patients, respectively. The mean CD19+ percentage on OFB was 0.40 (± 1.87). Neurofilament light was the only biomarker to significantly decrease post switch (P=.02), with no changes in others, including glial fibrillary acidic protein.

CONCLUSIONS: OFB demonstrates a favorable safety profile with minimal relapse and MRI activity in a real-world setting.

DISCLOSURES: *Kiranpal S. Sangha: TG Therapeutics (advisory board). Sara Esmaeili, Ravneet S. Sangha, Kiret S. Sangha, Alexander Mirzoev, Joseph LaPorta: Nothing to disclose. W. Daniel Chapman: Amgen, EMD Serono/Merck (consulting fee); Biogen (consulting fee, speakers' bureau); Novartis (contracted research). Lawrence Goldstick: Biogen, Roche/Genentech, Sanofi-Genzyme (consulting fee, contracted research); Bristol Myers Squibb, EMD Serono (consulting fee); Horizon/Amgen, TG Therapeutics (speakers' bureau, consulting fee). Aram Zabeti: Alexion/AstraZeneca, Bristol Myers Squibb, Sanofi, TG Therapeutics (speakers' bureau).*

KEYWORDS: Disease-Modifying Treatments in MS, Ofatumumab, Efficacy, Safety, Real-World Study

(DMT45) Adherence and Persistence With Infusion Disease-Modifying Therapies and Travel Burden in Patients With Multiple Sclerosis on Medicare

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BACKGROUND: Ofatumumab, ocrelizumab, natalizumab, alemtuzumab, and ublituximab, which are generally considered high-efficacy disease-modifying therapies (DMTs) for multiple sclerosis (MS), are all administered by intravenous infusion, except ofatumumab, which is an at-home self-injectable DMT. Travel to an infusion center may pose a burden for patients with MS and could impact their adherence and persistence to therapy.

OBJECTIVES: To assess adherence and persistence to infusion DMTs and evaluate the impact of travel burden.

METHODS: Medicare fee-for-service data were used to identify adult patients with MS who received an infusion DMT of interest (see list above; index = first DMT claim date) from January 2017 to September 2024 with 12 months or more of preindex continuous enrollment. The travel (ie, commuting) distance was based on the 5-digit zip codes of the patient's residence and the infusion facility. Persistence was defined as the number of days from index until treatment discontinuation or DMT switch (maximum allowed gap of 90 days). Kaplan-Meier survival analysis was used to describe persistence. Adherence was based on the proportion of days covered and was set at 0.8 or greater. Logistic regression and Cox proportional hazards regression were used to identify the factors impacting 24-month adherence and persistence, respectively.

RESULTS: Among 20,961 included patients, the mean (SD) age was 57 (12) years, 69% were women, 80% were White, 80% resided in urban areas, and 84% received ocrelizumab. Adherence at 24 and 36 months was 43% and 35%, respectively. Persistence to index infusion DMT at 24 and 36 months was 43% and 29%, respectively. There was an approximately 10% (OR, 0.90; 95% CI, 0.84-0.96) decrease in adherence for rural patients with 2-way travel distance between 61 and 120 miles compared with those with 60 or fewer miles of travel from the infusion center. In addition, 75% of DMT recipients were not receiving their infusion(s) at their nearest infusion facility, traveling an average additional 2-way distance of 52 miles.

CONCLUSIONS: Among Medicare beneficiaries with MS, adherence and persistence to infusion DMTs were low, with more than 50% of patients nonpersistent after 2 years and more than two-thirds of patients nonpersistent after 3 years. Travel burden was associated with lower adherence, particularly in rural areas. High-efficacy DMTs administered at home may provide a more suitable option for Medicare beneficiaries with MS who are at risk for nonadherence due to travel burden.

DISCLOSURES: *Karishma Thakkar, Ming-Hui Tai, Swetha R. Palli, Brandon Brown, Luo Li, Cheng Shi, Abhijit Gadkari: Novartis (salary).*

KEYWORDS: Disease-Modifying Treatments in MS, Travel Burden, Adherence, Persistence

EPIDEMIOLOGY AND GENETICS

(EP101) Exploring the Association of Immune Checkpoint Inhibitors and Multiple Sclerosis: Insights From the Food and Drug Administration Adverse Event Reporting System Database

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BACKGROUND: Immune checkpoint inhibitors (ICIs) have revolutionized cancer therapy by improving prognosis. But they are associated with increased risk of autoimmunity or exacerbation of preexisting autoimmune diseases.

OBJECTIVES: The aim of this study was to explore the association of ICIs with multiple sclerosis (MS) and/or MS relapses using the United States Food and Drug Administration Adverse Event Reporting System (FAERS) database and to compare that association with other autoimmune neurological adverse events (AEs).

METHODS: We conducted a disproportionality analysis of FAERS data spanning the 4th quarter of 2003 to the second quarter of 2024 using OpenVigil 2.1. The ICIs analyzed (grouped as a single drug class for this analysis) included pembrolizumab, nivolumab, cemiplimab, dostarlimab, atezolizumab, durvalumab, avelumab, ipilimumab, and tremelimumab. The AE terms searched for were *multiple sclerosis* (and/or *multiple sclerosis relapse*), *myasthenia gravis* (and/or *myasthenia gravis crisis* and/or *immune-mediated myasthenia gravis*), *Guillain-Barre syndrome*, and *autoimmune encephalitis*. Analyses were restricted to reports where ICIs were identified as the primary suspect drugs for AEs. A signal was detected when the number of drug-AE reports was 3 or more, the proportional reporting ratio (PRR) was 2 or greater, and the x^2 value was 4 or greater. Results were presented as reporting ORs (RORs) with corresponding 95% CIs for each AE. The ROR represents the odds of a specific AE occurring with the drug of interest compared with the odds of the same AE occurring with all other drugs in the database.

RESULTS: There were 48 reports of MS or MS relapse in association with ICIs. These patients had an average age of 56.1 years (± 14.5) years, with 24 women, 18 men, and 6 of unknown sex. The ROR for MS and/or MS relapse was 0.09 (95% CI, 0.068-0.12), whereas the RORs for other autoimmune neurological AEs were 21.05 (95% CI, 19.287-22.974) for myasthenia gravis, 8.075 (95% CI, 6.677-9.766) for Guillain-Barre syndrome, and 29.03 (95% CI, 23.564-35.764) for autoimmune encephalitis.

CONCLUSIONS: Our findings do not suggest a significant safety signal for MS or MS relapse with ICIs, unlike myasthenia gravis, Guillain-Barre syndrome, and autoimmune encephalitis, where safety signals were detected. Prospective studies are needed to confirm these results, investigate mechanisms underlying the differential safety profiles of ICIs across autoimmune neurological AEs, and identify predictors of such AEs associated with ICIs.

DISCLOSURES: *Afsaneh Shirani: TG Therapeutics (consulting fee). Olaf Stuve: Current Treatment Options in Neurology (section editor). Biomedical Laboratory Research and Development, EMD Serono, National Multiple Sclerosis Society, United States Department of Veterans Affairs (grants); EMD Serono, Novartis, Octave Bioscience (advisor); Genentech-Roche, Novartis (data monitoring committees); Therapeutic Advances in Neurological Disorders, Expert Review of Clinical Immunology (editorial boards).*

KEYWORDS: Epidemiology of MS, Immune Checkpoint Inhibitors and MS, Immunology and MS

(EP102) Misdiagnosis of Adult-Onset Leukodystrophies as Multiple Sclerosis: The Need to Prioritize Genetic Testing in Clinical Workup

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BACKGROUND: Due to shared clinical and neuroimaging manifestations, many adult-onset neurological disorders are inaccurately diagnosed as multiple sclerosis (MS). Literature from MS centers suggests that 20% to 30% of patients who receive an initial diagnosis of MS are misdiagnosed. Inaccurate diagnosis can result in treatment-related morbidity, delay in accessing suitable therapies, and challenges in identifying participants for clinical trials. Important differential diagnoses for MS include adult-onset leukodystrophies. Overlapping symptoms and imaging findings result in up to 40% of patients with leukodystrophy being misdiagnosed, frequently as MS. Misdiagnosis of adult-onset leukodystrophies as MS may be avoided by recognizing clinical or neuroimaging findings suggestive of alternative diagnoses and genetic testing for leukodystrophy-associated genes. Indeed, the McDonald criteria were developed to identify MS "once other diagnoses have been deemed unlikely." However, detailed characterization of red flags to prompt consideration of other diagnoses and genetic testing in MS clinics is lacking.

OBJECTIVES: To characterize clinical and radiological red flags leading to prioritizing genetic testing for leukodystrophies in patients with suspected MS.

METHODS: A systematic literature review was performed to identify published cases of adult-onset leukodystrophies with presentations mimicking MS. Eligible studies were screened to identify clinical and imaging findings differentiating leukodystrophies from MS.

RESULTS: Literature review identified 58 cases of patients with adult-onset leukodys-

trophies mimicking MS, many of whom were initially misdiagnosed. Of these cases, adult-onset leukoencephalopathy with axonal spheroids and pigmented glia was the most common final diagnosis (37.9%), followed by cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (27.6%). Red flags for differential diagnoses included cognitive and behavioral changes, family history of neurological disease, and/or atypical imaging findings.

CONCLUSIONS: Adult-onset leukodystrophies are frequently misdiagnosed as MS due to overlapping clinical and radiological presentations. However, several red flags should prompt genetic testing for leukodystrophies. We recommend prioritization of genetic testing for leukodystrophy-associated genes in patients with suspected MS with a family history of neurological disorders, brain abnormalities atypical of MS, or early-onset cognitive changes.

DISCLOSURES: *Donald M. McLaren, Clarissa Martinez-Rubio, Cynthia Cassandro, Ali Toumadj: Vigil Neuroscience (salary). Holly Rutherford: Vigil Neuroscience (consulting fee).*

KEYWORDS: Differential Diagnosis

(EP103) Demographic Survey of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease in an Adult Hispanic Population in South Texas

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BACKGROUND: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an autoimmune disorder of the central nervous system that can result in demyelination of the brain, optic nerves, and spinal cord. Although it shares clinical features with multiple sclerosis and neuromyelitis optica spectrum disorder, MOGAD is diagnosed using cell-based assay to detect antibodies directed against MOG. As a recently discovered clinical entity, little is known about the epidemiology of MOGAD and how it differentially affects patients of various ethnic backgrounds.

OBJECTIVES: Our objective is to evaluate the presentation and disease course of MOGAD in an adult Hispanic population in South Texas.

METHODS: We are conducting an ongoing retrospective chart review identifying patients with MOGAD at The University of Texas San Antonio Health Center. Baseline demographics, clinical presentation, and patient outcomes are recorded for each patient.

RESULTS: At present, 33 adult Hispanic patients with MOGAD have been identified through chart review. Within the Hispanic population, we observed a female-to-male ratio of 2.66:1 (24 women and 9 men). The average age is 45 years (range, 22-83). A total of 81.8% presented with optic neuritis (54.5% unilateral and 27.3% bilateral). The relapse rate was 62.5% for women and 55.5% for men. Of those tested, oligoclonal bands were present in 7 of 27 (25.9%). Cell-based assay MOG antibody titers were at least 1:100 in 22 of 32 patients (68.8%).

CONCLUSIONS: We will provide valuable epidemiological data for Hispanic patients with MOGAD in South Texas. Data on MOGAD historically have been obtained predominantly from White patients. This study provides valuable demographic data for an underrepresented population that may be used to help guide prognosis and treatment decisions.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: MOGAD

(EP104) Prevalence and Odds of Bipolar Disorder in Patients With Multiple Sclerosis: A Systematic Review and Meta-Analysis

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BACKGROUND: Patients with multiple sclerosis (MS) experience a wide range of physical and psychiatric disorders. Literature shows increased prevalence of bipolar disorder (BD) in patients with MS.

OBJECTIVES: To estimate pooled prevalence and odds of BD in patients with MS.

METHODS: PubMed, Scopus, Embase, Web of Science, PsycINFO, and Google Scholar were systematically searched by 2 independent researchers on March 1, 2024.

RESULTS: A literature search revealed 2228 records. A total of 107 full texts were evaluated, and 34 studies were included in the systematic review. The prevalence of BD in included studies ranged between 1% and 20%, and the pooled prevalence was estimated as 3% (95% CI, 2%-4%; $I^2 = 99\%$; $P < .001$). The pooled prevalence of BD in patients with MS was estimated as 3% (95% CI, 1%-5%) in America and Europe (95% CI, 1%-8%) and 2% (95% CI, 1%-3%) in Asia. The OR of BD in cases with MS ranged between 2.17 and 17.9, and the pooled OR was estimated as 3.84 (95% CI, 1.75-8.41; $I^2 = 93\%$; $P < .01$).

CONCLUSIONS: The results of this systematic review demonstrate that the prevalence of BD in patients with MS is high and that patients with MS are at a 3-fold higher risk of developing BD. The pooled prevalence was the lowest in Asia compared with America and Europe.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Bipolar Disorder, Epidemiology of MS

(EP105) Epidemiological Profile of Patients in a Multiple Sclerosis Association

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BACKGROUND: Multiple sclerosis (MS) is a chronic, progressive demyelinating disease characterized by inflammation of the central nervous system that predominantly affects young adults. Over the years, the disease results in the accumulation of motor, sensory, visual, and cognitive sequelae (Schaffer et al; 2015) and is the leading cause of disabilities in this age group in Western countries. In Brazil, the prevalence of MS is estimated to range from 1.36 per 100,000 inhabitants in Recife, Pernambuco, to 27.2 per 100,000 inhabitants in Santa Maria, Rio Grande do Sul (da Gama Pereira ABCN, Sampaio Lacativa MC, da Costa Pereira FFC, Papais Alvarenga RM. Prevalence of multiple sclerosis in Brazil: a systematic review. *Mult Scler Relat Disord*. 2015;4(6):572-579. doi:10.1016/j.msard.2015.08.004). In the city of São Paulo, it is estimated that approximately 15 per 100,000 inhabitants are diagnosed with MS (Callegaro D, Goldbaum M, Morais L, et al. The prevalence of multiple sclerosis in the city of São Paulo, Brazil, 1997. *Acta Neurol Scand*. 2001;104(4):208-213. doi:10.1034/j.1600-0404.2001.00372.x), although this figure is believed to be an underestimation.

OBJECTIVES: The objective of this study is to understand the epidemiological profile of patients enrolled in an MS patient association in São Paulo, Brazil.

METHODS: Data collection occurred between April 2023 and December 2024 and included a total of 295 individuals.

RESULTS: Among the patients included in the nongovernmental MS association, 72.5% were women and 27.5% were men, with an average age of 46 years. In terms of ethnicity, 64.4% identified as White and 28.1% as Brown. Regarding educational attainment, 25.1% held a postgraduate degree or a master's degree/doctorate, 33.9% had completed higher education, 12.9% had some college education but did not complete their degree, and 24.1% had completed high school. In terms of relationship status, 40.3% were single, 38.6% lived with family members, and 13.2% lived alone (single or divorced). Among the respondents, 44.7% reported having some form of employment, 19.3% were unemployed, and 8.8% received sickness benefits. Of those employed, 34.1% were self-employed. The family income of the majority (66.5%) did not exceed 4 times the minimum wage.

CONCLUSIONS: The patients participating in the MS association are primarily women, White, educated, and employed, with many identifying as self-employed. The high level of education among these individuals is noteworthy, potentially indicating access to information or recognition of the importance of involvement in a patient association that offers complementary therapeutic services such as physiotherapy, reflexology, psychology, and shiatsu. The social circumstances of these patients, including being single and living with family members, may arise from the limitations imposed by the disease or financial constraints. Understanding the socioeconomic landscape of these patients can contribute to the formation of public policies that more effectively address the realities faced by individuals living with chronic incurable diseases.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Epidemiology of MS, Brazil, MS Association

(EP106) Studying the Genetic Architecture of Multiplex Families With Multiple Sclerosis in Newfoundland and Labrador

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BACKGROUND: The majority of individuals in Newfoundland and Labrador (NL) in Canada are descended from a small number of English and Irish immigrants who settled the province in the 18th and 19th centuries. The population has remained relatively isolated over the past 3 centuries, preserving the genetic structure associated

with this population bottleneck. Within NL, there are large families with high numbers of multiple sclerosis (MS) diagnoses. Although MS has not been associated with a single gene, findings from twin studies have demonstrated higher disease concordance for identical twins (~ 25%-30%) compared with fraternal twins (3%-5%), suggesting underlying genetic risk factors may be present in these multiplex families.

OBJECTIVES: The disease prevalence and unique demographic history make the population of NL well suited for identification of genetic risk factors associated with MS. We aimed to design and deploy a study of NL families, with the eventual goal of identifying putative risk factors underlying MS in NL.

METHODS: We identified study participants by working with the Recovery and Performance Laboratory (RPL) at Memorial University in NL and recruited families in collaboration with this group and local neurologists. Study participants seen at RPL have undergone deep phenotyping; we also collected personal and family history information via medical record review and participant interviews, including construction of detailed pedigrees. Families must have at least 2 individuals diagnosed with MS to be enrolled and are offered the option to receive research-grade medically actionable secondary findings. Blood samples collected from participants are used for whole-genome sequencing (WGS). Participants with MS diagnoses are categorized as "affected" for genetic analysis; this designation may also be assigned to obligate carriers and/or individuals with highly suggestive phenotypes.

RESULTS: A total of 103 individuals from 25 families have been enrolled, including 45 individuals diagnosed with MS; pedigrees span over 5 generations in some cases. The largest family includes 6 affected individuals within first- and second-degree relations, with an additional 4 cases in the extended family. The study's geographic range spans NL, and sampling has been extended to relatives from 5 other Canadian provinces and the United States. Over 85% of participants have consented to receive secondary findings, and approximately 80% have consented to be included as controls in future studies.

CONCLUSIONS: This is the largest WGS family-based study of the genetic basis of MS to date. WGS and the association of rare variants with disease status are ongoing, and continued sample collection is adding to the level of detail. Results of these analyses will provide fundamental information about the etiology of the disease, thereby aiding in development of future treatments for MS as well as providing an example of effective collaboration between industry, academia, and provincial health care systems.

DISCLOSURES: *Margaret MacMillan, Diane Power, Tom Barber: Sequence Bioinformatics (ownership interest, salary). Cameron M. Nugent: Sequence Bioinformatics (ownership interest, salary); Bridge Informatics (consulting fee). Bari Ballew: Sequence Bioinformatics (ownership interest, salary); Blackjack Biotechnologies (contracted research, ownership interest).*

KEYWORDS: Epidemiology of MS, Etiology of MS, Genetics and MS

(EP107) Attitudes Toward Genetic Information Sharing Among Patients With Multiple Sclerosis

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BACKGROUND: Genetic data can provide valuable insights in the study of multiple sclerosis (MS). The success of these research initiatives depends on individuals' willingness to share genetic information, which often is viewed as more sensitive than other personal information.

OBJECTIVES: To assess the willingness of persons with MS to securely share and store genetic information for research purposes and explore associated characteristics.

METHODS: A fall 2023 survey asked participants of the North American Research Committee on Multiple Sclerosis Registry about their willingness to share genetic information. Response options were "yes," "perhaps," "depending on circumstances," "no," "unsure/undecided," or "prefer not to answer." Demographic factors (age, sex, race, education, income, marital status, employment) and clinical characteristics (disease duration, disability level, comorbidities, prior clinical trial participation) were collected. A multivariable multinomial logistic regression was used to identify factors associated with willingness to share genetic information. For regression analyses, "no" and "unsure/undecided" were collapsed and the "prefer not to answer" group was excluded. We may consider an additional analysis where it is added to the "no" and "unsure/undecided" group.

RESULTS: Among 4805 respondents (mean age, 66.1 years; 81.4% women; 37.3% with severe disability), 33.7% responded "yes," 27.2% "perhaps," 18.9% "no," 10.3% "unsure," and 9.9% "prefer not to answer." On multivariable analysis, men had 26% increased odds of responding "yes" vs "no" or "unsure" (OR, 1.26; 95% CI, 1.03-1.55). Both part-time workers (OR, 1.70; 95% CI, 1.20-2.40) and those not employed (OR, 1.51; 95% CI, 1.16-1.97) were more likely to respond "yes." Participants from areas with higher deprivation indices (OR, 1.61; 95% CI, 1.21-2.15) and those with previous clinical trial participation (OR, 1.60; 95% CI, 1.33-1.94) showed greater willingness to share genetic information. Higher alcohol consumption (OR, 2.19; 95% CI, 1.65-2.92) and not being physically active (OR, 1.35; 95% CI, 1.13-1.61) were associated with increased willingness. Disability was not associated with willingness. Every 10-year increase in disease duration was associated with a reduced odds of responding "perhaps" vs "no" or "unsure" (OR, 0.89; 95% CI, 0.81-0.99).

CONCLUSIONS: Many individual characteristics are related to willingness to share genetic information. Understanding these sociodemographic and clinical factors can help develop targeted strategies to address barriers in MS research.

DISCLOSURES: *Mudita Sharma, Gary R. Cutter: Nothing to disclose. Robert J. Fox: AB Science, Bristol Myers Squibb, Eli Lilly, EMD Serono, Genentech, Greenwich Biosciences, Immunic, INmune Bio, Janssen, Siemens, TG Therapeutics (consulting fee); Biogen, Novartis, Sanofi (consulting fee, research support). Ruth A. Marrie: Arthritis Society, Biogen Idec, Canadian Institutes of Health Research, Consortium of Multiple Sclerosis Centers, Crohn's and Colitis Canada, MS Canada, National Multiple Sclerosis Society, Public Health Agency of Canada, Research Manitoba, Roche Canada, US Department of Defense (research funding). Amber Salter: Consortium of Multiple Sclerosis Centers, Multiple Sclerosis Society of Canada, National Multiple Sclerosis Society, US Department of Defense (research funding); Abata Therapeutics, Gryphon Bio, Sora Neuroscience (consulting fee); Owl Therapeutics (equity).*

KEYWORDS: Genetics and MS

(EP108) Understanding the Burden of Illness in People With Primary Progressive Multiple Sclerosis in the United States: A Matched Cohort Study

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BACKGROUND: Primary progressive multiple sclerosis (PPMS) is characterized by steady accumulation of disability from the onset and affects 10% to 15% of people with multiple sclerosis (PwMS). Although PwMS experience a substantially lower quality of life and greater health care resource utilization (HCRU) than the general population, data on the clinical and economic burden of PPMS are limited.

OBJECTIVES: To assess the real-world clinical and economic burden in people with PPMS in the United States.

METHODS: A retrospective matched cohort study was conducted using a US-based administrative claims database from January 1, 2018, to June 30, 2023. People with PPMS were identified via a validated algorithm and matched to unique MS-free controls based on age, sex, insurance type, and region (1:1). Demographics, comorbidities, HCRU, and health care costs (HCCs) were compared (costs in 2023 US$) with matched controls during the 2-year observation period.

RESULTS: The final cohort was 3587 people with PPMS and 3587 matched controls (mean ± SD age, 57.5 ± 12.0 years; female: 75.9%). The mean Charlson Comorbidity Index score (2.1 vs 0.9) and the proportion of people with infections (81.8% vs 49.3%), leukopenia (2.6% vs 0.7%; all $P < .001$), and elevated liver transaminase level (1.1% vs 0.5%; $P = .003$) were significantly higher in the PPMS cohort vs controls. The most common MS-related comorbidities in the PPMS cohort vs controls were abnormal gait (66.7% vs 3.4%), malaise/fatigue (56.9% vs 15.7%), depression (36.5% vs 11.3%), muscle weakness (34.4% vs 2.8%), and urinary incontinence (30.1% vs 3.0%; all $P < .001$). Use of ambulatory devices (74.3% vs 9.8%) and physical (67.5% vs 16.1%), occupational (75.4% vs 19.4%), and speech therapy (3.2% vs 0.2%) were more frequent in the PPMS cohort than controls (all $P < .001$). Hospitalizations (33.3% vs 11.0%), emergency department (ED) visits (45.4% vs 18.3%), and mean number of physician visits (40.0 vs 13.4) were also significantly greater in the PPMS cohort vs controls (all $P < .001$) at follow-up. The PPMS cohort had significantly higher total mean HCCs than controls ($147,443 vs $21,842), mainly due to cost of medical claims ($105,917 vs $16,213) and non-ED outpatient services ($82,360 vs $9458; all $P < .001$).

CONCLUSIONS: People with PPMS had more comorbidities and significantly higher HCRU and HCCs vs controls, resulting in a substantial clinical and economic burden in a population for whom very limited approved therapies exist.

DISCLOSURES: *Nupur Greene, Inès Hemim: Sanofi (salary). Ashis K. Das, Eunice K. Chang, Marian H. Tarbox: ADVI Health (salary).*

KEYWORDS: Burden in Primary Progressive MS, Economic Issues and MS, Epidemiology of MS

INTERNET AND INFORMATION SERVICES

(IIS01) Systematic Collation of Individual Patient Data Within the Electronic Health Record Improves Efficiency in Metrics Related to Multiple Sclerosis Care

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BACKGROUND: The advent of electronic health records (EHRs) was supposed to make it faster and easier to find information in patient charts. In practice, key details about a patient's clinical history are not aggregated, often requiring substantial time for care team members to refamiliarize themselves with the details each time an encounter occurs. At the Johns Hopkins Multiple Sclerosis (MS) Precision Medicine Center of Excellence, we created a snapshot tool in Epic called MS SmartForm and have been utilizing it for over 5 years. Retrospective data are populated in SmartForm, and clinicians subsequently add new information as it becomes available. The experience of our care team has been that the tool saves valuable time by reducing the need to locate scattered results to prepare for a clinic appointment or to respond to a patient query, and we hypothesized that other MS centers might also experience time savings using the MS SmartForm.
OBJECTIVES: To evaluate whether having access to a standardized data collection tool within the EHR saves time for clinicians who require rapid access to details about a given patient's MS course.
METHODS: Four MS centers with populations of at least 1000 unique MS patient visits per year participated in the study. First, study teams used randomly selected visit dates to identify 40 charts. Three clinicians at each site then completed a blinded, timed questionnaire for each chart. Next, the information technology team at each institution integrated the SmartForm into their local EHR. Subsequently, SmartForm data were populated for 1000 charts at each site, and the same clinicians completed the blinded, timed questionnaire a second time for the same 40 patients. We used a mixed-methods model to compare the pre- and post-SmartForm questionnaire completion times.
RESULTS: Clinicians spent 3.04 fewer minutes completing the questionnaires post vs before SmartForm (95% CI, 2.63-3.45; $P < 2.2e-16$).
CONCLUSIONS: The results support the hypothesis that the MS SmartForm saves time for clinicians seeking core details about a person's MS history; for an average 30-minute appointment, for example, 10% more time would become available for other important aspects of care. In future work, we plan to analyze clinicians' satisfaction with the EHR and their perceptions of quality of care provided before and post SmartForm implementation.
DISCLOSURES: *Ellen M. Mowry: Biogen, Genzyme (research funding); Teva (medication for a clinical trial); UpToDate (royalty). Thomas Grader-Beck: Argenx, Novartis (consulting fee). Soha Fardad, Kasturi Ganesh Barki, Tirisham Gyang, Alicia Hill, Yishang Huang, Susan Robles, Willard W. Will III: Nothing to disclose. Kate Fitzgerald: SetPoint Medical (consulting fee). Jennifer Graves: ABM, Atara Biotherapeutics, Biogen, EMD Serono (contracted research); Google (consulting fee); Horizon, TG Therapeutics (advisory board participation); Novartis (contracted research, pediatric clinical trial steering committee). William Meador: Bristol Myers Squibb, Patient-Centered Outcomes Research Institute (contracted research). Yujie Wang: Genentech, National Institute of Neurological Disorders and Stroke, uniQure (contracted research); TG Therapeutics (consulting fee).*
KEYWORDS: Comprehensive Care and MS, Methods of Care

(IIS02) Multiple Sclerosis Health Care Providers Are Not Leading Online Resource: Analysis of Online Multiple Sclerosis Sources, Searches, and Sites

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BACKGROUND: Research demonstrates that those living with multiple sclerosis (MS) use the internet for health education. The sources and qualifications of online MS education are not well-known.
OBJECTIVES: The study has 3 aims. The first aim is to clarify and compare the top 5 online sources of 9 MS-related search terms (STs) on 6 online sites (OSs). The second aim is to compare the sources across the 6 different OSs. The third aim is to determine whether the requester of information changes the search results.
METHODS: Three medical students (MedSs) each searched 2 websites (eg, Twitter, Instagram, YouTube, TikTok, Facebook, and Google) on both a personal account (MSA) and a newly created account (PSA) for 9 MS-related STs. The searches were completed from October 2024 through January 2025. The 9 STs were *multiple sclerosis*, *MS*, *#multiplesclerosis*, *#MS*, *multiple sclerosis cause*, *multiple sclerosis prognosis*, *multiple sclerosis child*, *multiple sclerosis symptoms*, and *multiple sclerosis treatment*. The sources were defined as personal (P), patient advocate (PA), physician (MD), other health care provider (OHP), academic (A), and unknown. The MedSs coded in a shared Excel spreadsheet, indicating source, ST order, MedS, ST, and OS. All data were public, so no review board was involved. Data were analyzed using x^2 analysis to calculate a *P* value comparing the source, OS, and ST.
RESULTS: There were 540 data points. Chi-square analysis ($P = 2.237e-67$) indicated the top MS STs of the 6 OSs are significantly associated with the source. Across all online searches, P sources were the most common overall (n = 248), followed by PA groups (n = 100) and then A sources (n = 86). The most prominent overall source on each social media platform was P (Twitter, Facebook, Instagram, TikTok), A (Google), and MD (YouTube). Of the top 5 searches, 34.4% were related to health care (MD, A, OHP). Notably, YouTube results were 53.3% related to health care. There was no significant difference ($P = .5185$) in search results between MSA and PSA accounts.
CONCLUSIONS: MS search terms were answered most commonly by personal online accounts, followed by patient advocacy groups and lastly by health care sources. A sources were the top sources only on Google and never the top 5 sources on Facebook. Individual health care providers were the top source on YouTube only. The requester account did not alter the search results significantly. Health care providers have an opportunity to provide MS online resources.
DISCLOSURES: *Finley Kocher, Julia Grandinetti, Luke Wisniewski: Nothing to disclose. Mary Rensel: Brain Fresh LLC (ownership interest).*
KEYWORDS: Comprehensive Care and MS, Internet Education in MS

IMAGING

(IMG01) Myelin Integrity as a Predictor of Backward vs Forward Walking Performance in Multiple Sclerosis

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BACKGROUND: Multiple sclerosis (MS) is marked by axonal demyelination that may lead to motor impairments and increased fall risk. Although forward walking (FW) is often used to assess fall risk in MS, backward walking (BW) offers greater sensitivity in distinguishing fallers from nonfallers due to its higher postural and cognitive demands. Despite evidence linking myelin damage to fall risk, the relationship between myelin content and BW performance remains underexplored. Identifying tract-specific associations to BW deficits is vital for understanding the neurological mechanisms driving mobility challenges in MS.
OBJECTIVES: To explore how myelin content in key motor tracts relates to BW performance in MS.
METHODS: This study enrolled 43 individuals with relapsing-remitting MS (ages 18-65; Patient-Determined Disease Steps [PDDS] score<6), excluding those with relapses within 3 months. Participants completed FW and BW assessments on a 25-foot walkway to measure gait velocities. Myelin water imaging data were acquired at 3T, and the outcome measurements included myelin water fraction (MWF) values from 4 critical neural regions: body of the corpus callosum (CCbody), superior cerebellar peduncles (SCP), inferior cerebellar peduncles (ICP), and corticospinal tracts (CST). A multivariate regression model analyzed these regional MWF values as predictors of BW and FW performance, with age and PDDS score as covariates.
RESULTS: In the SCP, there was a significant positive association between MWF and BW velocity ($\beta = 0.414$; $P = .026$), whereas MWF of other tracts, including the CCbody ($\beta = 0.220$; $P = .094$), CST ($\beta = -0.036$; $P = .821$), and ICP ($\beta = -0.218$; $P = .284$), were not significant. This model explained 55.3% of the variance in BW velocity. For FW velocity, MWF of the CCbody was a significant predictor ($\beta = 0.294$; $P = .030$), whereas MWF values of the SCP ($\beta = 0.232$; $P = .208$), CST ($\beta = -0.008$; $P = .960$), and ICP ($\beta = -0.102$;

P=.617) were not significant. This model explained 54.1% of the variance in FW velocity. In both models, greater disease severity (PDDS) was a significant covariate, consistently associated with slower walking performance (BW: β=−0.550; P<.001; FW: β=−0.563; P<.001).

CONCLUSIONS: These findings suggest that BW and FW rely on distinct neural networks, with the SCP predicting BW velocity and the CCbody predicting FW velocity. Identifying these neural correlates may guide targeted rehabilitation strategies to enhance mobility and fall risk prediction in MS. By identifying neural correlates of BW performance, this research aims to inform targeted rehabilitation strategies to improve mobility and fall risk prediction in MS.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Complementary/Alternative Therapies in MS, Rehabilitation, Imaging and MS

(IMG02) Diagnosing Pediatric Multiple Sclerosis From Visual Evoked Potentials With Artificial Intelligence

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BACKGROUND: The optic nerve is affected in most individuals with multiple sclerosis (MS), with up to a quarter of patients developing optic neuritis. Visual evoked potentials (VEPs) are commonly used to evaluate optic nerve pathology in individuals with MS. These pathological changes are reflected in alterations to the morphology of VEP peaks, with patterns such as the "w" wave attributed to MS. Clinically, standardized thresholds based on P100 latencies are used to identify anomalous VEPs. Machine learning (ML) models may enhance the accuracy of current VEP-based morphological assessments in diagnosing MS.

OBJECTIVES: To develop and evaluate ML models that can distinguish between pediatric patients with MS and noninflammatory controls using VEP scans.

METHODS: Consecutive children with MS (n = 116; female n = 83) followed at the pediatric neuroinflammatory clinic at The Hospital for Sick Children and children with no neuroinflammation (n = 23; female n = 12) received pattern-reversal VEP according to American Clinical Neurophysiology Society Guidelines on Evoked Potentials. P100 latencies were calculated per standard protocol from VEP scans. For the ML assessment, scans were split into training (75%) and testing (25%) data sets and the Synthetic Minority Oversampling Technique was applied to balance the class distribution. Waveforms were processed through a ResNet1D encoder to extract 32 features, which were then used for the binary classification. Four ML models were used: Gradient Boosting Classifier, Random Forest Classifier, K-Nearest Neighbors Classifier, and C-Support Vector Classifier. Receiver operating characteristic area under the curve (AUC) is used to evaluate the models' performance, with an unweighted average of class accuracies.

RESULTS: The study included 188 scans from patients with MS (average age, 15.3; SD, 2.5) and 28 scans from noninflammatory controls (average age, 13.7; SD, 3.8). Average P100 latency was 110.5 milliseconds (SD, 12.5) in patients with MS and 106.2 milliseconds (SD, 9.3) in healthy controls. Using clinical thresholds of delayed P100 latency of 115 milliseconds or greater in either eye or an intereye latency difference 10 milliseconds or greater as the cutoff for anomalous VEPs, we were able to accurately identify 73.5% of noninflammatory scans and 47.0% of MS scans. Of the 4 models, Gradient Boosting Classifier performed best, with an AUC of 0.62, achieving 42.9% accuracy for controls and 80.9% accuracy for MS. Other models showed varying AUC from 0.39 to 0.57. However, all models demonstrated limited performance in identifying healthy controls compared with patients with MS.

CONCLUSIONS: ML models predict MS in children with greater accuracy than traditional methods based on P100 latency and intereye differences. Future studies will incorporate multimodal data to improve the accuracy of these ML models in diagnosing MS in youth.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Imaging and MS, Machine Learning and MS

(IMG03) Linking Local Cortical Demyelination to Language Impairment in Early Multiple Sclerosis

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BACKGROUND: Due in part to variability in lesion location within the central nervous system, multiple sclerosis (MS) can produce a spectrum of symptoms affecting motor, sensory, visual, and cognitive function. Although motor and cognitive dysfunctions in people with MS (PwMS) have been extensively studied, language impairments have received comparatively less attention. These deficits are common in PwMS, with word-finding difficulty being the most frequent language complaint in early disease, yet the mechanism for this impairment is unclear. Cortical lesions are common and can be extensive in MS, and recent evidence suggests that cortical lesions may frequently be located in cortical regions implicated in language function.

OBJECTIVES: To identify whether cortical lesions in regions known to be important for language are associated with language deficits in early MS.

METHODS: Twenty-three PwMS within 1 year of diagnosis underwent 7T brain MRI and cognitive testing, including a validated task of lexical retrieval speed/word finding (antonyms: participants rapidly state the antonym for multiple stimulus words; scores adjusted for reading speed assessed with control task). All included participants reported English as their first language. Cortical lesions were identified manually on T1- and T2*-weighted images (0.5-mm^3 resolution). 7T T1-weighted images were segmented into cortical parcels (FreeSurfer) according to the Human Connectome Project brain atlas, and for each participant, cortical lesions were mapped to individual parcels. Group comparisons were used to identify associations between lesion presence and language impairment. Cortical parcels of interest were chosen based on previously described subnetworks of regions active during semantic, syntactical, and speech processing.

RESULTS: The analyzed cohort included 17 women and 6 men (mean time since diagnosis, 0.9 ± 0.4 years; mean age, 35 ± 9 years). Cortical lesions were identified in 19 people (83%), and 16 (70%) had cortical lesions in cortical regions implicated in language function. Presence of cortical lesions in language regions was associated with slower lexical retrieval speed/word finding (antonyms mean time, 22.0 ± 2.8 vs 31.4 ± 11.1 seconds; P=.046). Presence of cortical lesions in language regions was not associated with worse performance on other cognitive or language tasks, and neither total cortical lesion volume nor total white matter lesion volume were significantly associated with performance on any language task.

CONCLUSIONS: In early MS, cortical lesions in language regions may account, in part, for expressive language deficits (ie, word-finding difficulty).

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Cognitive Outcomes and MS, Imaging and MS

MULTIDISCIPLINARY CARE

(MDC01) Austin Regional Clinic Nurse Navigator Program: A Bridge to Optimal Care for Patients With Multiple Sclerosis

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BACKGROUND: Multiple sclerosis (MS) is a chronic and progressive disease that can lead to multiple neurological symptoms and disability. Because of the disease's complexity, patients with MS require coordinated care from multiple specialists. Austin Regional Clinic (ARC) is a multispecialty group with 35 locations across central Texas that serve more than 700,000 patients. The clinic's patient demographics make up approximately 28% of people living in the Austin metropolitan area (approximately 2.47 million people) and mirrors its diverse population. Since August 2023, a neuroimmunologist has cared for almost 200 people with multiple sclerosis (PwMS).

OBJECTIVES: This study examined the impact of physician and nurse navigator coordinated care on the health outcomes and quality of life of PwMS. The aim was to assess patient progress, care plan adherence, medication adherence, and overall satisfaction with proactive nurse check-ins not only for MS-related needs but also for broader health concerns. It was conducted in 2024 at ARC.

METHODS: As a part of ARC Population Health Program, the nurse navigator program connects patients with chronic conditions to specialized nursing professionals who provide personalized care coordination, education, and access to resources such as rehabilitation, mental health support, and financial assistance. Utilizing the same nurse navigation model that proved successful at ARC for other patients with chronic conditions, ARC Neurology and ARC Population Health collaborated to expand this approach for PwMS. In 2024, nurse navigators received specialized training on how to address and support the needs of PwMS.

RESULTS: Preliminary results suggest that the nurse navigator program can be effective in improving outcomes and serve as a bridge to optimal care for PwMS. For example, a person newly diagnosed with MS who had a positive tuberculosis test

(not previously treated) and polysubstance abuse reported adherence to prescribed medication, decreased substance dependence, and fewer avoidable hospitalizations. Another PwMS presented with uncontrolled hypertension, diabetes, and osteomyelitis. This led to a coordinated care approach, which included toe amputation prior to initiation of disease-modifying therapy, and included improved glucose control and better hypertension management.

CONCLUSIONS: The team-based care model connects PwMS with multiple resources and specialists, streamlining access to treatments and enhancing care coordination. Preliminary results shows that a nurse navigator program can improve patient adherence, reduce unnecessary emergency department visits and/or hospitalizations, and coordinate care next steps while enhancing patient care satisfaction. Based on these outcomes, ARC plans to expand the nurse navigation program to PwMS.

DISCLOSURES: *Diana Andino: Amgen, Genentech, Merck-EMD Serono, Multiple Sclerosis Association of America (consulting fee); DKBmed (speakers' bureau); TG Therapeutics (consulting fee, speakers' bureau).*

KEYWORDS: Comprehensive Care and MS, Nursing Management in MS

(MDC02) Identifying Opportunities to Support Nutrition in Routine Multiple Sclerosis (MS) Care: Perspectives From Health Care Professionals and People With MS Using a Design-Led Thinking Approach

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BACKGROUND: Nutrition plays an important role in the management of multiple sclerosis (MS) and its comorbidities. However, it is often overlooked in routine MS care, leading to a gap in comprehensive management of patient cases.

OBJECTIVES: To understand the perspectives of people with MS (PwMS) and health care professionals (HCPs) about supporting nutrition in routine MS care, and to cocreate solutions to provide more nutrition support.

METHODS: Over 3 months, two 2-hour workshops (n=14, PwMS; n=9, HCPs) and 10 semistructured interviews with HCPs were conducted online in Australia. A design-led thinking approach guided these, focusing on empathizing with the end user's needs, understanding experiences and challenges to define the problem, and encouraging ideation and brainstorming of solutions. Data collected included transcripts from the workshops and interviews and digital sticky notes from the workshops. The data were thematically mapped using an inductive, data-driven analysis.

RESULTS: Our study identified 4 main themes and 20 key considerations, reflecting participants' perspectives and corresponding design solutions. The first theme was *navigating health care barriers to integrating nutrition into MS care* and the support needed to address these barriers, including addressing educational gaps (misinformation, patient educational materials [PEMs], and HCPs' learning), overcoming health care system barriers (consultation time and dietetics services' costs and access), and bridging knowledge-evidence gaps (research on MS and diet and nutritional guidelines). The second theme emphasized the importance of *supporting shared and person-centered decision-making* by considering consumers' readiness and motivation to receive nutrition advice and respecting their choices and preferences by offering realistic options. The third theme encompasses ideas that *foster the accessibility and inclusivity of MS-specific resources* for both HCPs and PwMS, including resources such as an online website hosting downloadable PEMs and HCP learning materials that are credible and accessible. In addition, PEMs should be simple, with clear visual aids and inclusive to those with disabilities. The fourth theme underscores the importance of *continuing nutrition care with dietitians* to ensure that PwMS receive personalized advice while raising awareness about the role of dietitians among HCPs and addressing interdisciplinary knowledge gaps regarding dietitian referrals.

CONCLUSIONS: Our participatory approach to design thinking engaged stakeholders in creating human-centered, practical strategies and solutions for integrating nutrition care into routine MS care. Building on the opportunities identified, we successfully created educational resource prototypes that are ready for testing to support this integration.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Nutrition

(MDC03) Health Care Communication Perspective and Experiences of People With Multiple Sclerosis

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BACKGROUND: Multiple sclerosis (MS) is a chronic, progressive autoimmune disease that affects the central nervous system, leading to significant variability in symptoms and disease progression. Effective communication between health care providers and people with MS (PwMS) is essential to foster self-management, enhance patient-centered care, and improve health outcomes. However, communication challenges persist in health care delivery, particularly in addressing the complex needs of PwMS and ensuring culturally competent care.

OBJECTIVES: This study aimed to explore the perspectives and experiences of PwMS regarding in-person and electronic communication with health care providers and among health care systems. The goal was to identify strengths, gaps, and opportunities for improving communication practices to enhance patient satisfaction and outcomes.

METHODS: We conducted a national cross-sectional survey of 590 PwMS, focusing on their experiences with communication in MS care. The survey included open-ended questions and Likert-type items, and responses were analyzed using qualitative thematic analysis. Themes were developed iteratively through independent coding and team consensus. Demographic characteristics and additional details were reported to contextualize findings.

RESULTS: Three primary themes emerged from the analysis: (1) communication between patients and health care providers, (2) communication between health care providers and systems, and (3) cultural (in)competence of health care providers and staff. Although 62.9% of participants reported positive communication experiences, citing responsiveness, competence, and active listening, 37.1% described dissatisfaction due to inattentiveness, rushed interactions, and inadequate responses to patient concerns. Fragmented and uncoordinated communication across health care systems led to delays in care, increased patient stress, and a sense of administrative burden. Participants emphasized the need for integrated electronic health records (EHRs) and automated reminders to streamline care delivery. Although 71.7% of participants experienced culturally competent care, 28.3% encountered cultural incompetence. Issues such as racial, linguistic, sex, and weight biases were highlighted as significant barriers to effective communication and trust.

CONCLUSIONS: The findings underscore the importance of fostering empathetic, patient-centered communication, improving interprovider coordination, and addressing cultural competency gaps. Implementing technological solutions, such as EHR integration and telehealth platforms, alongside cultural competence training, can help mitigate these challenges. Addressing these areas will contribute to more equitable, effective, and satisfying care for PwMS.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Communication, Comprehensive Care and MS, Nursing Management in MS

METHODS OF CARE

(MOC01) Free Multiple Sclerosis Online Education for Social Workers and Other Professionals: A North Carolina Pilot Study

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BACKGROUND: Social workers are underrepresented in the multiple sclerosis (MS) arena. As opposed to social workers in large research centers/hospitals, they often learn about new topics online via free/low-cost education. Online webinars are efficient and cost-effective for delivering free continuing education units (CEUs) and information about emerging MS topics. An innovative case study is presented via a free online conference to increase knowledge about MS/resources (four 30-minute sessions/10-minute question-and-answer sessions).

OBJECTIVES: Increase knowledge about MS and available resources via an innovative free online webinar.

METHODS: The cross-sectional, correlational study included 20 participants who work in health care and non–health care settings. The Empowering Communities: Inaugural Multiple Sclerosis Conference in March 2024 was hosted by the University of North Carolina at Charlotte (UNCC) School of Social Work (SSW) and the National Multiple Sclerosis Society (NMSS) Greater Carolinas Chapter. The webinar included four 30-minute sessions, with 10 minutes for questions and answers. The sessions were (1) Multiple Sclerosis 101: What Patients and the Community Need to Know (keynote address by published author with a master's degree in social work who has MS), (2) MS Navigator Program (NMSS representative), (3) Social Work Roles in the MS Area of Specialization, (UNCC SSW faculty members), and (4) Medical Trauma and Chronic Illness (a licensed clinical social worker who is an expert in trauma). Participants

received 2.5 CEUs. The conference was advertised via listservs, emails, social media, and university publications.

RESULTS: Fifty percent of conference participants (n=20) completed the evaluation form. The diverse audience represented social workers/community practitioners, UNC system faculty/students, and NMSS members. Participants rated the 4 sessions using a 5-point Likert on 4 dimensions: content quality, presenter's knowledge/expertise, relevance to your interests, and overall presentation. The results of each session were overwhelmingly positive for all dimensions. All respondents (n=10) rated the session as *good*, *very good*, or *excellent* and would recommend the conference to others. Eighty percent (n=8) were *extremely satisfied* with the webinar. The quality of content and overall presentation of the keynote address were rated *excellent* by 6 people. Fifty percent (n=5) knew someone who has MS. Participants identified important takeaways such as "the lived experience with video was helpful" and "women/African Americans are particularly impacted." Some limitations were that only 20% of the target audience (n=100) was reached, and the short question-and-answer intervals provided limited opportunities for personal interaction.

CONCLUSIONS: Brief, online, free MS webinar interventions are easy to deliver, require limited delivery time for busy professionals, and increase geographic and economically accessible CEU training. Participants expanded their networks and increased their MS knowledge and available resources.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, MS and the Caregiver/Family, Psychological Issues and MS

(MOC02) Development of the Impact Clinic: A Wellness and Socialization Opportunity

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BACKGROUND: Research suggests that individuals with multiple sclerosis (MS) may experience decreased social support and limited socialization. Occupational therapists (OTs) are equipped to address social participation and use occupation-based interventions to promote quality of life. Subjectively, patients participating in OT report enjoying the personal contact therapy provides. Group-based interventions allow for improved discharge planning and care continuity without insurance limitations; however, many rehabilitation sites lack such programs. To address this gap, an OT supervisor and OT doctoral student created the Impact Clinic, a program designed to provide neurologic patients with socialization and therapeutic benefits in a group setting.

OBJECTIVES: Create a novel, sustainable, and recurrent wellness program offering occupation-based therapeutic benefits.

METHODS: Semistructured interviews with individuals with neurologic conditions (80% MS, 20% other) were used to assess social needs. Participants voluntarily engaged in a pilot 10-week, 90-minute weekly group session aimed at improving social participation and self-efficacy. Participants selected social participation goals at initiation of the pilot. After introductions, leaders facilitated relaxation techniques. Participants then engaged in structured activities, including crafts, a book club, and trivia. OTs used occupation-based strategies to facilitate participation such as targeted questions and contrived seating arrangements. To conclude, leaders educated participants on strategies to enhance visual, physical, and cognitive performance.

RESULTS: During the pilot phase, quantitative and qualitative data were collected using the PROMIS General Self-Efficacy Form and postsession satisfaction surveys. Two people with MS attended every session and completed pretests and post tests. Their baseline *t* scores indicated low self-efficacy. Postsession surveys highlighted enjoyment of selected activities and implementation of education provided.

CONCLUSIONS: Survey results revealed benefits for well-being and enhanced social participation. Engaging in a group program offers a supportive environment for social participation and leisure activity, which may promote health and quality of life for individuals with MS. OTs can address group therapeutic goals while cultivating meaningful relationships. By incorporating occupation-based strategies, OTs can empower individuals to participate in desired and meaningful activities.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Rehabilitation, Quality of Life

(MOC03) MRI Access Program 2.0: A Unique Research Database for Studying Outcomes in Underserved Multiple Sclerosis Populations

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BACKGROUND: The MRI Access Program, initiated by the Multiple Sclerosis Association of America, has provided essential diagnostic services to more than 10,000 individuals with multiple sclerosis (MS) based on diagnosis and financial need (300% of the federal poverty guideline) for more than 2 decades. Although the original program addressed significant gaps in MRI access, the next phase—MRI Access Program 2.0—aims to expand its impact by creating a comprehensive research database from this uniquely underserved population, which is rarely represented in clinical trials.

OBJECTIVES: Present the objectives and structure of MRI Access Program 2.0, which seeks to generate an unprecedented research database that offers insights into MS diagnosis, treatment, and disease progression among patients from underrepresented communities. This project will investigate these individuals' health outcomes and treatment patterns, offering critical data to support new research and improve MS care.

METHODS: MRI Access Program 2.0 will collect deidentified patient data from individuals who receive MRIs through the program. The icobrain artificial intelligence–powered quantitative MRI analysis will be used to generate objective information from the scans, including lesion load and brain volume changes. The patient-monitoring app icompanion will be used to gather patient-reported outcomes and information on treatment adherence. As such, a holistic overview of each patient will be presented to the participating health care practitioners, and the data will also be anonymized and shared with researchers.

RESULTS: This dataset will provide insights into the health outcomes and disease management of these particular people with MS, whose demographics and socioeconomic backgrounds often limit their participation in clinical trials. The scale of the program, serving nearly 1500 individuals annually, will enable meaningful statistical analyses that can inform future clinical and therapeutic strategies.

CONCLUSIONS: MRI Access Program 2.0 could have a profound impact on MS research by providing a unique dataset that has been difficult to gather through traditional clinical trials. This program not only continues to address health inequities in MS care but also offers a new resource for researchers aiming to improve MS diagnostics, treatment planning, and long-term outcomes.

DISCLOSURES: *Amanda Montague, Alexis Kline: Multiple Sclerosis Association of America (salary). Annemie Ribbens, Lars Costers, Rebecca Bartz: icometrix (salary).*

KEYWORDS: Economic Issues and MS, Equity of Care, Imaging and MS

(MOC04) Showcasing the Structure and Clinical Care Model of the Multiple Sclerosis Centers of Excellence

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BACKGROUND: The Multiple Sclerosis Centers of Excellence (MSCoE), established by the Veterans Health Administration (VHA), provide a multidisciplinary care model to improve outcomes for veterans diagnosed with multiple sclerosis (MS). Emphasizing evidence-based practice, veteran-centered care, and innovative research, MSCoE enhance access to high-quality, cost-effective care, education, informatics, and research opportunities across its regional centers.

OBJECTIVES: To present the organizational structure and clinical care model of the MSCoE, highlighting their role in delivering specialized care, fostering collaborations, and advancing MS research within the VHA.

METHODS: MSCoE are organized into 2 regional hubs, East and West, supporting care through a national network of affiliated MS Regional Specialty Programs (MS-RSPs). A national leadership team, including administrators, physicians, nurse coordinators, informatics specialists, researchers, and educators, oversees operations. The MS-RSPs utilize both virtual and in-person care to enhance accessibility for veterans, particularly those in remote areas. MSCoE employs a multidisciplinary approach to MS management, featuring comprehensive care teams (collaboration among neurologists, physiatrists, therapists, mental health professionals, social workers, and pharmacists to create individualized care plans); advanced diagnostics and treatment (access to state-of-the-art imaging, laboratory services, and disease-modifying therapies); education and support (programs for veterans and caregivers, mental health resources, and navigation assistance for MS-related challenges); telehealth integration (telecon-

sultation and remote monitoring to maintain continuity of care for veterans unable to attend in person); and informatics support (standardized documentation and quality improvement initiatives facilitated by informatics systems). MSCoE conducts pioneering research to enhance understanding and treatment of veterans with MS, collaborating with academic institutions, advocacy organizations, and industry to drive innovation in biomarkers, imaging techniques, and therapeutic interventions.

RESULTS: The integrated care delivery model of MSCoE highlights the VHA's commitment to improving the quality of life for veterans with MS. By combining clinical excellence, innovative research, informatics, and educational initiatives, MSCoE establishes a benchmark for MS care.

CONCLUSIONS: The VHA MS care model showcased by MSCoE provides insights into replicable strategies for enhancing care delivery and outcomes for individuals with chronic neurological conditions.

DISCLOSURES: *Anza B. Memon: Inlightened, Connected Research (consulting fee). Jodie K. Haselkorn, Rebecca Spain, Aaron P. Turner, Lindsey Wooliscroft, Suma Shah, Carolyn Bevan, Francesca R. Bagnato, Mitchell Wallin: Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, MS Care Model

(MOC05) Understanding the Learning Needs of People With Multiple Sclerosis

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BACKGROUND: The foundational pillars of the BARLO MS Center are research, excellence in clinical care, and excellence in education. Building excellence in education requires an understanding of the learning needs of people with multiple sclerosis (MS) and those who support them.

OBJECTIVES: To ensure the BARLO patient education program meets the learning needs of people with MS we sought to obtain robust input from the target audience and understand how learning needs differ between the newly diagnosed and those who attend the general population educational webinars.

METHODS: In October 2023, the BARLO MS Center launched a learning program for people with MS. The programs alternate monthly between sessions designed for those newly diagnosed with MS and general MS webinars covering various topics for all people with MS. All participants were asked to complete an evaluation that included an open-ended question asking for suggested topics for future educational sessions. Responses were analyzed to identify emerging themes related to suggestions for future topics.

RESULTS: From October 2023 to December 2024, 15 patient programs were conducted. Sessions for patients newly diagnosed with MS accounted for 8 of the events, and 7 were MS-related educational webinars. After the newly diagnosed education sessions, 48 of 69 attendees completed evaluations, a 70% response rate. Among completed evaluations, 23 of 48 respondents offered suggestions for future topics. On the other hand, 46 of 105 webinar attendees completed evaluations, representing a 36% response rate. Among completed evaluations, 24 of 46 respondents gave suggestions for future topics. Five themes for future topics emerged: symptoms, disease course and treatment, lifestyle and life issues, communication and access, and research and future directions. Results were similar across both groups.

CONCLUSIONS: Patient- and family-directed education programming is a critical factor in meeting the education needs of people with MS. Evaluation response rates align with what is reported in the literature, including a lower response rate for online sessions compared with what was observed with in-person sessions. Requests for information on symptoms and management are the most frequent request for all attendees. These findings will guide future educational program development at our center.

DISCLOSURES: *Aprile Royal, Nasser AlOhaly, Suzanne Ezekiel: Nothing to disclose. Jiwon Oh: Biogen Idec, F. Hoffmann-La Roche (consulting fee, contracted research); Bristol Myers Squibb, Eli Lilly, EMD Serono, Novartis, Sanofi Genzyme (consulting fee).*

KEYWORDS: MS Education

(MOC06) The Perspective of People With Multiple Sclerosis on Telemedicine

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BACKGROUND: During the COVID-19 pandemic, reimbursable telemedicine services expanded rapidly, including an increase in telemedicine utilization by people with MS (PwMS). Studies have explored the feasibility and utility of managing MS through telehealth visits, often from a health care system or provider perspective.

OBJECTIVES: In this study, we explored PwMS's current experience with telemedicine.

METHODS: PwMS who receive care at the University of Washington Multiple Sclerosis Center received a survey distributed both online with REDcap and on paper in person. We asked for demographic and disease-specific information as well as their opinions on the advantages and limitations of telemedicine. Descriptive statistics and correlations between demographic factors and preferences regarding telemedicine have been obtained.

RESULTS: Initial results showed 143 complete responses to the REDcap online survey. Of the participants, 85% have a diagnosis of MS. They were mainly aged 36 to 45 years (26%) and 56 to 65 years (22.4%); 73% identified as female; and 85.2% reported their race as White. English was the primary language of 64.2% of participants and 87.2% were residents of state of Washington. Private insurance coverage was reported by 69.2%. The majority had between 16 and 18 years of education. Full-time work was reported by 37.8%, and part-time work was reported by 8.3%. Of those employed, 41.4% work in-person, 21.4% work remotely, and 37.1% work a mix of in-person and remote. Appointments required 58.6% of participants to take leave from work, with 36% having to travel more than 50 miles for their appointments. A stable internet connection at home and the ability to independently navigate Zoom were reported by 95%. Difficulty with independently navigating MyChart and Zoom was reported by 5%. Of 143 participants, 113 had used telemedicine for an appointment, and their satisfaction level on a scale of 1 to 10 with 10 being *extremely satisfied* was a median of 9 (SD,1.59). Most participants (85%) listed *saves time* as an advantage of telemedicine, and 96% reported the biggest disadvantage was *provider not able to perform exam*. For *routine follow-ups* and *consultations regarding medicines*, 75% of participants thought that telemedicine could replace in-person appointments.

CONCLUSIONS: This is an ongoing study, and additional data (especially from the in-person survey) are pending. The results of this real-world experience of telemedicine in PwMS after the COVID-19 pandemic can help inform future decisions about suitability and availability of ongoing telemedicine services for people facing challenges with having chronic disease.

DISCLOSURES: *Atika Paracha: Nothing to disclose. Annette Wundes: Benaroya Research Institute (contracted research). Gloria von Geldern: Contineum Therapeutics, Novartis, Sanofi. (contracted research).*

KEYWORDS: Economic Issues and MS, Telemedicine

(MOC07) The Relationship Between the Timed 25-Foot Walk, the Timed Up and Go, the Patient-Determined Disease Steps, and the Multiple Sclerosis Walking Scale

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BACKGROUND: Multiple Sclerosis (MS) is a relapsing progressive disorder that leads to a broad spectrum of disabilities characterized by subtle changes which may not be clinically visible. Traditional outcome measures like the Expanded Disability Status Scale often fail to capture these subtle changes in ambulation. Discrepancies can arise between examiner interpretation and patient-reported perceptions. Quantitative multidimensional measures that combine patient perception and performance are needed to better define disease progression and disability milestones. Patient-reported outcome (PRO) assessments, such as the Patient-Determined Disease Steps (PDDS), the Multiple Sclerosis Walking Scale (MSWS-12), the Activities-Specific Balance Confidence (ABC) assessment, the Modified Falls Efficacy Scale (MFES), and the Lower Extremity Functional Scale (LEFS), can provide insight into patient experiences and disability variations.

OBJECTIVES: To explore the relationship between Timed 25-Foot Walk (T25-FW) results and Timed Up and Go (TUG) scores and the PRO PDDS, MSWS-12, ABC, MFES, and LEFS.

METHODS: A cross-sectional retrospective analysis was conducted of both PRO and performance measurements gathered as part of routine MS care. Statistical analysis was performed using *t* tests and Pearson correlations.

RESULTS: The study included 241 people with MS aged 26 to 80 years (mean, 55.5); 71% of the participants were women. Significant differences were found between those younger and older than 55 years for T25-FW (P=.005), TUG (P=.03), and LEFS (P=.05). No significant differences were found in PDDS (P=.15), MSWS-12 (P=.12), ABC (P=.09), or MFES (P=.58) scores. The T25-FW strongly positively correlated with PDDS (r= 0.66l N=1169) and MSWS-12 (r=0.47; N=190) as well as negatively corelated with ABC (r= −0.52; N=195), LEFS (r= −0.61; N=177), and MFES (r=−048; N=195). TUG outcome scores positively correlated to both PDDS (r=0.61; N=1.69) and MSWS-12 (r=0.41; N=190). TUG outcome scores were negatively corelated with ABC (r=−0.54; N=195)

and LEFS (r=−0.56; N=177). TUG scores were insignificantly correlated with MFES scores (r=−0.14; N=195).

CONCLUSIONS: Timed performance measures such as the T25-FW and TUG accurately reflect patient perspective of disease impact as indicated by scores on the PDDS, ABC, MFES, MSWS-12, and LEFS. In PwMS, greater confidence in the ability to perform tasks and less severe perceptions of MS symptoms are correlated with greater efficiency at performing timed walking tests. Combining PROs and timed performance measures provides greater insight into disease impact and progression that traditional examination techniques may miss. Integrating these measures into routine practice can enhance the tracking of granular changes in disease and inform treatment decisions as the disease evolves.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Management of Activities of Daily Living in MS, Patient-Reported Outcomes

(MOC08) There Is Nothing New Except What Has Been Forgotten

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BACKGROUND: Syphilis, the "great mimicker," is caused by the spirochete bacterium *Treponema pallidum*; it can manifest in any organ with frequent multiorgan involvement. A steady increase in disease incidence has been documented in the United States since 2019, with rates of infection per 100,000 people increasing from 43.7 in 2019 to 88.8 in 2023 in Texas alone. Ocular syphilis, a rare manifestation of the disease, may occur at any stage of the disease, leading to delayed diagnosis and treatment with the potential for poor outcomes that are fully preventable. Ocular syphilis can have variable clinical presentations, including pan uveitis, anterior and posterior uveitis, and refractory chronic retinal disease. Optic nerve involvement includes perineuritis, anterior or retrobulbar optic neuritis, and papilledema.

OBJECTIVES: This abstract describes 3 cases of optic neuropathy secondary to syphilis with the aim of increasing awareness of ocular manifestations of the disease and emphasizing the need for a high level of clinical suspicion.

METHODS: Case series of 3 patients admitted to inpatient neurology service for the work-up and management of suspected optic neuritis in September 2024 and eventually determined to have ocular syphilis.

RESULTS: Mean age of patients was 31.3 years; 2 were women; 2 were heterosexual. At presentation, 2 had bilateral symptoms of variable duration. All had optic nerve head edema on ophthalmological exam, 2 of them bilaterally. None reported other manifestations of the disease or had coinfection with HIV. All of them received treatment with intravenous penicillin via a neurosyphilis regimen with complete resolution of subjective symptoms as well as objective findings on subsequent ophthalmological examination.

CONCLUSIONS: Given the rising rates of syphilis in the US, independent of age and racial/ethnic groups as well as various clinical manifestations, it should always be part of the differential diagnosis when patients present with ocular symptoms concerning optic neuritis and optic neuropathy. Timely recognition, diagnosis, and treatment of ocular syphilis is imperative to prevent long-term ocular and systemic complications.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Clinical Manifestations; Ocular Syphilis

(MOC09) Developing Multiple Sclerosis (MS) Nurse Onboarding and Training Materials With the MS Nurse Education and Roundtable Discussions Program

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BACKGROUND: The multiple sclerosis (MS) Nurse Education and Roundtable DiscussionS (NERDS) program was initiated during the COVID-19 pandemic to help Canadian MS nurses stay updated on evolving MS data. This educational and discussion-based forum evolved into quarterly virtual meetings that expanded nationally. In 2023, at the annual meeting of the Consortium of Multiple Sclerosis Centers, the first in-person event was held. Entitled "Striving for GOLD in Canadian MS Nursing Management," nurses discussed common challenges and best practices in patient management and developed a checklist for nurses to audit their practices. The 2024 in-person meeting was called "Addressing the Gaps in MS Nurse Onboarding and Training."

OBJECTIVES: Assess the effectiveness of the 2024 NERDS program for developing MS nurse onboarding and training materials.

METHODS: A presurvey was distributed to gather participants' thoughts on discussion topics. Data collected from the survey was analyzed to tailor meeting content to nurses' needs. The in-person program combined didactic sessions and interactive discussions. These included polling questions and open conversations to engage participants and facilitate knowledge exchange. Based on the discussions, a tool or reference material was developed to support their clinical practice. Participants completed a postmeeting evaluation survey.

RESULTS: Overall, 15 nurses attended the 2024 session and completed the premeeting survey, compared to 7 nurses in 2023. In the premeeting surveys, nurses identified current onboarding practices and unmet needs among MS nurses and discussed best practices for improvement. The chairs developed a proposed outline for MS nurse onboarding, followed by polling and roundtable discussion on additions and changes. At the end of the session, a customizable onboarding template, along with a list of best practices and resources for MS nurses, was distributed. Of the 10 nurses who completed the postprogram evaluation survey, 7 strongly agreed and 3 agreed that the discussions were valuable and relevant to their clinical practice. Based on the event, 9 of 10 were likely or extremely likely to propose changes to their institutions' onboarding and training.

CONCLUSIONS: The NERDS program is a unique, interactive, nurse-led program that provides MS nurses with up-to-date information on relevant topics, promotes team building, facilitates sharing of best practices across Canadian MS clinics, and develops valuable tools for daily practice.

SUPPORT: *This program was supported by Biogen.*

DISCLOSURES: *Donna Kuipers: Apotex, Biogen, EMD Serono, Novartis, Roche, Sentrex (consulting fee). Quyen James: Biogen (ownership interest, salary). Bonnie Blain: Biogen, EMD Serono, NKS Health, Novartis, Roche (consulting fee).*

KEYWORDS: Nursing Management in MS

(MOC10) Geographic Disparities in Spatial Access to Outpatient Infusion Centers Among People With Multiple Sclerosis in the United States

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BACKGROUND: Access to intravenous (IV) high-efficacy disease-modifying therapies among people with multiple sclerosis (PwMS) can be limited by distance to infusion providers, leading to disparities in care and outcomes. Ocrelizumab is an anti-CD20 therapy approved for relapsing or primary progressive multiple sclerosis (MS) that is now available in IV or subcutaneous formulations. Data on disparities in spatial access to infusion providers are needed to inform policy decisions on access to effective therapies with flexible delivery options. Such policies would prioritize tailored therapy for individual PwMS while improving practice efficiency.

OBJECTIVES: To identify disparities in spatial access to outpatient infusion providers relative to MS prevalence in the US and to understand differences in county-level demographics and social determinants of health (SDOH) in areas with varying access.

METHODS: This cross-sectional study used 2022 US county-level, age-adjusted MS prevalence estimates (Institute for Health Metrics and Evaluation) and infusion provider zip codes to calculate ratios of infusion providers within reasonable access per 1000 PwMS. Reasonable access was based on county classifications and corresponding maximum drive times and distance standards for outpatient infusion facilities (Centers for Medicare and Medicaid Services) from each census tract centroid using HERE Isoline Routing API v8. Access ratios were spatially mapped. County-level SDOH characteristics (American Community Survey) were compared across access ratio quartiles.

RESULTS: Of 3105 counties, 2000 had infusion access ratios below the national average. Of 775 counties in the bottom twenty-fifth percentile, 57% were classified as rural or counties with extreme access considerations. Median differences in SDOH were compared vs remaining counties. In the bottom twenty-fifth percentile, more PwMS self-identified as Hispanic or Latino (+23%; P<.001) and had household incomes of less than $10,000 (+4%; P<.001) and access to 1 vehicle (+4%; P<.001). Notable disparities were found among metro bottom quartile counties; more PwMS reported ambulatory difficulty (+12%; P<.001), household incomes of less than $35,000 (+11%; P<.001), and access to no or 1 vehicle (+18% or+7%; P<.001 for both).

CONCLUSIONS: Access to therapies with established efficacy and long-term safety profiles that provide flexibility in the site of care, route, and time of administration, combined with SDOH assessments, may help facilitate more equitable care

and outcomes.

DISCLOSURES: *Elmor D. Pineda, Thomas Majda, Zhiyu Xia, Rongrong Wang: F. Hoffmann-La Roche (royalty); Genentech (salary).*

KEYWORDS: Disease-Modifying Treatments in MS

(MOC11) MRI Findings Suspicious for Progressive Multifocal Leukoencephalopathy Post Radiofrequency Rhizotomy

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BACKGROUND: Trigeminal neuralgia is commonly experienced in patients with multiple sclerosis (MS). Patients who do not have success with pharmacological treatment may undergo a surgical procedure. Natalizumab is a high-efficacy disease-modifying therapy (DMT) used to treat multiple sclerosis (MS). Patients treating their MS with natalizumab are at increased risk for progressive multifocal leukoencephalopathy (PML).

OBJECTIVES: To describe the abnormal brain MRI findings that are suspicious for PML in a patient treated with natalizumab post radiofrequency rhizotomy.

METHODS: Encephalomalacia of the temporal lobe has been reported in patients post radiofrequency rhizotomy. PML is a rare and often fatal disease characterized by progressive inflammation or damage of the white matter of the brain. Patients on immunomodulatory therapy, such as natalizumab, are at risk for PML. Patients who have a high-resolution MRI less than 1 month post rhizotomy may have abnormal findings on imaging suspicious for PML within the temporal white matter of the treated side.

RESULTS: A 64-year-old male with relapsing-remitting multiple sclerosis (RRMS) developed a new MRI lesion in the inferior right temporal subcortical white matter consistent with PML. This finding was reported shortly after the patient had a right-sided radiofrequency rhizotomy for ongoing trigeminal neuralgia. He had received 117 doses of natalizumab and tested serum John Cunningham virus (JCV) antibody-negative 2 months prior to the abnormal MRI. A prior MRI from January 2024 was stable. An MRI of the brain prior to his rhizotomy (June 2024) was also stable. As part of our required monitoring for patients exceeding 24 doses of natalizumab, he repeated his brain MRI in August 2024, which noted that the right temporal subcortical lesion was consistent with PML. He did not develop any new symptoms. He was evaluated in the emergency department. His lumbar puncture was negative for JCV polymerase chain reaction. His repeat serum JCV antibody was negative. A repeat brain MRI completed approximately 2 weeks later showed interval resolution of the lesion or edema in the right temporal subcortical white matter.

CONCLUSIONS: There is little clinical information regarding MRI findings following treatment of trigeminal neuralgia by radiofrequency rhizotomy. According to 1 study, encephalomalacia can occur in the temporal lobe adjacent to the trigeminal cave post radiofrequency rhizotomy. Trigeminal neuralgia is common in people with MS, and some patients require radiofrequency rhizotomy. A brain MRI of a patient on natalizumab post radiofrequency rhizotomy treatment contained findings concerning for PML. These findings resolved on follow-up MRI 2 weeks later. Accurate and prompt diagnosis of PML is imperative. However, clinicians should be aware of abnormal MRI findings that may occur in patients post gamma knife or radiofrequency rhizotomy treatment.

DISCLOSURES: *Meagan A. Adamson: Biogen, Bristol Myers Squibb (speakers' bureau); Genentech, Genzyme, TG Therapeutics (consulting fee). James Simsarian: Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Imaging and MS, Immunology and MS

(MOC12) Compelling Need for Health and Wellness Coaching in Multiple Sclerosis Care

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BACKGROUND: The impact of comorbidities related to unhealthy lifestyle behaviors is a growing concern in multiple sclerosis (MS) care. Numerous studies demonstrate causality between cardiometabolic comorbidities, chronic lung diseases, and psychiatric diseases with less optimal MS outcomes. When compared with individuals who do not have MS, there is an increased prevalence of earlier onset of comorbidity and earlier deaths for individuals with MS, which suggests that comorbidity management is a crucial component of MS care. Health and wellness coaching (HWC) addresses these challenges. HWC is a credentialed, rapidly growing, intervention that has proven effective. HWC models focus on advancing health, wellness, and behavior change by using motivational interviewing (MI) and other competencies to guide patients through self-directed, lasting changes aligned with their values, strengths, and beliefs in their capacity for change. Individuals are empowered to be experts in their own lives. The American Medical Association (AMA) approved 3 category III Current Procedural Terminology (CPT) codes for HWC and allows reimbursement of the services to be offered under physician supervision. MS centers choosing to combine education with HWC have the potential to significantly impact all aspects of MS care and to receive financial reimbursement, making this a cost-effective model.

OBJECTIVES: (1) To examine the potential impact of HWC on comorbidities and patient outcomes; and (2) to identify opportunities, benefits, and financial considerations of incorporating HWC into multidisciplinary patient care.

METHODS: Using the PubMed database, a search of peer-reviewed medical and integrative observational reviews published since 2010 was conducted. The focus was on systematic reviews regarding the impact of comorbidities on MS and other chronic illnesses and the role of HWC in these populations. To better understand the HWC model and gain competence in HWC, the author completed the Mayo Clinic wellness coach training program and achieved the status of national board-certified health and wellness coach (NBC-HWC).

RESULTS: The review of current literature supports HWC as an effective intervention leading to statistically significant improved outcomes in patients with chronic illnesses with and without comorbidities. Current studies are ongoing to evaluate long-term effectiveness and explore various models for implementing HWC.

CONCLUSIONS: The results support HWC as a rapidly growing and impactful intervention for all patients. There is a high probability of having significant positive outcomes in all aspects of MS care. This, combined with the AMA approval of 3 category III CPT codes for HWC, highlights the opportunity to offer cost-effective integration of HWC into multidisciplinary teams and improve patient outcomes.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Lifestyle Comorbidity, Nursing Management in MS

(MOC13) Creating a Multiple Sclerosis Multidisciplinary Rehabilitation Clinic to Improve Access to Specialized Therapy Services

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BACKGROUND: Evaluation by outpatient rehabilitation therapy services can play an important role for people with MS by optimizing function, symptom management, and safety. Access to rehabilitation specialists who are familiar with multiple sclerosis (MS) can be a challenge in rural and underserved areas. Our clinic is the only comprehensive MS center in Idaho and serves a wide geographic region, including eastern Washington and western Montana.

OBJECTIVES: We aimed to create a multidisciplinary rehabilitation clinic to allow patients from rural areas and patients with advanced disabilities to be evaluated by a neurologist, physical therapist (PT), occupational therapist (OT), and speech therapist (SLP) during a single visit. The goal was to provide initial evaluations for multiple therapy services and recommendations for continuing therapy, additional diagnostics, or home programs when appropriate.

METHODS: We created a planning committee with the goal of implementing a quarterly clinic. Our committee included 2 members of the International Organization of MS Nurses, an MS specialist and advanced practice provider, a PT, an OT, an SLP, and leadership. Five patients are selected per session. Previsit, there is a telephone evaluation focused on social history, home activities of daily living, and visual and hearing abilities. A mailed packet with Eating Assessment Tool-10 screening, Mayo-Portland Adaptability Inventory, the Modified Fatigue Impact Scale, and the 12-item MS Walking Scale are completed prior to the clinic visit. Patients are seen in the outpatient rehabilitation gym, with disciplines rotating through 45-minute blocks. The day concludes with a debrief to coordinate recommendations and referrals.

RESULTS: We have successfully completed 3 multidisciplinary sessions, serving 15 patients. Of these patients, 11 (73%) were referred for ongoing PT, with 2 specifically for vestibular rehabilitation; 9 (60%) were referred for ongoing OT; 12 (80%) were identified as having possible oropharyngeal dysphagia and sent for additional testing (9 with modified barium swallow and 5 with fiberoptic endoscopic evaluation).

CONCLUSIONS: Patients have expressed satisfaction with the overall experience of the multidisciplinary clinic. Many have found it beneficial to make a single trip for therapy evaluations. If distance is a concern, therapists can tailor home programs when appropriate. There are still ongoing access challenges when patients who would benefit from ongoing specialty rehabilitation therapy are unable to coordinate regular therapy visits. Telehealth services for these patients are being explored.

DISCLOSURES: *Kaelianne Newbold, Katherine Gwin, Abigail Schwarte, Emma Chafin,*

Kara Purcelley, Guadalupe Owen, Elissa Diaz, Vivien Spyra, Kimberlee Wassink, Sue Donaghue: Nothing to disclose. R. Chase Cullen: TG Therapeutics (consulting fee). Nina Bozinov: EMD Serono (consulting fee, speakers' bureau); Genentech (consulting fee).

KEYWORDS: Comprehensive Care and MS, Management of Activities of Daily Living in MS

(MOC14) Adherence to Dietary Guidelines in People With Multiple Sclerosis: Development of the Australian Dietary Guidelines Adherence Tool

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BACKGROUND: People diagnosed with multiple sclerosis (MS) often try to make lifestyle changes, including diet. Despite interest in specialized diets for MS, they are currently advised to follow national dietary guidelines. As research into the role of diet in MS continues, a tool to measure adherence to dietary guidelines in people with MS is needed.

OBJECTIVES: Develop a tool to measure adherence with the Australian Dietary Guidelines (ADG) in studies collecting dietary intake data using a food frequency questionnaire (FFQ).

METHODS: The Dietary Questionnaire for Epidemiological Studies version 2 (DQES) is a semiquantitative FFQ that has been used to capture dietary intake in a range of epidemiological studies in Australia, including in individuals with MS. The ADG database was previously developed to compare food consumption reported in the 2011-2013 Australian Health Survey with dietary guidelines. This study developed a ready reckoner by matching DQES food items with ADG food items by food descriptions. The matching process was systematic, whereby the final match resulted from a direct match to a single food; a direct match to a summary food, identified by a description containing *not further defined*; or an average of multiple matches in the ADG database. Excluded were items with all values equal to 0, items included in a *not further defined* summary item, mixed dish items, overgeneralized items, or inappropriately prepared items.

RESULTS: The ADG-AT provides a ready reckoner for the 101 food items reported by the DQES, providing the number of servings per 100 g of the following food groups: vegetables, fruits, grains, meats/alternatives, dairy/alternatives (to consume); and discretionary foods (to limit). The ADG-AT can be applied to dietary intake data to determine the total number of servings consumed by each participant per day for each food group. This can be compared with age- and/or sex-specific recommendations to determine adherence to dietary guidelines.

CONCLUSIONS: The ADG-AT was developed to analyze food group intake and determine ADG adherence in studies using the DQES to collect dietary intake data. The tool can be used to explore dietary associations with health outcomes, including in people with MS, and may be adapted in other studies using different data collection methods and/or food composition databases.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Complementary/Alternative Therapies in MS, Dietary Guidelines, Epidemiology of MS

(MOC15) Closing the Nursing Gap: Creating Multiple Sclerosis (MS) Nurse Navigators as Part of a Rural MS Comprehensive Care Center.

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BACKGROUND: Our clinic is the only comprehensive multiple sclerosis (MS) center in Idaho and provides care to patients from Idaho, western Montana, and eastern Washington. When we sought to create the first center, defining and creating the MS nurse navigator role was at the foundation of our process. Recruitment of specialized nurses can be challenging in rural areas. In underserved health regions that span large geographic areas, services close to home are critical, as traveling can be challenging for those with higher disability and/or lower socioeconomic status. Navigators can facilitate laboratory monitoring, diagnostic testing, and referrals closer to home.

OBJECTIVES: We sought to develop a nurse navigator role that would incorporate MS disease process education, disease-modifying therapy (DMT) education, symptom management, referral review and triage, safety monitoring, coordination of local services, and community education. Part of this process included the creation of a timeline for nursing education, as well as obtaining relevant certification.

METHODS: At the onset of clinic development, 2 nurses without prior MS experience joined the MS specialist. Registered nurse (RN) education was obtained through available videos, articles, direct observation, Consortium of MS Centers (CMSC) annual meeting attendance, and participation in the National MS Society ECHO program. Work-flow standardization was created and optimized for referral review, symptoms triaging, and coordination with pharmacy for DMT initiation and medication safety monitoring. Patient education handouts and community education events were created to provide additional evidence-based education to patients.

RESULTS: Specialty certification was obtained through the CMSC after 1 year and through the International Organization of MS Nurses after 2 years. Pathways were developed that standardized the patient's experience. Of the 674 patients seen at our clinic in 2024, 168 of these patients established care. In 2024, 117 patients and family members attended our quarterly in-person community education events.

CONCLUSIONS: Two RNs obtained specialized certification and became MS nurse navigators over the course of 2 years. They have been instrumental in providing specialty care to MS patients, navigating many unique resource challenges. Establishing pathways has created key touchpoints for patient education, such as new diagnosis education or DMT education, as well as standardizing symptom triage.

DISCLOSURES: *Katherine Gwin, Kaelianne Newbold: Nothing to disclose. R. Chase Cullen: TG Therapeutics (consulting fee). Nina Bozinov: EMD Serono (consulting fee, speakers' bureau); Genentech (consulting fee).*

KEYWORDS: Comprehensive Care and MS, Nursing Management in MS

(MOC16) Using Blood-Based Biomarkers to Monitor Discontinuation of Therapy in Individuals With Relapsing Multiple Sclerosis: A Case Series

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BACKGROUND: Discontinuation of disease-modifying therapies (DMTs) carries the risk of increased future disease activity, such as new or worsening symptoms and MRI changes. Currently, there are no established guidelines on DMT discontinuation in multiple sclerosis (MS), making decisions about treatment cessation highly individualized and dependent on factors such as disease history, current stability, and patient preference. Given the uncertainty surrounding the risks and benefits of discontinuing, ongoing monitoring strategies are necessary to promptly identify signs of increasing disease activity. Blood-based biomarkers have emerged as promising tools to customize treatment decisions in MS. The Octave Multiple Sclerosis Disease Activity (MSDA) test is a commercially available, analytically and clinically validated blood-based biomarker test that measures 18 proteins to determine 4 disease pathway scores and an overall disease activity score scaled from 1.0 to 10.0.

OBJECTIVES: The MSDA test was evaluated in routine clinical use in 6 patients before and after discontinuing treatment to understand its role in supporting discontinuation decisions and monitoring patients after discontinuation.

METHODS: Six patients with MS of various ages, disease durations, DMT use, and clinical/radiographic presentations were examined in this case series. Individuals were monitored between March 2022 and January 2024 with 2 or more MSDA time points. Clinical and radiographic data were collected from the patients' medical records.

RESULTS: After discontinuation, 5 patients remained stable with score changes of 1 point or less. One patient's score increased 3.5 points into the high category, prompting initiation of a new DMT, which brought the score down 4.5 points into the low category.

CONCLUSIONS: This study provides evidence that MSDA is a beneficial tool for clinicians in guiding treatment decisions for patients who discontinue DMTs. The MSDA test's ability to assess the likelihood of clinical and radiographic disease activity helps stratify patient risk and identify those who may benefit from timely reinitiation of therapy.

DISCLOSURES: *Jacqueline A. Nicholas: Nothing to disclose. Julie Burnham, Yassir Jassam: Octave Bioscience (consulting fee). Michael Sy: AstraZeneca, Octave Bioscience, Pliant Therapeutics, Roche (consulting fee); University of California Irvine (receipt of intellectual property rights/patent holder). Taylor Gonyou: EMD Serono, Genentech, Horizon Therapeutics, Sanofi (consulting fee). Yassir Jassam: Alexion-AstraZeneca, Amgen (speakers' bureau); Genentech, Novartis, Octave Bioscience, Sanofi (contracted research); TG Therapeutics (contracted research, speakers' bureau). Katherine Ruby, Patricia Izbicki, Sarah Eagleman, Ferhan Qureshi, Terrie Livingston: Octave Bioscience (salary).*

KEYWORDS: Biomarkers

(MOC17) Integration of Lifestyle Medicine in Multiple Sclerosis Care: Single-Center Experience and Outcomes

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BACKGROUND: Evidence suggests that factors such as regular physical activity, a nutrient-rich, anti-inflammatory diet, stress management, and adequate sleep can reduce fatigue, enhance mobility, and lower inflammation. Additionally, addressing modifiable risk factors and comorbidities may help slow the accumulation of disability and improve health outcomes in people with multiple sclerosis (MS).

OBJECTIVES: To develop and evaluate a novel program integrating lifestyle medicine into MS care to empower patients to actively participate in their health, fostering long-term well-being.

METHODS: The MS Lifestyle Medicine Program at The University of Texas Health Austin was established in January 2024. It is led by a physician who is board-certified in family medicine and lifestyle medicine and who has MS. As part of this program, patients are referred by MS clinicians for individual lifestyle consultations, which take place 1 day a week in the same space as neurology visits. During initial visits, a standardized lifestyle assessment is conducted using a validated tool. The physician and patient then work together to set SMART goals. Preventive care consultations are also provided as part of the visits. Follow-up visits take place via telehealth. In addition, starting in September 2024, all patients established at the Center are invited on a quarterly basis to participate in group-based, lifestyle educational sessions, following the PAVING the Path to Wellness curriculum.

RESULTS: The MS Lifestyle Medicine Program has served 69 patients and now has a 12-week wait time for new patients. Patients are most frequently referred for assistance in the management of comorbidities, fatigue, sleep difficulties, weight management, and/or sedentary lifestyle. Most patients have agreed to follow up with subsequent visits when indicated. No-show rates have remained below national averages for both primary care and neurology. Reimbursement has been strong, with no claim denials since the program's inception. Additional patient outcomes will be presented. In addition to individual visits, the program enrolled 14 participants in its initial cohort of the PAVING the Path to Wellness group sessions and has now enrolled its second cohort. Both cohorts enrolled within days of the program's announcement, and there is a wait list for the next cohort. Of 17 patients enrolled in the initial cohort, 14 completed the program. Based on survey results from the initial cohort (n = 11), all participants would recommend the program to others with MS, and most (n = 10/11) reported being more motivated to make healthy changes after participating in PAVING.

CONCLUSIONS: Integrating lifestyle medicine in MS care is feasible and helps address an unmet need for people with MS seeking to optimize their overall health, better manage symptoms, and improve their long-term outcomes. We demonstrate not only the feasibility but also the high demand for this kind of program.

DISCLOSURES: *Lisa Doggett: Sagility (senior medical director/hourly employee; note: Sagility does not provide services or products related to MS care). Alexandra Rossi: Can Do MS, Multiple Sclerosis Association of America (speakers' bureau); TG Therapeutics (consulting fee). Gabriella Cozzani: Nothing to disclose. Léorah Freeman: EMD Serono, Genentech, Hoffmann La Roche, Horizon Therapeutics, Sanofi, TG Therapeutics (advisory board participation, consulting fee). Genentech, Medscape, Merck, Multiple Sclerosis Association of America (honoraria for educational programs/speaking); EMD Serono, Genentech, National Institute of Neurological Diseases and Stroke, Patient-Centered Outcomes Research Institute, Sanofi (grant support).*

KEYWORDS: Comprehensive Care and MS, Lifestyle Medicine, Management of Activities of Daily Living in MS

(MOC18) Piloting a Comprehensive Neuroinflammatory Consultation Service: Identifying a Need

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BACKGROUND: Neuroinflammatory disorders (NID) encompass multiple sclerosis (MS) and other rare, chronic inflammatory degenerative conditions. Despite the significant advancement in diagnostics and therapies for people with NID, there is a significant impact on patients and health care systems, emphasizing the importance of expert diagnosis and effective management strategies to potentially reduce health care costs. Managing a busy schedule of clinic patients and coordinating their care while simultaneously attempting to consult on complex inpatient cases with devastating neurological consequences is not a sustainable model for safe and effective care.

OBJECTIVES: This preliminary study aimed to determine the needs of neuroinflammatory specialists when caring for hospitalized patients by implementing an e-consult service and a monthly urgent clinic staffed by fellows. The study characterized consultation frequency, patient demographics, diagnostic patterns, acuity level, and follow-up outcomes.

METHODS: This descriptive study identified details of neuroinflammatory specialists' inpatient consultations in an outpatient setting. Study data was collected and managed using REDCap electronic data capture tools hosted at Penn Medicine. A neuroinflammatory e-consult service leveraging Epic Chat and a monthly urgent fellows' clinic was created. We characterized the number of consults per month, patient demographics, acuity (intensive care unit [ICU] vs non-ICU), initial diagnosis vs diagnosis after consultation, and number of patients discharged without a typical inflammatory disorder (MS, neuromyelitis optica, myelin oligodendrocyte glycoprotein antibody-associated disease, sarcoidosis). Follow-up data included the rate of patients lost to follow-up, time to follow-up, and utilization of the urgent clinic.

RESULTS: Over 19 months, 60 consults were completed, with an average of 3.2 consults per month. Of these, 28% required ICU-level care; 45% of the diagnoses changed post consultation; 23% were lost to follow-up; and 10% utilized the urgent clinic. In addition, the average time to follow-up was 4 weeks.

CONCLUSIONS: The results underscore the need for neuroinflammatory specialist expertise in high-acuity settings. The implementation of specialized services, including e-consults and urgent clinic follow-ups, is an opportunity for timely and accurate diagnosis, reducing unnecessary testing, and expediting outpatient follow-up and treatment initiation. Improvements in patient conversion rates to the outpatient setting are necessary. Future studies should explore the opportunity cost and specialist time; the impact of a neuroinflammatory consult service on inpatient length of stay; readmission rates; and health care utilization to support NID specialist effort, staff support, or relative value unit generation for this needed service.

DISCLOSURES: *Maria C. Adair, Laura Naydovich, Noellie Rivera-Torres: Nothing to disclose. Rohini D. Samudralwar: Amgen, EMD Serono, Genentech, TG Therapeutics (advisory board).*

KEYWORDS: Comprehensive Care and MS, Economic Issues and MS, Quality of Care

(MOC19) Impact of Interprofessional Clinical Education for Patients With Multiple Sclerosis

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BACKGROUND: It is known that interdisciplinary patient care improves patient outcomes and patient experience. The traditional education system for medicine, nursing, pharmacy, and social work provides practicum experiences within each of those specialties, rather than having students work together to provide patient care. The University of Oklahoma (OU) Health and Science Center College of Medicine, Nursing, Pharmacy, and Social Work partnered with the OU Health outpatient neurology clinic to provide an interprofessional clinic for 6 adults who have multiple sclerosis (MS).

OBJECTIVES: To evaluate the impact on student education and patient care for those with MS in an interprofessional outpatient setting.

METHODS: Two separate cohorts of 3 previously diagnosed people with MS were selected and agreed to participate in their regularly scheduled follow-up outpatient appointment with an interdisciplinary team consisting of a medical student, a nursing student, a pharmacy student, and a social work student. A licensed preceptor worked alongside each student. The patient first saw the nursing student to gather vital signs and document current concerns. The social services student then spoke with the patient about social determinants of health and current needs. The medical and pharmacy students saw the patient together, and the medical student performed an assessment. Afterward, the students and preceptors met for a brief interprofessional discussion of the most important items to address and to develop the plan of care for the patient. All participants then met with the patient to discuss the options and gave any necessary education or resources.

RESULTS: At the end of the clinical experience, students and preceptors completed a 13-question assessment rated on a 1 to 7 Likert Scale (1, *needs improvement*, to 7, *exceptional*) and 5 open response questions. Patients completed a 5-question survey at the end of their appointment. All surveyed patients (100%) stated they would want to engage in an interdisciplinary clinic appointment in the future, and they believed having an interdisciplinary care team could significantly or moderately improve their health outcomes.

CONCLUSIONS: Patients, preceptors, and students saw the value and impact of interprofessional education and patient care as a way to collaborate, learn from other

disciplines, and improve patient outcomes.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Interprofessional Care, Psychological Issues and MS

(MOC20) Evaluating the Impact of Refill Channels on Medication Adherence in Patients With Multiple Sclerosis at a Specialty Pharmacy

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BACKGROUND: Medication adherence is crucial for effective management of multiple sclerosis (MS), as consistent use of disease-modifying therapies can reduce relapse rates and slow disease progression. Despite the availability of effective treatments, many people with MS experience suboptimal adherence, leading to poorer health outcomes. Specialty pharmacies play a vital role in supporting adherence by offering various refill methods, including telephonic communication, text messaging, and patient portals. Digital refill methods, such as text messaging and patient portals, provide automated and convenient ways for patients to manage their medication refills. Evaluating their effectiveness can guide strategies to enhance adherence and improve clinical outcomes for patients with MS.

OBJECTIVES: This study examines how refill channels impact medication adherence among patients receiving MS medications.

METHODS: This is a retrospective review of adherence using the proportion of days covered (PDC) across 3 refill channels for prescriptions filled between January 1, 2024, and December 31, 2024. Patients who received an MS medication from AcariaHealth during this period were included. Patients were categorized according to the refill method utilized for each refill (ie, phone, portal, or text). PDC rates for phone compared to portal and text were analyzed for significant differences ($P<.05$) using 2-sample *t* tests.

RESULTS: The analysis included 23,303 patients (mean age 51.78 ± 14.05; 75.62% women) with 19,161 phone refills, 532 portal refills, and 3,610 text refills. Mean PDC adherence rate comparisons between telephone and digital (ie, portal and text) refill channels were 92.93% phone, 94.36% portal ($P<.05$), and 94.32% text ($P<.05$).

CONCLUSIONS: Clinical evidence supports a PDC threshold of 80%. Our findings demonstrate high adherence rates in our MS patient population across all refill channels, with digital channels demonstrating a statistically significant increase compared to phone. These findings emphasize the importance of offering a range of accessible and convenient refill options to support consistent and on-time medication adherence, a critical factor in MS management. Future research should focus on strategies to increase patient enrollment in digital refill channels, enabling more robust comparisons across groups and further optimizing adherence strategies.

DISCLOSURES: *Rachel Wiechert, Allison Watson, Robert Allender, Parag Bhosale, Thomas Pouliot: AcariaHealth Specialty Pharmacy (salary).*

KEYWORDS: Comprehensive Care and MS, Medication Adherence, MS and the Caregiver/Family

(MOC21) Atypical Presentation of Human Herpes Virus 6 Infection in a Patient With Multiple Sclerosis

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[1]Wayne State University School of Medicine, Detroit, MI; [2]Michigan State University College of Human Medicine, Lansing, MI; [3]Michigan State University College of Osteopathic Medicine, Lansing, MI; [4]University of Michigan School of Medicine, Ann Arbor, MI; [5]University of Michigan, Ann Arbor, MI; [6]Michigan State University, Lansing, MI; [7]MI; [8]Department of Neurology, Wayne State University, Detroit Medical Center, Detroit, MI; [9]Department of Neurology, Wayne State University School of Medicine, Detroit, MI; [10]Creighton University Medical School, Omaha, NE

BACKGROUND: Multiple Sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system and a potential cause of severe disability in adults. Human herpes virus 6 (HHV6) is a member of the family *Herpesviridae* known to cause various illnesses in humans. A previous study reported that HHV6 might be present in a dormant phase.

OBJECTIVES: To underscore the significance of maintaining a heightened suspicion for infectious causes in patients exhibiting new or worsening neurological symptoms under immunosuppressant therapy. Additionally, we aim to emphasize the specific risks linked to HHV6 virus infection in people with multiple sclerosis (PwMS).

METHODS: A case report and literature review

RESULTS: A 26-year-old patient with MS and prior left optic neuritis taking ocrelizumab infusion therapy presented with progressive gait instability and right leg weakness over a few months. At presentation, a brain MRI showed large ring-enhancing lesions on the left side more than the right side, with marked vasogenic edema and mass effect, suggestive of active tumefactive demyelinating plaques. Cerebrospinal fluid studies showed 13 nucleated cells, while herpes simplex virus, John Cunningham virus, varicella zoster virus, HIV polymerase chain reaction, hepatitis panel, and syphilis tests were negative. The patient was treated with steroids, intravenous immunoglobulin, and plasmapheresis but had persistent encephalopathy and neurological decline, which led to the diagnosis of HHV6 encephalitis confirmed by brain biopsy. Despite treatment and extensive interventions, the patient remained encephalopathic with neurological decline without significant improvement.

CONCLUSIONS: Our study underscores the occurrence of HHV6 encephalitis in PwMS on ocrelizumab, which may result in significant disability. Clinicians should be aware of this rare complication.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, MS and HHV6

NEUROIMMUNOLOGY AND DISEASE MODELS

(NDM01) In Preclinical Models, Vidofludimus Calcium Exhibits Potential Neuroprotective Effects in Multiple Sclerosis By Modulating Nuclear Receptor-Related 1

Amelie Schreieck,[1] Evelyn Peelen,[1] Hongmin Wu,[2] Alexandra Herrmann,[1] Tanja Wulff,[1] Mehrnoosh Jafari,[1] Christian Gege,[3] Andreas Muehler,[3] Daniel Vitt,[3] Zuoming Sun,[2] Hella Kohlhof[3]
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BACKGROUND: Nuclear receptor-related 1 (Nurr1), a transcription factor, regulates genes that enhance neuronal survival and reduce neurotoxic mediators produced by microglia and astrocytes. Growing evidence supports its protective role in neurodegenerative diseases. In people with multiple sclerosis (PwMS), Nurr1 gene expression levels in blood were shown to be reduced. However, these levels revert to normal in pregnant PwMS, which coincides with a reduction in disease activity (Gilli F, Lindberg RL, Valentino P, et al. Learning from nature: pregnancy changes the expression of inflammation-related genes in patients with multiple sclerosis. *PLoS One*. 2010;5(1):e8962. doi:10.1371/journal.pone.0008962). Also, findings by Pansieri et al (Pansieri J, Pisa M, Yates RL, Esiri MM, DeLuca GC. A potential protective role of the nuclear receptor-related factor 1 [Nurr1] in multiple sclerosis motor cortex: a neuropathological study. *Brain Commun*. 2023;5[2]:fcad072. doi:10.1093/braincomms/fcad072) highlighted a potential protective role of Nurr1 in the postmortem motor cortex of people with progressive forms of MS. Vidofludimus calcium (VidoCa), currently in phase 2 and 3 clinical trials for progressive and relapsing MS, respectively, has been shown to be a potent Nurr1 activator.

OBJECTIVES: To demonstrate the potential neuroprotective effects of VidoCa through activating Nurr1.

METHODS: Neuronal survival by VidoCa was assessed in vitro by flow cytometry after apoptosis induction by either 6-hydroxydopamine in SH-SY5Y cells or tumor necrosis factor alpha with cycloheximide in neuro-2A cells. Mice immunized with MOG_{35-55} to induce experimental autoimmune encephalomyelitis (EAE) were treated with VidoCa. From these mice, T helper (Th) cells were examined by flow cytometry, gene expression was evaluated by RNA sequencing or quantitative reverse transcription polymerase chain reaction and peripheral brain derived neurotrophic factor (BDNF) and neurofilament light chain (NfL) levels were determined by enzyme-linked immunosorbent assay.

RESULTS: VidoCa enhanced neuronal survival under proapoptotic conditions. This effect was associated with a higher expression of Nurr1 target genes and reduced NfL levels in the supernatant of the cells. VidoCa effectively attenuated EAE disease severity and led to reduced Th cell infiltration, including decreased numbers of pathogenic Th cells producing IL-17A, granulocyte-macrophage colony-stimulating factor, and interferon-gamma in the central nervous system (CNS) as well as reduced frequencies of these cells in the spleen. In plasma, higher VidoCa levels correlated with reduced clinical symptoms and NfL levels and with increased levels of the peripheral Nurr1 activation biomarker brain-derived neurotrophic factor. In addition, enhanced expression of Nurr1 and its target genes superoxide dismutase 1, tyrosine hydroxylase, and cytochrome c oxidase subunit 5B have been observed in the CNS.

CONCLUSIONS: In conclusion, these data indicate that VidoCa activates Nurr1 both in vitro and in vivo, potentially enhancing neuroprotection.

DISCLOSURES: *Amelie Schreieck: Immunic AG (shares, stock options, salary). Evelyn Peelen: Immunic AG (shares, stock options, salary, receipt of intellectual prop-*

erty rights/patent holder). Hongmin Wu, Zuoming Sun: Immunic AG (work support). Alexandra Herrmann, Tanja Wulff, Mehrnoosh Jafari: Immunic AG (shares, stock options, salary). Christian Gege: Immunic AG (receipt of intellectual property rights/patent holder, shares, stock options, salary). Andreas Muehler, Hella Kohlhof: Immunic AG (shareholder, salary, receipt of intellectual property rights/patent holder, ownership interest). Daniel Vitt: Immunic AG (shareholder, salary, receipt of intellectual property rights/patent holder, ownership interest).

KEYWORDS: Disease-Modifying Treatments in MS, Neuroprotection

(NDM02)The Path to Diagnosis and Treatment Among Patients With Neuromyelitis Optica Spectrum Disorder: Health Disparities Among People From Marginalized Groups From Project ASPIRE

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BACKGROUND: People from marginalized groups often experience barriers to health care access, particularly in diagnosis and treatment of rare diseases. Project ASPIRE aims to eliminAte diSparities and Promote equIty in Rare diseasE.

OBJECTIVES: Identify barriers to timely diagnosis for patients with neuromyelitis optica spectrum disorder (NMOSD), assess whether disadvantaged groups are disproportionately affected, and propose solutions to mitigate barriers.

METHODS: ASPIRE recruited patients through advocacy groups and referrals. Some patients completed surveys only, including the Depression Anxiety Stress Scale-21, while some participated in surveys and interviews (n=42). Health care providers (HCPs; n=12) were interviewed.

RESULTS: Survey respondents were predominantly female (93%) with an overall median age of 46 years, and from diverse ethnic backgrounds (50% White, 38% Black, 10% Hispanic/Latinx, and 2% American Indian and Alaskan Native). Respondents experienced a mean (SD) journey time of 49.0 (92.8) months from symptom onset to NMOSD diagnosis; most delays occurred after seeking care. White respondents had shorter total journeys than people from other ethnic backgrounds (27.1 [55.4] vs 72.3 [118.2] months). Common (≥ 10% of respondents) reported reasons for delayed diagnosis were difficulty navigating insurance coverage (24%), impediments to accessing specialty care (12%), lack of provider knowledge (12%), race/ethnicity (12%), and lower income (10%). Mean (SD) number of HCPs seen for all respondents was 4.8 (5.1). People from marginalized groups and women reported that HCPs dismissed their symptoms as emotional problems, comorbidities, or drug-seeking behaviors. Most (74%) survey respondents reported their journey was *stressful* or *very stressful* (*very stressful*: people from marginalized groups, 57%; White, 43%). Patients and HCPs identified solutions to overcoming barriers that included increasing knowledge about NMOSD, accessing health care appointments, and accessible medical records for HCPs.

CONCLUSIONS: The diagnostic path for NMOSD can be long and arduous, with the average journey to diagnosis extending over 4 years. People from marginalized groups experienced 2.7 times longer mean total journey time compared with White respondents. Project ASPIRE identified barriers and solutions to promote health equity by bringing awareness to inequities faced by patients with NMOSD.

DISCLOSURES: *Benjamin J. Osborne: Alexion Pharmaceuticals, Biogen, Bristol Myers Squibb, Horizon Therapeutics (speakers' bureau); Peter Angelos Law Firm (expert witness); publication related to health care (royalty). Jacqueline Rosenthal: Alexion Pharmaceuticals (consulting fee, fees for non-CME/CE services); Amgen (advisory board, speakers' bureau); National Multiple Sclerosis Society Georgia Chapter (board member); TG Therapeutics (advisory board). Iosin James, Barbara Mungin: Alexion, AstraZeneca Rare Disease (employee, stock or stock options, salary). Kristi Mitchell, Sheila Fifer, Lee Ann Prebil: Atlas Clarity (employee, salary). Evanthia Bernitsas: Biogen, Janssen Pharmaceuticals (speaker's bureau); Roche/Genentech (research support to institution).*

KEYWORDS: Health Disparities, Diagnostic Journey

(NDM03) FKBP5 Inhibition Ameliorates Neuroinflammation by Modulating Microglial Activation in a Preclinical Model of Multiple Sclerosis

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BACKGROUND: FK506 binding protein 5 (FKBP5), a co-chaperone in the glucocorticoid receptor complex, modulates glucocorticoid signaling through a negative feedback mechanism that is critical for maintaining stress response homeostasis. Dysregulation of FKBP5 has been implicated in neuropsychiatric disorders, including major depressive disorder and posttraumatic stress disorder, conditions often associated with hypothalamic-pituitary-adrenal (HPA) axis disruptions. Notably, HPA axis imbalances have been reported in people with multiple sclerosis (PwMS), potentially contributing to dysregulated glucocorticoid signaling. The altered regulation of FKBP5 in MS may indicate a mechanistic link between stress pathway dysregulation via the HPA axis and MS disease progression.

OBJECTIVES: Determine the role of FKBP5 in the dysregulation of myeloid cells in MS pathogenesis via the experimental autoimmune encephalomyelitis (EAE) animal model and human specimens.

METHODS: We conducted single-cell ribonucleic acid (RNA) sequencing on cerebrospinal fluid (CSF) cells from PwMS and healthy controls (HCs), along with bulk RNA sequencing of central nervous system-derived myeloid cells from EAE mice. To investigate FKBP5's role in EAE, we administered SAFit2, a selective FKBP5 inhibitor. Additionally, we conducted RNA sequencing of FKBP5 (shFKBP5) knockdown BV2 microglia and SAFit2-treated bone marrow–derived macrophages (BMDM), along with in vitro phagocytosis assays.

RESULTS: We demonstrated that FKBP5 is significantly upregulated in CSF microglia-like and macrophage cells from PwMS vs HCs, and at the peak of disease in the myeloid cells infiltrating the central nervous system (CNS) in EAE mice. Preventive SAFit2 treatment after myelin oligodendrocyte glycoprotein (MOG_{35-55}) immunization significantly decreased the clinical course of EAE mice and lowered infiltrating cells in the CNS when compared with control mice. CNS microglia from SAFit2-treated mice showed lower levels of MHC-II and CD11c, which are important markers for microglia activation. Bulk RNA-seq of shFKBP5 BV2 microglia cells and SAFit-2-treated BMDMs revealed significant downregulation of pathways associated with interferon signaling, complement activation, and phagosome formation. In vitro functional assays further demonstrated a marked reduction in phagocytic activity and interferon-gamma response in shFKBP5 BV2 cells and SAFit-2 treated BMDMs vs HCs. Additionally, SAFit2-treated cells exhibited superior myelin phagocytic capacity but slightly decreased myelin degradation compared with control BMDMs.

CONCLUSIONS: These preliminary findings suggest that FKBP5 might play a role in microglia cell activation and phagocytosis during CNS inflammation in the EAE model.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Glial Biology, Immunology and MS

(NDM04) Socioeconomic and Racial Disparities in Myelin Oligodendrocyte Glycoprotein Spectrum Disorder: Leveraging Cosmos to Study This Rare Disease

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OBJECTIVES: This study examines the impact of socioeconomic and racial factors on the prevalence of myelin oligodendrocyte glycoprotein antibody disease (MOGAD), highlighting disparities related to social vulnerability.

METHODS: A retrospective study was done using the Epic Cosmos database, which contains over 280 million de-identified patient records. MOGAD patients seen between January 2020 and November 2024 were identified using *International Classification of Diseases*-10 code G37.81. Patients who had at least 2 encounters with abnormal MOG antibody lab test results were classified as confirmed cases. To refine the cohort, we included patients with optic neuritis (ON) or transverse myelitis (TM), along with those receiving intravenous immunoglobulin (IVIG) or rituximab. After excluding records with unspecified demographics, the final cohort consisted of 897 patients. Social Vulnerability Indices (SVI; Swaminathan SS, Medeiros FA. Socioeconomic disparities in glaucoma severity at initial diagnosis: a nationwide electronic health record cohort analysis. *Am J Ophthalmol.* 2024;263:50-60. doi:10.1016/j.ajo.2024.02.022) were used to stratify patients by overall vulnerability, socioeconomic status (SES), racial/ethnic minority status (REMS), household characteristics (HC), and rural-urban commuting area (RUCA) codes (United States Department of Agriculture. Rural-urban commuting area codes. Updated January 6, 2025. Accessed April 15, 2025. https://www.ers.usda gov/data-products/rural-urban-commuting-area-codes). Multivariate regression assessed the impact of demographic and socioeconomic factors on MOGAD prevalence. The risk factors studied were demographics, SVIs, and RUCA. Socioeconomic

disparities were also compared among the MOG patients with ON (Dos Passos GR, Oliveira LM, da Costa BK, et al. MOG-IgG-Associated optic neuritis, encephalitis, and myelitis: lessons learned from neuromyelitis optica spectrum disorder. *Front Neurol*. 2018;9:217. doi:10.3389/fneur.2018.00217) (Amatya et al, 2024) and TM.

RESULTS: Of 897 patients with MOGAD (mean age, 40; SD=18), 64% were women. Stratification by SVI quartiles showed 34% in the highest quartile, with 30% of Black or African-American patients concentrated in this group. MOGAD was more prevalent in urban areas. The age groups of 41 to 60 (odds ratio [OR]=0.99; *P*=.0002) and over 60 (OR=0.99; *P*<.0001) had slightly lower odds of MOGAD compared with the age group 18 to 40. Living in a rural area increased the odds of MOGAD (OR=1.01; *P*=.00019). Lower SES quartiles were associated with increased odds of MOGAD (*P*=.00077). Patients with TM had significantly lower SES (*P*=.018), poorer household conditions (*P*=.001), and higher overall social vulnerability (*P*<.001) compared with patients with ON. Among the 453 patients analyzed, 410 (90.5%) had ON, and (9.5%) had TM. The difference in proportions was statistically significant (x^2=297.33, *P*<.001), indicating a significantly higher prevalence of ON in this MOGAD cohort.

CONCLUSIONS: This study emphasizes the role of socioeconomic and racial factors in MOGAD prevalence. Identifying these associations may inform screening programs and improve early detection and care in neurology clinics.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Immunology and MS, Myelin Oligodendrocyte Glycoprotein Antibody Disease, MOGAD

(NDM05) Tracking Choroid Plexus Volume Changes in Experimental Autoimmune Encephalomyelitis: A Longitudinal Imaging Study of Neuroinflammation

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BACKGROUND: The involvement of immune cells residing in the central nervous system (CNS) in the pathogenesis of multiple sclerosis (MS) is well-established. Choroid plexus (ChP), vascularized epithelial tissues within the brain's ventricles, are thought to regulate the trafficking of immune cells into the CNS, serving as a critical entry point for circulating leukocytes. Recently, ChP enlargement has been observed across various subtypes of MS, correlating with disease severity. However, the pathophysiological relevance of these findings remains unclear, mostly due to the lack of longitudinal data.

OBJECTIVES: This study aims to longitudinally evaluate changes in ChP volume in the murine experimental autoimmune encephalomyelitis (EAE) model of MS; to identify individual ChP volume change trends; and to explore its association with disease onset, clinical scores, and underlying neuroinflammation. Whether alterations in ChP volume could serve as a predictive biomarker for disease diagnosis and clinical outcomes was assessed.

METHODS: Active EAE among C57BL/6 mice was evaluated via MRI at 4 different points: (1) baseline at 2 days prior to immunization, (2) preonset (PO) at 8 days post immunization (PI), (3) during the acute phase at 72 hours after clinical onset, and (4) during the chronic phase at 3 weeks post onset (or 40 days PI in those without clinical onset).

RESULTS: The mean ± SD baseline ChP volume in mice was 0.78 ± 0.13 and was not correlated to their weight (*P*=.80). All EAE mice exhibited ChP enlargement during the PO and acute phases of immunization when compared with baseline, independent of clinical disease. During the chronic phase, all mice with clinical symptoms exhibited a decrease in ChP volume compared with the acute phase, however volumes remained higher than baselines. The change in ChP volume (ΔV) between the PO and acute phase was significantly correlated with the time of clinical onset (*r*=−0.96; *P*=.002). Moreover, the time of clinical onset affects the ΔV between the acute phase and chronic phase (*r*=0.87; *P*=.02); ΔV between the acute and chronic phases was negatively correlated with the clinical score during the acute phase (*r*=−0.96; *P*=0.002).

CONCLUSIONS: ChP volume changes could predict disease onset and clinical severity. Associated inflammatory biomarkers, along with MRI, may improve the potential prognostic yield of this emerging concept.

DISCLOSURES: *Naghmeh Abbasi Kasbi, Janaka Wansapura, Rehana Z. Hussain, Sergiu Groppa, Gabriel Gonzalez-Escamilla: Nothing to disclose. Olaf Stuve: Current Treatment Options in Neurology (section editor); EMD Serono, National Multiple Sclerosis Society, US Department of Veterans Affairs Biomedical Laboratory Research and Development (grants); EMD Serono, Novartis, Octave Bioscience (advisor); Genentech-Roche, Novartis (data monitoring committees); Therapeutic Advances in Neurological Disorders, Expert Review of Clinical Immunology (editorial boards).*

KEYWORDS: Imaging and MS, Immunology and MS, MRI

(NDM06) Comparison of Clinical Features and Demographics Between Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease and Neuromyelitis Optica Spectrum Disorder

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BACKGROUND: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) and neuromyelitis optica spectrum disorder (NMOSD) are demyelinating disorders of the central nervous system with diverse demographics and clinical features. Their overlapping symptoms can complicate diagnosis, and the comparison of their features remains underexplored.

OBJECTIVES: To assess for clinically significant associations between MOGAD and NMOSD, to guide clinicians in the future.

METHODS: A retrospective analysis of adults with MOGAD (n=55) and NMOSD (n=49) was conducted using electronic health records. Clinical features, demographics, and imaging findings were compared, with a comparison of proportions to assess significant associations.

RESULTS: Regarding demographic features, people with NMOSD, when compared with people with MOGAD, had a lower proportion of diagnoses before 18 years old (n=2 vs n=10; 4.1% vs 18.2%, *P*=.025) and had a lower proportion of men (n=5 vs n=23; 10.2% vs 41.8%, *P*<.001). There were fewer White patients with NMOSD vs patients with MOGAD (n=9 vs n=25, 18.4% vs 45.5%; *P*=.003), but also a higher proportion of Black patients (n=22 vs n=10; 44.9% vs 18.2%; *P*=.003). Regarding clinical features, a lower proportion of patients with NMOSD vs patients with MOGAD had optic nerve lesions at diagnosis (n=13 vs n=33; 32.5% vs 61.1%; *P*=.006). Patients with NMOSD vs patients with MOGAD had greater proportions of neuropathic pain (n=36 vs n=25; 73.5% vs 45.5%; *P*=.004), weakness (n=28 vs n=19; 57.1% vs 34.6%; *P*=.021), and eye pain (n=11 vs n=19; 84.6% vs 34.6%; *P*=.001). There were no significant differences in the prevalence of psychiatric symptoms between the 2 groups (*P*=.425).

CONCLUSIONS: Demographic and clinical features differ significantly between patients with NMOSD and those with MOGAD: Patients with NMOSD exhibited a lower proportion of early diagnoses, were less likely to be male, and were more likely to be Black. Patients with MOGAD were more likely to be White. These findings are consistent with current literature, which suggests that NMOSD affects more women and individuals from diverse racial backgrounds, particularly Black individuals. Clinically, people with NMOSD are more likely to experience neuropathic pain, weakness, and eye pain, aligning with known presentations of the disease, while patients with MOGAD typically present with a higher frequency of optic nerve lesions. These findings are also in line with established clinical observations. These results emphasize the need to consider both demographics and clinical features in diagnosis and treatment.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Immunology and MS

(NDM07) Time to Vaccination After Rituximab Discontinuation in Patients With Anti–Aquaporin-4 Antibody-Positive Neuromyelitis Optica Spectrum Disorder: A Post Hoc Analysis of the CHAMPION-NMOSD Trial

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BACKGROUND: Rituximab is often prescribed off-label for patients with anti–aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4-Ab+NMOSD), and patients may transition to ravulizumab, an approved therapy. Vaccination against *Neisseria meningitidis* (*Nm*) is the primary risk-mitigating strategy for complement inhibitors. Although meningococcal vaccines trigger a T-cell response, prior anti–B-cell therapy may attenuate responses to clinically relevant vaccines. CHAMPION-NMOSD (NCT04201262)

is a global, open-label, phase 3 study evaluating ravulizumab in patients with AQP4-Ab+NMOSD, approximately one-third of whom had rituximab exposure.

OBJECTIVES: To characterize the time from the last rituximab dose to the first administered meningococcal vaccine in patients from the CHAMPION-NMOSD trial previously on rituximab.

METHODS: Descriptive post hoc analyses were performed in a subgroup of patients on ravulizumab who received meningococcal vaccinations (MenACWY or MenB) after their last rituximab dose (N=19). Clinical laboratory parameters, vaccine administration, and time to first meningococcal vaccination and ravulizumab dose after receiving rituximab are summarized.

RESULTS: Patients were primarily White (63.2%), from North America (68.4%), and female (94.7%). Lymphocytes were within normal limits in most patients (13/14, 92.3%); lymphocyte subsets were not collected in this study. All patients received 1 or more meningococcal vaccines 2 or more weeks prior to ravulizumab initiation. Most patients (68.4%) received their first meningococcal vaccinations either 0 to 3 months (15.8%) or 3 to 6 months (52.6%) after their last dose of rituximab prior to ravulizumab. Most patients (84.2%) received both MenACWY and MenB vaccinations at the same visit; 4 patients (21.0%) received multiple doses of either vaccine. There were no reports of meningococcal infection in patients whose initial *Nm* vaccination occurred after their last dose of rituximab.

CONCLUSIONS: Most patients received a meningococcal vaccination 6 or fewer months after their last dose of rituximab, with MenACWY and MenB vaccines at the same visit. Total lymphocyte counts were normal in most patients, with no reports of meningococcal infection or NMOSD attacks in patients who received their initial *Nm* vaccination after their last rituximab dose.

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KEYWORDS: Immunology and MS, Neuromyelitis Optica Spectrum Disorder

NONIMAGING BIOMARKERS

(NIB01) Comparison of Natalizumab, Ocrelizumab, and Diroximel Fumarate in Patients With Relapsing-Remitting Multiple Sclerosis to Characterize Proteomic, Radiomic, and Clinical Trajectories: Interim Study Results

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BACKGROUND: The Octave Precision Care Solution, developed to improve management of multiple sclerosis (MS), consists of (1) a blood-based multibiomarker MS disease activity test (MSDA), (2) enhanced MRI reporting, and (3) a clinical insights program providing support to patients through digital monitoring via apps, wearables, and nurse engagement.

OBJECTIVES: To report interim results of a study performed to characterize proteomic, radiomic, and clinical trajectories of people with relapsing-remitting MS (PwMS) who are stable on natalizumab (NTZ), ocrelizumab (OCR), or diroximel fumarate (DRF) using the Octave Precision Care Solution.

METHODS: This open-label, observational study aims to examine PwMS on 1 of 3 disease-modifying therapies (DMT) in a real-world setting across 3 MS centers in the United States. A total of 78 participants were included in this interim analysis. All participants had completed their 6-month visit, with all data collected by the cutoff date (October 14, 2024). Thirty participants were treated with OCR, 32 with NTZ, and 16 with DRF. To examine the longitudinal stability of MSDA scores across DMT subgroups, scores at baseline and 6 months were evaluated for equivalency using 2 one-sided *t* tests (TOST). Results from electronic patient-reported outcomes (ePROs) were analyzed to evaluate a feel-good effect (FGE) and a wearing-off effect (WOE) for NTZ and OCR. Quality of Life in Neurological Disorders (Neuro-QoL) survey scores for all PwMS on all 3 DMTs were also collected. Initial lesion volumetrics from MRI scans collected up to the month 6 visit were processed using the Cortechs.ai algorithm and were reviewed by a neuroradiologist. Notifiable events, including number of events per category (ie, suspected relapse, symptom change, missed DMT), number of events per site, and number of events per DMT were captured.

RESULTS: Mean MSDA scores at baseline and 6 months were determined to be equivalent (within 1.5 score units) for each of the DMT subgroups ($P<.002$ for each TOST). The odds of positive sentiment, indicating an FGE, were 4.58 times higher for NTZ than for OCR ($P<.0001$). Interim analysis results at 6 months for WOE and NeuroQoL ePROs were not significantly different across groups, but these outcomes may require additional follow-up to detect differences. Only 17 MRI studies across the 3 sites were eligible for the interim analysis, and a limited number of notifiable events (n=39) were recorded.

CONCLUSIONS: For all 3 DMT groups, there were no significant trends in MSDA score in the first 6 months of the study, indicating stable disease activity as measured by the MSDA. Patients treated with NTZ were 4.58 times more likely to report positive sentiments (FGE) than those treated with OCR. WOE ePRO and NeuroQoL score analyses were inconclusive. Limited interim analysis data were available for the MRI and notifiable events analysis. The final analysis for this study is expected by the end of 2025.

DISCLOSURES: *John Foley: Biogen, TG Therapeutics (consulting fee, contracted research, speakers' bureau); ImStem Biotechnology, Octave (contracted research); InterPRO Bioscience (founder). Gabriel Pardo: AbbVie, Adamas, Alkermes, Biogen Idec, EMD Serono, Novartis, Roche/Genentech, Sanofi-Genzyme, Teva (research support); Alexion, Biogen Idec, Celgene/Bristol Myers Squibb, EMD Serono, Horizon/Amgen, Novartis, Roche/Genentech, Sanofi-Genzyme, TG Therapeutics (speaker honoraria and/or consulting fees); Cadenza Bio, Progentec Diagnostics, (advisory board). Amparo Gutierrez: Biogen (contracted research). Jason P. Mendoza, James B. Lewin, Robin L. Avila: Biogen (salary). Elisa Sheng, David Brazel, Kelly Leyden, Franklin X. Faust, Sarah Eagleman, Ferhan Qureshi: Octave Bioscience (salary, employee).*

KEYWORDS: Disease-Modifying Treatments in MS, Imaging and Nonimaging Biomarkers

(NIB02) Design and Implementation of the Decentralized Immunological Substudy for the COVID-19 VaccinE Response in Multiple Sclerosis Project

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BACKGROUND: The survey-based study COVID-19 VaccinE Response in Multiple Sclerosis (COVER-MS) was launched with the iConquerMS people-powered research network in 2021 to help answer pressing questions about the effects of COVID-19 vaccines in people with MS (PwMS). To gain insights into the impact of factors such as vaccination timing and MS disease-modifying therapy (DMT) history on vaccine effectiveness, a substudy was launched in 2022 to collect longitudinal blood samples from vaccinated PwMS and measure spike and nucleocapsid antibodies and T-cell responses to the COVID-19 virus and vaccines.

OBJECTIVES: To design and implement a decentralized, repeatable process for collecting blood samples from PwMS across the United States for analysis at a central laboratory.

METHODS: The substudy was designed by a multistakeholder team and based on a decentralized clinical trial model to optimize inclusivity and convenience for participants. Participants were recruited from the COVER-MS study and consented online. Sample collection kits and tote bags were shipped to participants who then made appointments at their local Quest Diagnostics Patient Service Center (PSC). A Quest mobile phlebotomy provider collected samples from participants who could not travel

to a local PSC. Samples were shipped via FedEx to a Quest esoteric lab.

RESULTS: A total of 953 COVER-MS participants were contacted about the substudy, and 236 enrolled, representing 41 states and the District of Columbia. Of these, 228 had 1 blood sample collection, 206 had 2, and 189 had 3, resulting in 83% retention. Recollection was required for 36 samples due to problems such as underfilled or broken tubes or shipping delays. Participants could contact a Quest representative directly with questions or issues. They received gift cards for each collection and were notified of their individual antibody results via the COVER-MS study portal.

CONCLUSIONS: This substudy demonstrated the feasibility of collecting and shipping research blood samples from PwMS in a decentralized manner. Using a nationwide network of PSCs and a mobile phlebotomy service enabled the inclusion of PwMS for whom location, transportation challenges, or lack of mobility would prevent enrollment in a traditional clinic-based study. We recommend this model for future biomarker studies in which participant diversity, convenience of participation, and economical sample collection are desired.

DISCLOSURES: *Hollie Schmidt: EMD Serono, Novartis Pharmaceuticals, Quest Diagnostics, Sandoz (contracted research). Michael K. Racke, Julia Larsen: Quest Diagnostics (salary). Bruce Bebo, Phyllis Klein, Farren B.S. Briggs: Nothing to disclose. Stephanie Buxhoeveden: Genentech (consulting fee). Robert N. McBurney: Autoimmunity BioSolutions, EMD Serono (consulting fee).*

KEYWORDS: Decentralized Trials, Disease-Modifying Treatments in MS, Immunology and MS

(NIB03) Clinical Application of Serum Neurofilament Light Chain in Multiple Sclerosis Management

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BACKGROUND: Serum neurofilament light (sNfL) has recently become available in the clinical setting in Australia; however, there is still debate about its practical use for patients with multiple sclerosis (MS).

OBJECTIVES: This presentation is designed to discuss the potential of this important biomarker and empower the clinician by providing practical information about how it can be used to support clinical decision-making.

METHODS: One hundred individual patient results were collected, and trends based on type of treatment, time on treatment, and disease phenotype will be presented. Two case studies will also be discussed, exemplifying the use of sNfL in practice.

RESULTS: Results show the effects of treatment over time. The longer the patients were on therapy, the lower the sNfL level overall. There are also differences in response to medication and MS phenotype that will be displayed. The case studies discuss usefulness in treatment escalation and de-escalation and highlight the ethical considerations.

CONCLUSIONS: sNfL is a long-awaited biomarker that will contribute clinically useful information about prognosis and efficacy of therapeutic treatments in MS. There is now considerable evidence for this biomarker to be used along with MRI and clinical measures of disease progression as a decision-making tool for MS patient management. Regular monitoring in patients with MS can be attended to determine changes from baseline and predict subclinical disease activity. As clinical access to this testing became available to the general population in Australia in October 2024, it is important to discuss the strengths and limitations of sNfL and its growing role in clinical practice.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Etiology of MS, Serum Neurofilament Light Chain

(NIB04) Association of Serum Neurofilament Light Chain Deviation Levels to New Lesions on MRI in People With Multiple Sclerosis

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BACKGROUND: Serum neurofilament light chain (sNfL) is a promising biomarker for monitoring disease activity in people with multiple sclerosis. Prior studies have shown an association of higher sNfL levels with the occurrence of new lesions on MRI scans. Limited data are available on the association of changing sNfL levels over time with the likelihood of new MRI lesions.

OBJECTIVES: To characterize sNfL level deviation over time in the context of new lesions on MRI.

METHODS: Data were obtained from Vitamin D to Ameliorate Multiple Sclerosis (VIDAMS), a multisite, randomized controlled trial of high vs low vitamin D supplementation as an add-on to glatiramer acetate. sNfL was measured using a high throughput, scalable immunoassay at months 0 (baseline), 3, 6, 12, 18, and 24; MRI scans were obtained at months 0, 12, and 24. We used generalized estimating equations to characterize the relationship of within-person and between-person change in sNfL and the rate of new gadolinium-enhancing lesions and new/enlarged T2 lesions on MRI.

RESULTS: We included 153 participants in the study in which 782 sNfL levels were assessed for an average of 5.1 (SD: 1.3) assessments per person and 372 corresponding MRI scans with lesion data. A within-person doubling of the levels of sNfL deviation were associated with an increased rate of gadolinium-enhancing lesions (RR 3.88; 95% CI, 2.46-6.11; $P<.001$) and increased rate of new or enlarged T2 lesions (RR 2.62; 95% CI, 1.31-5.24; $P=.01$).

CONCLUSIONS: Higher within-person fluctuations in sNfL over time are associated with an increased likelihood of developing a new MRI lesion. These results will help to increase our knowledge of the potential clinical application of sNfL as a biomarker in MS.

DISCLOSURES: *Karla Gray-Roncal, Sandra D. Cassard: Nothing to disclose. Kathryn C. Fitzgerald: SetPoint Medical (consulting fee). Ellen M. Mowry: Biogen, Genzyme (research funding); Teva (medication for a clinical trial); UpToDate (royalty).*

KEYWORDS: Biomarkers of MS, Imaging and MS

(NIB05) Revolutionizing Gait Quality Monitoring in Multiple Sclerosis: An Instrumented Shoe Insole Solution

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BACKGROUND: Spatiotemporal gait metrics significantly differ between healthy people (HP) and people with multiple sclerosis (PwMS), especially as PwMS experience worsening disability. If such changes, which are often subtle before they become manifest, are captured at regular intervals, they can become powerful biomarkers to monitor disease progression and evaluate intervention efficacy. However, performing frequent and regular gait analyses is challenging to incorporate into the standard of care, as is incorporating gait metrics into new data-driven models of care.

OBJECTIVES: To demonstrate an instrumented insole framework (IF) that automatically identifies ambulatory activities, performs gait detection, and calculates spatiotemporal gait metrics to produce a gait quality composite index (CIn; 0-100) to monitor longitudinal and acute changes in gait.

METHODS: Twenty-seven HP and 45 PwMS were recruited, of which 26 PwMS and 6 HP followed a 6-month protocol. HP completed 6-minute treadmill walks while PwMS took 15-minute free-living walks; the remaining 21 HP and 19 PwMS performed laboratory tasks (6-m and 500-m walks, stair navigation). For all tasks, participants wore instrumented shoe insoles (pressure+inertial measurement units, 50 Hz; ReGo; Moticon) that streamed raw data to a smartphone application (Celestra Health Systems, Canada). Laboratory data were used to train an artificial neural network (ANN) to identify walking, standing, stair ascent/descent, and turning. Sixty-eight gait metrics were identified using logical algorithms and validated against a motion capture (MoCap) system (Vicon, United Kingdom). Through a series of feature selection processes (ie, reliability and significance testing, partial least squares regressions), 15 latent variables from the 500-m walks were used to train a support vector machine (SVM) to classify 10-second walking segments as HP or PwMS. The CIn is the z score of the projected location in the SVM.

RESULTS: The ANN had an activity recognition accuracy of 94.6%. Compared with MoCap, the average intraclass correlation (2,1; ICC) of the logical algorithms was 0.862, with a temporal and spatial bias of 0.01 seconds and 1.7%. The SVM had an accuracy of 89.9% and F1 score of 92.4%. The CIn had an ICC (3,1) of 0.869 over 6 months for HP. The CIn correlations to Expanded Disability Status Scale (EDSS) scores, 12-item Multiple Sclerosis Walking Scale, Symbol Digit Modalities Test, 9-Hole Peg Test, and Timed 25-Foot Walk were 0.822, 0.799, 0.654, 0.586, and 0.819, respectively, in the free-living PwMS. The CIn also captures significant degradations in gait quality in PwMS over 500 m (distance: $P=.040$; EDSS level: $P<.001$; interaction: $P=.869$).

CONCLUSIONS: The IF accurately identifies activities, produces valid gait metrics, generates CI scores comparable to the standard of care, and identifies significant fatigue-related changes to gait quality, making it a practical solution to longitudinally and unobtrusively monitor gait quality of PwMS in clinical and free-living conditions.

DISCLOSURES: *Matthew P. Mavor, Alexandre Mir-Orefice: Celestra Health Systems (ownership interest). Victor C.H. Chan: Nothing to disclose. Gauruv Bose: Celestra Health Systems (contracted research); EMD Serono, Novartis, Sanofi-Genzyme, Teva*

Pharmaceuticals (consulting fee). Heather J. Maclean: Celestra Health Systems (spouse cofounder/executive); EMD Serono, Novartis (consulting fee, speakers' bureau); Immunic Therapeutics, Janssen, Sanofi (contracted research); Roche (consulting fee, contracted research, speakers' bureau). Tanuja Chitnis: BrightFocus Foundation, Celestra Health Systems, EMD Serono, I-Mab Biopharma, Sanofi-Genzyme, Tiziana (contracted research); Bristol Myers Squibb, Genentech, Novartis AG, Octave Bioscience (consulting fee, contracted research); Cabaletta Bio, Cycle Pharmaceuticals, F. Hoffmann-La Roche, Janssen, Merck KGaA, MJH Life Sciences, Novartis Pharma K.K., Sanofi, Siemens, UCB (consulting fee); Intellisphere LLC, Prime Education, LLC (speakers' bureau). Mark S. Freedman: Abata Therapeutics, Amgen, AstraZeneca, Celltrion, Find Therapeutics, Sentrex (consulting fee, advisory board member); Moderna (member of data safety monitoring board); Autolus, Bayer Healthcare, Celestra Health Systems, NeuroGenesis, SetPoint Medical (advisory board member); EMD/EMD Serono/Merck Serono, Novartis (consulting fee, speakers' bureau, advisory board member); Hoffman La-Roche (consulting fee, speakers' bureau, member of data safety monitoring board, advisory board member); Sandoz, Teva Canada Innovation (consulting fee); Sanofi-Genzyme Canada (consulting fee, contracted research, advisory board member). Ryan B. Graham: Celestra Health Systems (ownership interest, company scientific advisory board).

KEYWORDS: Disease Monitoring in MS, Equipment in MS

(NIB06) Plasma Neurofilament Light Chain Level Is Associated With Cognition and Brain Volume in Patients With Early Relapsing Multiple Sclerosis

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BACKGROUND: Neurofilament light chain (NfL) is a cytoskeletal component of neurons and a marker of axonal damage and neuronal death.

OBJECTIVES: Assess relationships between plasma NfL level, cognition, and brain volume in the ENLIGHTEN trial of ozanimod.

METHODS: ENLIGHTEN (NCT04140305) is an ongoing, open-label, single-arm study assessing the effects of ozanimod 0.92 mg for 3 years on cognitive processing speed in patients with early multiple sclerosis (MS). Cognitive assessments—the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test Second Edition (CVLT-II), and the Brief Visuospatial Memory Test–Revised (BVMT-R)—and MRI are performed yearly. Impaired cognitive performance was defined as less than 1.5 SD below healthy normative values. Baseline and 1-year whole-brain volume (WBV), cortical grey matter volume (CGMV), thalamic volume (TV), and lateral ventricular volume (LVV) were quantified using SIENA, SIENAX multitime point, or VIENA and divided into tertiles. Baseline plasma NfL concentrations were evaluated via Quanterix Neurology multiplex assay. Wilcoxon-Mann-Whitney 1-sided tests were performed to evaluate NfL levels in patients with and without cognition impairment as well as cognitive scores between NfL tertiles (low, medium, high) and NfL levels in high vs low BV tertiles.

RESULTS: Of 162 patients analyzed, 78% were female, 68% were treatment naive, mean (SD) age was 39.7 (10.4) years, mean years since MS onset was 4.0 (5.6), and mean number of relapses in the 12 months prior to enrollment was 0.73 (0.72). Baseline NfL levels were significantly higher in patients with impaired vs unimpaired cognition (SDMT: P=.005; BVMT-R: P=.005; CVLT-II: P=.008). Baseline cognitive scores were significantly higher in the low vs high NfL tertile group (SDMT: P=.0015; BVMT-R: P=.0006; CVLT-II: P=.0014). Baseline NfL level was significantly higher in those with low vs high CGMV (P=.0114) and TV (P<.0001) but not WBV (P=.0527) and was significantly lower in those with low vs high LVV (P=.0001) at baseline. The same relationships were seen between baseline NfL level and low vs high BV tertiles at year 1 of ozanimod, except that WBV was also significant (WBV: P=.036; CGMV: P=.0131; TV: P<.0001; LVV: P=.0006).

CONCLUSIONS: Plasma NfL, a marker of neurodegeneration, is associated with cognitive outcomes and regional brain atrophy in early MS.

FUNDING: *This study was sponsored by Bristol Myers Squibb.*

DISCLOSURES: *Robert Zivadinov: 415 Capital, Janssen, Sanofi (consulting fee, speakers' bureau); Bristol Myers Squibb, EMD Serono, Mapi Pharma, Novartis (consulting fee, contracted research, speakers' bureau); CorEvitas, Protembis, V-Wave Medical (contracted research). John DeLuca: Biogen (consulting fee, speakers' bureau); Bristol Myers Squibb, Janssen, Novartis (consulting fee); Canadian MS Society, Genentech, National Institutes of Health, National MS Society (grant funding); Consortium of MS Centers, EMD Serono (speakers' bureau, grant funding). Lauren P. Shapiro, Aditi Basu Bal, Jon V. Riolo, Sarah Harris: Bristol Myers Squibb (employee and/or shareholder).*

KEYWORDS: Biomarkers of Cognitive Impairment in MS, Disease-Modifying Treatments in MS, Imaging and MS

(NIB07) Real-World Utilization of a Novel Multianalyte Blood-Based Biomarker Panel: The Octave Multiple Sclerosis Disease Activity Test in Clinical Practice in the United States

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BACKGROUND: The complexity of multiple sclerosis (MS) underscores the urgent need for reliable and accessible biomarkers to improve disease management and patient care. Blood-based biomarkers offer a minimally invasive, cost-effective, and scalable solution for monitoring disease activity and guiding personalized treatment strategies. They hold potential for identifying inflammatory and neurodegenerative processes, treatment response, and subclinical disease activity. Incorporating blood-based biomarkers into routine care can enhance early diagnosis, optimize therapeutic interventions, and improve long-term outcomes for individuals living with MS.

OBJECTIVES: To describe the real-world utilization of the Octave Multiple Sclerosis Disease Activity (MSDA) test, a clinically validated, multianalyte blood-based biomarker panel for MS in clinical practice across the United States.

METHODS: We conducted a retrospective descriptive analysis of data elements collected and reported from the Octave MSDA test. Demographic and disease-related data on the transmission form include sex, age, race and ethnicity, current disease-modifying therapy (DMT), reason for test, and date of MS diagnosis.

RESULTS: The Octave MSDA test has been commercially available since 2022. As of December 2024, we are reporting on 10,394 patients with MS who have been tested with MSDA. Baseline demographics include mean age of 51.9 years, 77% female sex, mean disease duration of 13.8 years, 79.7% White, 15.6% Black, and 4.2% Hispanic. Of the 10,394 patients, 44% were treated with a high-efficacy DMT (anti-CD20s, natalizumab, cladribine, alemtuzumab) and 32.1% reported not currently being on a DMT. A total of 12,833 MSDA tests have been ordered from 122 institutions and 205 health care providers (HCPs). The MSDA test provides a quantitative, objective, validated disease activity (DA) score with established thresholds corresponding to low (0-4), moderate (4.5-7), and high (7.5-10) levels of disease activity. MSDA scores from this cohort are 63.5% low, 29.6% moderate, and 6.9% high, with a mean DA score of 3.8. The majority, 80.2%, had 1 MSDA test; 16.8% had 2 tests; and 3% had 3 or more. The top HCP-reported indications for use include routine/longitudinal monitoring, pretherapy/posttherapy, relapse assessment, and baseline evaluation.

CONCLUSIONS: This report highlights the increasing adoption of the MSDA in clinical practice across the US, underscoring its potential to transform MS care. However, continued research is critical to unlocking the full potential of the Octave MSDA, ensuring its seamless integration into clinical workflows and its ability to revolutionize the management of MS care.

DISCLOSURES: *Jennifer Graves: Octave Bioscience (contracted research). Terrie Livingston: EMD Serono (salary, former employee). Terrie Livingston, Gargi Datta, Ferhan Qureshi, David Brazel, Katherine Ruby, Matt Burrill: Octave Bioscience (salary).*

KEYWORDS: Blood-Based Biomarkers, Comprehensive Care and MS, Immunology and MS

NEUROPHYSIOLOGY, NEUROPSYCHOLOGY, AND NEUROPSYCHIATRY

(NNN01) Sex Differences in Multiple Sclerosis Neuropsychiatry

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BACKGROUND: In people with multiple sclerosis (PwMS), sex differences exist in vulnerability to MS and disease progression. Although depression, anxiety, fatigue, perceived deficits, and cognitive dysfunction vary by sex in the general population, there is mixed evidence for these differences in PwMS.

OBJECTIVES: To evaluate for sex differences in the neuropsychiatric sequelae of MS.

METHODS: A consecutive sample of 1530 PwMS (diagnosed per the McDonald criteria) aged 18 to 65 years routinely completed neuropsychological testing at a tertiary

neuropsychiatry clinic in Toronto, Ontario, Canada, from 2005 to 2025. Demographic data included age, education, Expanded Disability Status Scale (EDSS) scores, disease duration, and disease subtype. Neuropsychiatric measures included the Hospital Anxiety and Depression Scale for anxiety (HADS-A) and depression (HADS-D), the Modified Fatigue Impact Scale (MFIS), the Perceived Deficits Questionnaire (PDQ) for subjective cognitive concerns, and the Minimal Assessment of Cognitive Function in MS (MACFIMS) cognitive battery. Linear regression models predicted neuropsychiatric raw scores from sex, adjusted for all previously mentioned demographics ($P < .01$).

RESULTS: Seventy-three percent of participants were women. Mean age was 43.2 years (SD, 10.6), mean education was 15.8 years (SD, 3.0), median EDSS score was 2.0 (IQR, 1.5-3.5), mean disease duration was 9.7 years (SD, 8.4), and 83.3% had relapsing MS (RMS). Women had lower EDSS scores and longer disease duration and were more likely to have RMS than men (all $P < .01$). Controlling for demographics, women had higher scores than men on the MFIS, PDQ, and tests of verbal learning and memory (California Verbal Learning Test) and visuospatial learning (Brief Visuospatial Memory Test) but lower scores on tests of visuospatial processing (Judgment of Line Orientation) and working memory (Paced Auditory Serial Addition Test) (all $P < .01$). No significant sex differences were found in HADS-A, HADS-D, or other MACFIMS scores.

CONCLUSIONS: On average, women with MS experience more fatigue and subjective cognitive concerns compared with men but outperform men in learning and verbal memory. Men perform better than women in visuospatial processing and working memory. Symptoms of anxiety and depression do not differ by sex. Limitations include a bias toward relapsing illness and lack of data on hormonal changes across lifespan. Although sex differences in fatigue and cognition align with general population trends, the null findings for anxiety and depression in MS do not, meriting future exploration.

DISCLOSURES: *David E. Freedman: Nothing to disclose. Jiwon Oh: Biogen Idec, Roche (consulting fee, contracted research, speaking); Bristol Myers Squibb, Eli Lilly, EMD Serono, Novartis, Sanofi-Genzyme (consulting fee, speaking). Anthony Feinstein: Amadeus Press, Cambridge University Press, Glitterati Editions, John Hopkins University Press (royalty); MS Society of Canada (grant); Novartis (speakers' bureau).*

KEYWORDS: Comprehensive Care and MS, Epidemiology of MS, Psychological Issues and MS

(NNN02) A Puerto Rican Hispanic Multiple Sclerosis Population: Baseline Cognitive Characteristics and Factors Predicting Positive Cognitive Outcomes for Patients on Natalizumab or Diroximel Fumarate

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BACKGROUND: Multiple sclerosis (MS) is a chronic neurological disease that damages the central nervous system. In addition to neurologic disability, many patients experience some degree of cognitive impairment. Although cognitive impairment in MS is well studied in White populations in the United States and Europe, little research has been done on how MS affects cognition in underserved populations. Our study was developed to provide a comprehensive analysis of the cognitive functioning and deficits in a large, underserved Hispanic population with MS in Puerto Rico. The study was also designed to analyze the efficacy of disease-modifying treatment (DMT) on cognitive functioning in Puerto Rican patients with MS.

OBJECTIVES: A main goal of our ongoing research project is to determine the pretreatment, baseline neurocognitive characteristics of Puerto Rican patients with MS using a comprehensive neuropsychological evaluation that included gold-standard paper/pencil measures as well as a standardized, validated computerized cognitive measure.

METHODS: Participants enrolled in the study are those about to start natalizumab (Tysabri) or diroximel fumarate (Vumerity). A primary goal is to follow participants over 2 years to determine the response to their respective DMT pertaining to cognitive functioning and available MRI parameters. At baseline, we are collecting a large amount of socioeconomic and health information (and obtaining samples to look at biomarkers, such as neurofilament light chain, in an attempt to determine whether there are factors that predict better outcomes on DMT).

RESULTS: This is a work in progress, and enrollment began about 2 years ago. The ultimate goal is to enroll approximately equal numbers of participants treated with natalizumab or diroximel fumarate (up to a total of 75) as well as 15 nonneurologic controls. The first presentation of this series will include baseline demographic and cognitive data for all participants enrolled through the spring of 2025. There will be a discussion of the pretreatment cognitive similarities and differences between this Puerto Rican population of patients with MS and a mainland US population. The number of patients who will have completed 1- and 2-year assessments by spring 2025 will be presented as initial data regarding medication effects, and any relevant trends in data will be discussed. We will also evaluate early correlation and regression data to determine whether there are insights into demographic and health factors that might help to predict medication efficacy or lack thereof. Although biomarker and MRI data will not be included in this preliminary presentation, such data will be analyzed in future posters/papers.

CONCLUSIONS: This is a work in progress.

DISCLOSURES: *Jeffrey Wilken: Bayer (consulting fee); Biogen (contracted research); EMD Serono, Serono (speakers' bureau). Angel R. Chinea, Timothy Fratto, Robert L. Kane, Viviana Martinez-Maldonado, Ivonne Vincente: Biogen (contracted research). Tamar Kalina, James B. Lewin, Jason P. Mendoza: Biogen (salary).*

KEYWORDS: Cognition, Disease-Modifying Treatments in MS, Psychological Issues and MS

(NNN03) Mobility Impairment and Concern About Falling Are Predictive of Wayfinding Ability in People With Multiple Sclerosis

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BACKGROUND: Complex everyday navigation behaviors depend on cognitive wayfinding processes and mobility function that are vulnerable to decline in persons with multiple sclerosis (PwMS). Although previous research suggests a role for mobility in the physical act of navigation, it remains unclear whether mobility impairment and the awareness of mobility constraints, which may include a potential concern about falling (CAF), could affect underlying cognitive processing essential for the creation and adaptation of one's memory of the environment in support of successful navigation.

OBJECTIVES: To determine the relation between mobility function, CAF, and recall of environment details as a component of wayfinding ability in PwMS.

METHODS: A clinical sample of 44 individuals (79.5% women; 31-65 years) with relapsing-remitting MS completed a virtual adaptation of the Morris Water Maze while seated, with subsequent assessment of free recall of environment details. Participants underwent a comprehensive assessment of mobility function and completed the Falls Efficacy Scale-International (FES-I) to evaluate potential CAF. A model of multivariate regression was used to determine probable predictors of recall of environment details. Candidate predictors included disease severity (Patient Determined Disease Steps), FES-I, Timed 25-Foot Walk, and the Mini Balance Evaluation Systems Test (MiniBEST).

RESULTS: The multivariate regression model was significant ($F=3.17$; $P=.02$), accounting for 25.0% of the variance in recall of environment details. The model revealed FES-I ($b=.09$; $\beta=.39$; $P=.03$) and MiniBEST ($b=.32$; $\beta=.69$; $P=.02$) as significant predictors, with rank-order comparisons suggesting MiniBEST had the larger unique effect.

CONCLUSIONS: Together, these findings underscore the importance of considering mobility function, including perceptions of mobility constraints in assessment of navigation, as modifiable risk factors that have the potential to shape our memory of the environment.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Spatial Navigation in MS

NEUROPATHOLOGY AND PATHOGENESIS

(NPP01) Multiple Sclerosis Prodrome From a Patient Perspective

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BACKGROUND: The report presents data from a questionnaire conducted from September 2024 focusing on patients' experiences and symptoms prior to their first multiple sclerosis (MS) diagnosis. It explores the prodromal phase of MS to identify early signs, comorbid conditions, and patient pathways to diagnosis and treatment.

OBJECTIVES: (1) To identify common symptoms and conditions experienced by individuals in the prodromal phase of MS; (2) to analyze the diagnostic journey, including general practitioner consultations and referral timelines; and (3) to gather patient feedback for improving MS diagnosis and treatment initiation.

METHODS: A survey was distributed to patients with MS, collecting data on demo-

graphics (age, sex), MS type and duration since diagnosis, medical history (comorbid conditions and symptoms prior to the first MS attack), interactions with health care providers (general practitioner visits and referral times), and feedback on improving diagnosis and treatment pathways.

RESULTS: Pending study completion.

CONCLUSIONS: Pending study completion.

DISCLOSURES: *Mavis Ayer: Biogen, Janssen, Merck, Novartis, Roche, Sanofi (consulting fee, speakers' bureau); MS Academy (speakers' bureau); Neuraxpharm (consulting fee).*

KEYWORDS: Epidemiology of MS, Etiology of MS, Genetics and MS

PROGRAMS

(PGM01) Development and Pilot Test of a Virtual Computer-Assisted Cognitive Rehabilitation Program

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BACKGROUND: The effects of multiple sclerosis (MS) on cognition have gained increasing recognition as major disabling symptoms. Despite their impact on quality of life, limited attention has been given to strategies that might help manage the cognitive changes commonly experienced by people with MS (PwMS). In our prior work (R01NR014362), we tested a cognitive rehabilitation intervention that combined the powerful effects of group interventions to build self-efficacy for new cognitive strategies with individual home computer practice of cognitive skills. Our multisite clinical trial, the 8-week Memory, Attention, and Problem-Solving Skills in MS (MAPSS-MS) trial, showed the significant effects of the use of compensatory strategies on cognitive performance as measured by neuropsychological tests.

OBJECTIVES: We adapted the existing in-person MAPSS-MS intervention for virtual delivery and are conducting a pilot study to evaluate the feasibility of remote recruitment, screening, data collection, and intervention delivery. A randomized wait list control design was selected to obtain preliminary estimates of efficacy.

METHODS: PwMS who meet inclusion criteria, including self-reported cognitive concerns, are being recruited for the study. Participants will be randomly distributed to the experimental group (8 weekly sessions via video conference plus prescribed practice of BrainHQ exercises) or the wait list control group. Participants will complete measures of MS severity, self-efficacy, depression, perceived cognitive function, compensatory strategy use, perceived stress, pain, fatigue, and sleep via REDCap and neuropsychological performance tests using the CNS Vital Signs core computerized neurocognitive test battery. Data will be collected at baseline, immediately post intervention, and 6 weeks post intervention.

RESULTS: Existing MAPSS-MS protocols and intervention manuals have been adapted for remote delivery. Sample recruitment is ongoing; 60% of the participants have been recruited to date. The virtual intervention will be launched in February 2025, and postintervention data will be available in May 2025.

CONCLUSIONS: Findings will allow us to determine the feasibility and efficacy of the adapted virtual MAPSS-MS cognitive rehabilitation intervention in improving overall neurocognitive competence, self-efficacy for cognitive tasks, and use of compensatory cognitive strategies.

ACKNOWLEDGMENT: This project was supported in part by the 2024 International Organization of MS Nurses Nightingale Award.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Nursing Management in MS, Psychological Issues and MS

(PGM02) My Health in Motion: Pioneering Mobile Health Equity and Clinical Trial Awareness for Racial and Ethnic Minority Patients With Multiple Sclerosis

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BACKGROUND: Multiple sclerosis (MS) disproportionately affects Black and Brown communities, often compounded by health care disparities, limited health literacy, and underrepresentation in clinical trials. EMD Serono's My Health in Motion (MHIM) initiative addresses these challenges through an innovative, mobile approach to health education and resource provision.

OBJECTIVES: To evaluate the initial impact of MHIM on health literacy, patient empowerment, health care engagement, and clinical trial awareness among Black and Brown patients with MS in underserved communities during a 6-month pilot program.

METHODS: Launched in February 2025, MHIM is a mobile unit with 4 educational stations going to 15 cities over 6 months. The program utilizes culturally sensitive materials in both Spanish and English, interactive technology, and personalized body scans. The 4 stations focus on (1) common health issues and risk reduction for racial and ethnic minority patients, (2) artificial intelligence–assisted doctor-patient communication practice, (3) importance of diversity in clinical trials, and (4) personalized body composition analysis. Participants will complete surveys before the visit, immediately post visit, and 4 weeks after their visit to assess changes in health literacy, self-efficacy, intention to engage in health care decisions, and interest in clinical trials.

RESULTS: Preliminary data from the first 3 months of the pilot program will be available in August. We anticipate significant improvements in MS-related health literacy, self-reported confidence in health care decision-making, and intention to discuss treatment options with health care providers. A key performance indicator will track the number of participants who enroll in or inquire about clinical trials as a result of MHIM. Initial qualitative feedback is expected to highlight the program's accessibility and cultural relevance. Specific metrics to be reported include percentage increase in health literacy scores, percentage of participants expressing increased confidence in communicating with health care providers, and the number of clinical trial inquiries or enrollments resulting from MHIM participation.

CONCLUSIONS: MHIM represents a novel, scalable model for addressing health disparities in MS care through mobile, culturally tailored education. This pilot initiative aims to enhance health literacy, empower patients to actively participate in their care, and increase representation in clinical trials, potentially improving long-term outcomes for racial and ethnic minority patients with MS. By providing accessible, culturally sensitive education and resources, MHIM has the potential to bridge significant gaps in MS care for underserved communities. Full results from the 6-month pilot will inform future expansions and adaptations of the program, with the ultimate goal of creating a more equitable landscape in MS treatment and research.

DISCLOSURES: *Marie-Ange Noué: EMD Serono (salary).*

KEYWORDS: Comprehensive Care and MS, Management of Activities of Daily Living in MS, MS and the Caregiver/Family

(PGM03) Empowering Women Navigating Multiple Sclerosis During Lactation: A Specialized Educational Program in Egypt

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BACKGROUND: Breastfeeding (BF) support may be an opportunity for a preventive intervention for women with multiple sclerosis (MS), particularly in limited-resource settings with a significant population of patients with MS and a high incidence of early-life adversities. Lactating women with MS struggle to manage their condition while seeking adequate infant care. Physically, these women may have exacerbated MS fatigue, postpartum relapses, and medication safety issues. Psychological aspects include postpartum depression and heightened anxiety of MS occurrence in their children. The demands of balancing BF and pumping schedules with MS treatment add significant stress on nursing women. Handling BF and MS through education and support is pivotal to empowering mothers with MS. For mothers, BF acts as an immunomodulator and reduces postpartum relapse risk. For newborns, BF supports long-term developmental programming and reduces MS chances by shaping a healthy gut microbiome. Egyptian mothers with MS have a hard time finding accessible, culturally sensitive, and evidence-based resources. A novel educational program is needed to help mothers deal with MS and streamline the maternity experience.

OBJECTIVES: (1) Develop a specialized program for lactating mothers with MS in Egypt and deliver tailored, interactive educational sessions and bilingual handouts; (2) provide these women with up-to-date information, opportunities, and ongoing connection and support; and (3) promote informed decision-making at the intersection of BF and MS.

METHODS: The proposed program builds upon an 11-year-old course offered by the LactAid Center, a leading lactation center in Egypt. The course has been specially updated for lactating mothers with MS, with guidance from a multidisciplinary team of lactation consultants, neurologists, and pediatricians. Interactive sessions focus on the benefits of BF for the overall health of the mother-baby dyad along with common concerns, myths, and safety issues. Practical strategies for managing MS symptoms, fatigue, and relapses are also shared. Easy-to-read, supportive, and visually engaging Arabic-English handouts are distributed to and evaluated by program participants.

RESULTS: Comparative pre– and post–educational session surveys have assessed

the program's impact. Quantitative and qualitative analysis techniques have measured changes in participants' knowledge, perceived competency, and acquired confidence. The handouts have also been assessed for accessibility, clarity, and cultural relevance. Complete data will be presented at the annual meeting.

CONCLUSIONS: Our program enhances health care equity and highlights the value of tailored, comprehensive MS patient education programs. Integrating educational sessions with bilingual handouts equips lactating mothers with essential knowledge and actionable measures to break cycles of intergenerational adversity and maintain health resilience.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Management of Activities of Daily Living in MS, Psychological Issues and MS

(PGM04) National Multiple Sclerosis Society Clinical Programs: Clinical Fellowships and Medical Student Mentorship Program

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BACKGROUND: The National Multiple Sclerosis Society (NMSS) provides early career support and funding to train physicians in the comprehensive care of people living with MS through our Sylvia Lawry Physician Fellowships, which began in 1998; Clinical Care Physician Fellowships, which began in 2004; and our Institutional Clinician Training Awards, which began in 2014. Through 2024, the NMSS' fellowship programs have supported the training of 360 physicians. In addition, NMSS supports upstream engagement with medical students by providing a mentorship program. Since 2008, NMSS has facilitated the mentorship of 177 medical students.

OBJECTIVES: The goals of the clinical fellowship program are to expand the neurology and neuroimmunology workforce and train physicians in the diagnosis and comprehensive care of people with MS, thereby increasing access to MS care. The goals of the mentorship program are to raise awareness about the complexities experienced by people with MS and advancements in treatment and management of MS and to generate interest in a career in MS care.

METHODS: We gathered information from participants in each of our fellowship and mentorship cohorts via surveys to understand the impact these programs have had on participants' career trajectories and, ultimately, the MS community. An administrative health claims data set using Komodo Healthcare Map was analyzed in Prism to identify the number of patients being cared for by our former fellows. Prism is a data analytics platform that allows access to medical claims data.

RESULTS: NMSS clinical fellowships and mentorships have influenced the number of physicians caring for individuals living with MS. In data from 2022 to 2024, 280 former NMSS fellows are active in a neurology practice in 43 states. These 280 providers have seen 58,650 unique patients with MS over a 2-year span. Of the 177 mentorship participants, we have been able to follow 120, and 34% are either practicing neurologists or are in neurology residency. For those who have completed their neurology residency, 33% of them specialize in MS care.

CONCLUSIONS: NMSS clinical programs are valuable and effective in stimulating interest and training early career students and physicians in the fields of neurology, neuroimmunology, and MS care. Future iterations of our programs should focus on how NMSS can help address the neurologist shortage in the United States and increase accessibility to MS care for people living with MS, especially in rural and neurology desert areas.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Employment in MS

(PGM05) Improving Access to Disease-Modifying Therapies Through a Financial Assistance Program: A 4-Year Review

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BACKGROUND: People with multiple sclerosis (MS) can experience a high financial burden from disease-modifying therapies (DMTs) as well as specialty prescriptions for symptomatic management. Affordability of medications plays a pivotal role in treatment access and adherence rates. Patients may be unable to fill medication prescriptions due to cost, or their provider may have to select an alternative, less-preferred treatment. Our Kootenai specialty pharmacy team helps navigate the financial burden for those patients by offering financial assistance (FA) to every patient who may require additional support to obtain specialty medications. They also assist in signing patients up for eligible grants.

OBJECTIVES: To review our specialty pharmacy financial assistance program and its impact on improving patient access to specialty medications, including disease-modifying therapies. To evaluate which types of prescriptions require financial assistance due to high costs.

METHODS: We utilized the EPIC enterprise reporting tool function to generate a report of patients enrolled in our specialty pharmacy FA program from January 1, 2021, to December 24, 2024. This included DMTs and symptomatic prescriptions from our MS clinic providers. Duplicate medication fills were removed, and categories were created for fills through Kootenai Health FA and grants. As a marker for the socioeconomic situation, we evaluated employment status.

RESULTS: We found that 136 of our patients have benefited from financial assistance and have not had gaps in therapy due to affordability. There were 190 unique specialty prescriptions filled through Kootenai Specialty Pharmacy: 132 (69.5%) were DMTs, including 11 infusion therapies, and 58 (30.5%) were prescriptions for symptomatic treatment (walking fatigue, overactive bladder, pseudobulbar affect, and migraine). Only 3 (2.2%) patients were uninsured; 77 (56.6%) patients had commercial insurance and 56 (41.2%) had Medicare. As for employment, 44 (32.4%) patients were disabled, 59 (43.4%) were employed, 2 (1.5%) were unemployed, 21 (15.4%) were retired, and 10 (7.4%) were homemakers.

CONCLUSIONS: Patients who receive FA are more likely to maintain consistent treatment without experiencing interruptions due to financial barriers. This continuity is crucial in optimizing outcomes and ensuring long-term MS management. Additionally, offering FA for symptomatic control medications further supports our clinic and specialty pharmacy's goal of comprehensive care for our MS patient population.

DISCLOSURES: *Tyler Cress, Nicole Dooda, Cindy Smith, Autumn Ramsrud, Brittany Kreifels, Michelle Roff, Mary Thibodeau, Barbara Conti, Angie Critchfield, Mandy Matheney: Nothing to disclose. R. Chase Cullen: TG Therapeutics (consulting fee). Nina Bozinov: EMD Serono (consulting fee, speakers' bureau); Genentech (consulting fee).*

KEYWORDS: Access to Medication, Economic Issues and MS

PSYCHOSOCIAL FACTORS

(PSY01) Hair Cortisol as a Biomarker of Chronic Stress in Adults With Multiple Sclerosis: A Feasibility Study

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BACKGROUND: Chronic stress may accumulate over time for people with multiple sclerosis (PwMS) and may influence disease progression and increase susceptibility to additional stressors. Although hair cortisol concentration (HCC) has emerged as an objective measure of chronic stress, most research has relied on saliva and blood samples.

OBJECTIVES: (1) To evaluate the feasibility of hair sample collection for cortisol analysis. (2) To investigate factors influencing participation in hair sample collection. (3) To explore the relationship between HCC and health promotion variables in community-dwelling individuals with longstanding MS.

METHODS: The data were collected as part of an ongoing longitudinal study examining health promotion in PwMS, initially recruited in 1996 from 2 Texas chapters of the National Multiple Sclerosis Society. Participants were asked to consent to providing a hair sample; those who consented received hair collection kits with standardized instructions for sample collection. Returned hair was examined to determine eligibility for cortisol analysis. Statistical analysis included calculating feasibility indicators (eg, completion rate, eligibility rate), comparing factors influencing participation, and examining correlations between HCC and self-report measures.

RESULTS: Of 203 survey respondents, 151 returned informed consent for hair collection, and 90 of those (59.6%) returned hair samples. After the quality assessment, 76 samples were assayed for HCC, with an eligibility rate of 84.4% (76/90). Although there were no significant differences between hair sample respondents (n=90) and nonrespondents (n =113), participants who returned eligible hair samples for cortisol analysis were younger ($t[88] = 2.47$; $P = .016$; $d = .72$) and had shorter MS diagnosis duration ($t[88] = 2.15$; $P = .049$; $d = .86$) than those whose samples were excluded. After log-transformation, there were no significant associations of HCC with perceived stress, other demographic variables, health-promoting behaviors, and health outcomes.

CONCLUSIONS: Hair sample collection for cortisol analysis is feasible in community-dwelling individuals with long-standing MS and can be incorporated into ongoing

longitudinal studies. Future research should employ multimethod approaches to collect hair samples from older adults with long-standing MS and carefully consider the impact of measurement windows between HCC and self-reported stress measures.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Psychological Issues and MS

(PSY02) Targeted Approaches for Minority Engagement in Multiple Sclerosis Research: Exploration of Barriers to Clinical Trial Participation and Strategies for Engagement Among Black Adults With Multiple Sclerosis

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BACKGROUND: There has been a notable increase in the number of Black adults diagnosed with multiple sclerosis (MS), and the disease may present differently and progress faster in Black than in White patients. Black people are historically underrepresented in MS clinical trials, which has resulted in underestimates of disease prevalence and limited understanding of disease course and treatment in this population. To fully understand the differences in the disease within this group, we need to develop targeted approaches to engage Black patients in MS clinical trials.

OBJECTIVES: To identify barriers to research participation among Black patients with MS and strategies to increase their engagement in clinical trials.

METHODS: We used a qualitative phenomenological design with 4 sequential phases: narrative literature review, expert panel of scientists, expert panel of community leaders, and interviews with Black people with MS who had previously participated in clinical trials. Data from each phase were analyzed at the end of that phase and results were used to inform the questions asked in the subsequent phase.

RESULTS: Three major themes related to participation barriers among Black patients were identified: personal or internal barriers, environmental barriers, and health care provider and health care system barriers. Strategies for increasing participation were matched to each theme and included building trust in the research process; assembling a diverse research team that reflects the race and other characteristics of the desired study sample; using trusted sources to disseminate information about research opportunities; offering study participants low-tech and convenient options for study activities and compensation for travel and other costs; educating health care providers about the high prevalence of MS in Black people; and informing providers about research opportunities for their patients with MS.

CONCLUSIONS: The underrepresentation of Black patients in MS research has limited the understanding of its prevalence, disease course, and treatment in this group. Strategies that build trust between investigators and the MS community and lower the burden of research participation may increase engagement of minority groups in clinical trials of the disease.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Epidemiology of MS, Health Equity in MS, MS and the Caregiver/Family

(PSY03) Patients' Perceptions of Women's Health Issues in Demyelinating Diseases of the Central Nervous System

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BACKGROUND: Demyelinating diseases of the central nervous system (CNS) have a propensity to affect women more than men, although there are very limited data discussing women's health issues in these patients. Most of the available research focuses on pregnancy in patients with multiple sclerosis (MS) but does not include other women's health issues or include patients with myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) or neuromyelitis optica spectrum disorder (NMOSD). Additionally, there remain gaps as many studies do not investigate other women's health issues, report the race/ethnicity of the patients, or include transgender patients who identify as women. Including these variables is important as there are data supporting different outcomes across race/ethnicity and biological sex.

OBJECTIVES: The objective of this study is to understand the beliefs and knowledge about women's health issues, including pregnancy, the postpartum period, breastfeeding, contraception use, sexual dysfunction, menopause, and cancer in women with demyelinating disease of the CNS at a tertiary referral center.

METHODS: Inclusion criteria required the patient identify as a woman and have a diagnosis of MS, MOGAD, or NMOSD. Patients completed an anonymous survey inquiring about their beliefs about women's health issues and how they relate to their diagnosis. Medical records were used to collect other pertinent clinical data.

RESULTS: Of 100 patients enrolled in the study, 99 were biological female and 1 patient was transgender female; 29 were minority and 71 were nonminority patients; 88 patients had MS, 5 patients had MOGAD, and 7 patients had NMOSD. There were 170 total pregnancies among 71 participants, and 3 women were pregnant at the time of the survey. The results of the questionnaire inquiring about patients' beliefs regarding women's health issues were diverse, indicating variable levels of understanding and education regarding these topics. For example, about 20% of participants did not believe they could pursue pregnancy or use assistive reproductive treatments because of their diagnosis.

CONCLUSIONS: This study aimed to investigate how women perceive and understand women's health issues in relation to their diagnosis of demyelinating disease of the CNS. The patients' responses about how their diagnosis affected women's health issues were highly variable and highlighted the fact that many patients may not receive the necessary counseling and education. Notably, these findings were not altered by patient education level. In the past 2 decades, there has been a surge of research focused on women's health issues in patients with demyelinating disease, but there also needs to be a focus on educating patients about these discoveries and advances. Patients need to be counseled routinely on all these subjects to ensure safety and to help improve quality of life in those with demyelinating diseases. Future directions include enrolling underserved and diverse patient populations at Parkland Hospital.

DISCLOSURES: *Caitlin Campbell, Nataliya Hall, Shelby Herr: Nothing to disclose. Lindsay A. Horton: Biogen, EMD Serono (consulting fee). Lauren M. Tardo: EMD Serono (consulting fee); MJH Life Sciences, NeurologyLive (paid support); The MOG Project (nonpaid medical adviser).*

KEYWORDS: Comprehensive Care and MS, Psychological Issues and MS, Women's Health Issues and MS

(PSY04) Identifying Predictors of Occupational Function in Military Personnel With Multiple Sclerosis

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BACKGROUND: A diagnosis of multiple sclerosis (MS) has major implications for United States military service members. Along with the risks of physical and psychological disability from MS that are well characterized for the general population, MS is currently considered a medically disqualifying condition in all branches of US military service due to its potential impacts on military readiness and the ability to deploy to austere environments. However, the disease course of MS and its effects on occupational functioning cannot be predicted by diagnosis alone, and some military members are able to receive waivers to continue serving in limited roles for some career fields. Despite existing data on the incidence of MS in the military, little is known about the clinical profiles of military members with MS and how modifiable factors, such as mood, fatigue, symptom management, and disease-modifying therapy (DMT) choice, may influence disability and unemployment rates in military members with MS.

OBJECTIVES: To examine the clinical characteristics of US military service members with MS and evaluate the impact of these characteristics on occupational functioning.

METHODS: US military service members with MS will complete demographic and MS history questionnaires, a computerized cognitive testing battery (Automated Neuropsychological Assessment Metrics), and patient-reported outcome surveys for fatigue (Modified Fatigue Impact Scale 5-item version), mood (Hospital Anxiety and Depression Scale), traumatic stress (Posttraumatic Stress Disorder Checklist for *Diagnostic and Statistical Manual of Mental Disorders* [Fifth Edition]), pain (Pain Effects Scale), quality of life (Multiple Sclerosis Impact Scale), and occupational functioning (Individual Work Performance Questionnaire). Hierarchical regression analyses will be performed to identify predictors of occupational functioning.

RESULTS: Data collection for this study is ongoing, with anticipated preliminary results available before May 2025. We hypothesize that US military service members with MS will report significant psychiatric comorbidities as well as medical comorbidities that contribute to occupational impairment. We hypothesize that shorter disease duration, use of DMTs, better mood, higher cognitive functioning, and use of symptom management strategies will predict better occupational functioning.

CONCLUSIONS: This study's findings will provide insight into the severity and functional impact of MS on service members and aid in assessing their fitness for duty and ability to continue military service. Additionally, we expect that the findings will inform more targeted and effective treatment recommendations to improve occupational functioning in military members with MS.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Employment in MS, Military, Psychological Issues and MS

(PSY05) Preliminary Understanding of Gender Considerations of Health and Well-Being for Women With Multiple Sclerosis in Canada: An Interpretive Phenomenological Analysis

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BACKGROUND: Canada has the highest rates for multiple sclerosis (MS), with over 90,000 cases, and women account for 3:1 compared with men. Gender is defined as a social, and not biological, construct that influences the identity, expressions, and behaviors of girls, boys, women, men, and gender-diverse people. Gender influences the distribution of societal resources and power, with women and gender-diverse people historically experiencing more barriers and stigmatization when accessing health care. Therefore, understanding how gender identity influences health may promote more equitable experiences for people with MS when accessing care.

OBJECTIVES: To identify the sociocultural factors related to gender that influence the lived experiences of the health and well-being of women with MS in Canada.

METHODS: van Manen's Interpretive Phenomenological Analysis was employed to investigate and understand the lived experiences for health and gender of 14 women with MS living across Canada. Semistructured interviews were conducted via videoconferencing and telephone, audio recorded, and triangulated with field notes taken by the research team.

RESULTS: Initial findings revealed that women with MS may have their health and well-being heavily influenced by the presence of traditional gender roles, especially if there were noted unconscious biases or assumptions for those in their social support network. This includes expectations where participants take on additional unpaid labor, such as caring for grandchildren or completing household chores, while on disability leave. Such tasks may exacerbate problematic symptoms like fatigue.

CONCLUSIONS: Clinicians supporting women with MS may benefit from understanding the influence of gender and how this intersects with the health and well-being of women with MS. This includes assessing the quality of social support systems for this population.

DISCLOSURES: *Nothing to disclose.*
KEYWORDS: Psychological Issues and MS, Women's Health

(PSY06) Gender Considerations for Women With Multiple Sclerosis: An Integrated Literature Review

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BACKGROUND: Gender differently influences the experiences of illness, social determinants of health (SDOH), and disability. Identifying as a woman was found to be a reliable predictor of having unmet health needs and of experiencing gender-based inequality with SDOH. Women are diagnosed with multiple sclerosis (MS) at 3:1 compared with men, yet the intersection of gender with health is largely unrecognized. This may contribute to inequitable health care practices for interprofessional teams caring for women with MS. Gender is a social construct that may intersect with health and MS, as there may be differences in how women and men experience health. This intersection was explored in an integrated literature review.

OBJECTIVES: To understand how gender as a construct is conceptually explored in recently published literature pertaining to the health and well-being of women with MS.

METHODS: Aspects of gender and women's health have recently been noted as being understudied; therefore, an integrated literature review was conducted to retrieve relevant scholarly articles to identify gaps in knowledge. This review was conducted using the following databases: PubMed, Scopus, and the Cumulative Index of Nursing and Allied Health. Additional grey literature located online was also included, using sites such as Google and Google Scholar. Combined keywords used for searching databases included *MS* and/or *women* and *gender*, which allowed for the retrieval of articles relevant to the health and well-being of women with MS that considered gender. Guided by the Public Health Agency of Canada's Critical Appraisal Toolkit, we analyzed the literature to identify themes pertaining to gender and how it intersects with the health of women with MS.

RESULTS: The search identified 422 articles on this subject that met the inclusion criteria, and 11 were selected based on the relevancy of scholarly evidence highlighting aspects of gender for women with MS. Most of the available literature pertains to gender for women with MS from a postpositivist lens employing quantitative methods. There is a gap in the literature about the topic using qualitative or mixed methods approaches or qualitative methods. Findings from the literature review study revealed 2 themes: implications for women with MS and considerations for the health of women with MS.

CONCLUSIONS: Gender considerations for the health and well-being of women with MS are currently in the literature. The nascent research conducted in this area suggests that women with MS benefit from clinicians effectively engaging in therapeutic communication, including empathetic and active listening to avoid dismissing and stigmatizing this population.

DISCLOSURES: *Nothing to disclose.*
KEYWORDS: Psychological Issues and MS, Women's Health

(PSY07) Implementation of a Depression Screening Protocol in People With Multiple Sclerosis

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BACKGROUND: According to estimates, around half of the individuals diagnosed with multiple sclerosis (MS) are likely to suffer from a major depressive episode. Regrettably, depression in people with MS often goes unnoticed or untreated. Additionally, the standardized mortality ratio highlights that the risk of suicide for people with MS is double that of the general population. Depression is highly correlated with poor health-related quality of life and negatively impacts treatment adherence, leading to poor prognosis and disability.

OBJECTIVES: The overarching goal of this project was to promote early detection, diagnosis, and treatment of depression in people with MS at an outpatient neurology practice. The primary objective was to screen more than 50% of all patients with MS for depression, and the secondary objective was to provide an intervention to more than 95% of all patients with a positive screening.

METHODS: The intervention was based on the Screening, Brief Intervention, and Referral to Treatment (SBIRT) method, which involves quick screening, a brief intervention to increase awareness, and referral to specialized treatment. A large body of evidence supports this method as it allows for early detection. A new workflow was created for the clinic, and the team was educated on the SBIRT method. The Patient Health Questionnaire was utilized to provide the screening and was administered by the medical assistant before a routine office visit. The neurologist reviewed the screening results with the patients at the end of the visit. Patients who screened positive were presented with treatment options in the form of medication or a referral for psychiatric evaluation if warranted.

RESULTS: The implementation phase lasted 60 days, during which 95% of patients with MS were screened for depression, meeting the primary objective; of those who screened positive, 87% received an intervention.

CONCLUSIONS: Using this approach in patients with MS for screening could increase detection and improve rates of referral and early treatment of depression, thereby contributing to an improved quality of life.

DISCLOSURES: *Jennifer Slonaker: Banner Life Sciences (employee).*
KEYWORDS: Comprehensive Care and MS, Depression, Psychological Issues and MS

(PSY08) Associations Among Anxiety, Depression, and Multiple Sclerosis Symptoms in Those Experiencing Pregnancy and the Postpartum Period

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BACKGROUND: Chronic health conditions such as multiple sclerosis (MS) regularly necessitate symptom management plans and increased task burden on patients, which can often contribute to deleterious effects on mental health. People with MS (PwMS) may experience myriad symptoms of anxiety, depression, and other psychological complications alongside MS disease-related symptoms. Completion of daily tasks, sleep hygiene, and cognitive functioning have been negatively correlated with anxiety and depression among PwMS.[1-3] Further, MS symptom relapse has been shown to decrease throughout pregnancy and exacerbate during the puerperium stage,

returning to baseline following this period.[4] The additional complexities that such a presentation brings to the process of childbearing and the postpartum experience suggest potential, additional mental health–related challenges for PwMS during this time as well and warrant further exploration.

OBJECTIVES: The current study aims to examine trends among mental health and MS symptomology throughout pregnancy and the postpartum period. We hope to highlight periods during which mental and physical health symptoms are most elevated vs when they are most well-controlled. We also seek to identify patient-specific variables that may be linked to symptom fluctuations, including but not limited to delivery type (eg, vaginal, elective/emergent cesarean delivery), discontinuation of disease-modifying therapies with pregnancy, and sociodemographic factors. Goals of the current research include broadening the understanding of these variables within this specific population of PwMS to better inform screening and clinical practice.

METHODS: The current research is a quantitative exploration of historical patient data, which will be analyzed using descriptive statistics and mixed effects linear regression models. Variables of interest will be captured through previously acquired Quality of Life in Neurological Disorders data, past MS symptom tests (eg, walking speed test), electronic medical record data, and other sociodemographic and disease-related information within our preexisting patient database. Preliminary hypotheses posit that both anxiety and depression symptoms will be positively associated with MS symptoms. Further, we hypothesize a reduction in all 3 symptomologies as pregnancy progresses, with all-encompassing symptom exacerbation in the postpartum period.

RESULTS: Data forthcoming.

CONCLUSIONS: Pending.

DISCLOSURES: *Kaila M. Kutz, Nicolas Thompson, Katherine B. Wood, Brianne N. Markley: Nothing to disclose. Grace E. Tworek: JTD Company (consultant). Amy B. Sullivan: EMD Serono, Novartis (consulting fee); Multiple Sclerosis Association of America (speakers' bureau, advisory board).*

KEYWORDS: Comprehensive Care and MS, Pregnancy/Parenthood and MS, Psychological Issues and MS

(PSY09) An Exploration of Trust and Patient-Reported Outcomes Among People With Multiple Sclerosis

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BACKGROUND: Trusting patient-provider relationships are increasingly recognized as a key factor in promoting positive health outcomes. In health care, trust is defined as the patient's belief that the provider will act in their best interests, which is particularly critical for people with multiple sclerosis (PwMS).[1] This subset of patients often experiences ongoing vulnerability, uncertainty, and dependence on health care providers due to the chronic nature of the disease and the complexity of treatment regimens.[2]

OBJECTIVES: The current study strives to understand the impact of trust within the patient-provider relationship on patient-reported outcomes (PROs) and to gain insight into areas for improvement in the treatment of MS. The results of this study will provide additional context about the patient-provider relationship, potentially leading to improved outcomes in PwMS. We aim to better understand how trust differs across sociodemographic variables and its relationship to PROs, as understanding how trust influences health care outcomes across diverse populations and contexts is essential to addressing disparities and improving health care delivery.

METHODS: The current research is a quantitative exploration of prospective patient reports and data, which will be analyzed using descriptive statistics and correlation analysis. Variables of interest will be captured both retrospectively and prospectively. Retrospective data will be collected through previously acquired Patient-Reported Outcomes Measurement Information System Global Health 10 and Quality of Life in Neurological Disorders data collected as standard of care during a Mellen Center office visit. Prospective data include the 13-Item Health Care Relationship Trust Scale Revised. Sociodemographic variables will be taken via electronic medical record data. Preliminary hypotheses postulate that high trust will be directly related to better PROs. Additionally, we hypothesize that trust will be statistically significant between sociodemographic variables.

RESULTS: Data forthcoming.

CONCLUSIONS: Pending.

DISCLOSURES: *Katherine B. Wood, Nicolas Thompson, Kaila M. Kutz, Andrew Schuster: Nothing to disclose. Grace E. Tworek: JTD Company (consultant). Amy B. Sullivan: EMD Serono, Novartis (consulting fee); Multiple Sclerosis Association of America (speakers' bureau, advisory board).*

KEYWORDS: Comprehensive Care and MS, Patient-Provider Relationships, Psychological Issues and MS

(PSY10) The Prevalence of Schizophrenia in Patients With Multiple Sclerosis: A Systematic Review and Meta-Analysis

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BACKGROUND: People with multiple sclerosis (MS) experience a wide range of psychological problems. Schizophrenia (SCZ) is a severe mental disorder that is conceptualized as a disorder of brain connectivity. Some patients with MS experience schizophrenia.

OBJECTIVES: To estimate the pooled prevalence of schizophrenia in people with MS.

METHODS: PubMed, Scopus, Embase, Web of Science, PsycINFO, and Google Scholar were systematically searched by 2 independent researchers on October 1, 2024.

RESULTS: A literature search revealed 7303 records; after deleting duplicates, 4515 remained. Eighty-two full texts were evaluated, and 20 studies were included in the review. The studies were published between 1969 and 2024. Most were conducted in Canada, followed by the United States, the United Kingdom, and Taiwan. Boesen et al included pediatric cases. One study was a case-control study, 7 were cross-sectional studies, and 12 were cohort studies. The pooled prevalence of schizophrenia in patients with MS was estimated as 1% (0%-1%; $I^2 = 98.1\%$; $P < .001$). The pooled prevalence of psychosis was estimated as 2% (95% CI, 1%-3%; $I^2 = 90.2\%$).

CONCLUSIONS: The results of this systematic review and meta-analysis showed that the pooled prevalence rates of schizophrenia and psychosis are 1% and 2% in people with MS, respectively.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Disease-Modifying Treatments in MS, Epidemiology of MS, Psychological Issues and MS

(PSY11) The Impact of Multiple Sclerosis on the Labor Situation in Brazil

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BACKGROUND: Multiple sclerosis (MS) is a disease that leads to the accumulation of motor, sensory, visual, and cognitive sequelae over time and is a leading cause of disability. In 2016, approximately 43% of people with MS had left their jobs within the first 3 years following diagnosis, and after 10 years, 70% were unemployed (MS International, 2016). The "Societal Cost of MS in Ireland" (2015) report highlighted that 70% of individuals with MS who were employed felt that their condition limited their career potential.

OBJECTIVES: The objective of this study is to understand the impact of MS on the employability of patients living in Brazil.

METHODS: A questionnaire assessing the impact of MS on employability was administered to 295 individuals participating in an association of patients with MS based in São Paulo, Brazil. Data were collected between April 2023 and December 2024.

RESULTS: Of the 295 respondents, 44.7% were employed, 28.1% were unemployed or received some form of sickness benefit, and 15.6% were retired. As of July 2024, the unemployment rate in Brazil was approximately 6.8% of the population (7.4 million individuals). In our sample, 229 patients engaged in some form of paid activity, with 48.9% holding steady jobs, 36.7% employed by private companies, and 12.2% employed in public sector positions (municipal, state, or federal). Approximately 78 individuals (34.1%) were self-employed, operating as microentrepreneurs or in the service provision sector. The majority of these individuals (38%) reported a family income of up to 2 Brazilian minimum wages (1 minimum wage=R$1412.00/$227.42), whereas 28.5% received between 2 and 4 minimum wages and 25.4% received between 4 and 10 minimum wages. Vanotti et al reported an unemployment rate of 30% among patients without cognitive impairment and 50% among those with cognitive impairment in Argentina, indicating a strong relationship between patients' socioeconomic status and their employment status.

CONCLUSIONS: MS significantly affects the employment situation of affected patients. Within the patient association for MS located in Brazil, only 44.7% of individuals are employed whereas the majority are either retired or unemployed. Nonetheless, 77.6% of participants engaged in some form of paid work due to the necessity of supplementing the family income, often in circumstances not regulated

by employment law. The overall employment situation in Brazil is challenging, and these issues are even more pronounced among patients with chronic disabling conditions, as evidenced by family income levels. Understanding the social and employment realities faced by these patients is crucial. It is imperative that both public and private social strategies be developed to enhance employment opportunities and implement career plans.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Economic Issues and MS, Employment in MS, MS and the Caregiver/Family

QUALITY OF LIFE AND OUTCOMES

(QOL01) Dairy Intake Is Modestly Associated With Physical Functioning Outcomes in Multiple Sclerosis

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BACKGROUND: There has been increasing interest in diet and dietary patterns among people with multiple sclerosis (MS), particularly with respect to lifestyle management for symptoms and disease progression, where quality of diet and adequate nutrient intake have been a key focus. There is currently limited and inconsistent evidence regarding dairy intake and its effect on MS symptoms and disease progression.

OBJECTIVES: This study examined whether the dairy component score of the Diet History Questionnaire (DHQ-III) Healthy Eating Index (HEI) was associated with physical functioning outcomes in MS.

METHODS: A sample of 367 participants remotely completed the DHQ-III and 3 measures of physical functioning, including the Patient Determined Disease Steps (PDDS), Multiple Sclerosis Walking Scale-12 (MSWS-12), and 30 Second Sit to Stand Test (30 Second STS). We examined Pearson bivariate correlations among the dairy component score of the DHQ-III HEI and physical function outcomes.

RESULTS: The dairy component score of the DHQ-III HEI was significantly associated with the PDDS score (r=–.15; P=.004), MSWS-12 score (r=–.14; P=.007), and total number of stands completed during the 30 Second STS (r=.19; P<.001). The significance of these associations persisted after controlling for age, sex, education level, annual household income, and the height of the chair utilized for the remotely conducted 30 Second STS.

CONCLUSIONS: Healthy consumption of dairy may be indicative of better physical functioning outcomes among people with MS. This contributes to the growing body of research regarding quality of diet and nutrient intake in MS.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Diet

(QOL02) Defeat Multiple Sclerosis (MS): A Patient and Community Education Campaign on Brain Health in MS

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BACKGROUND: The recently updated guidelines for standard of care in multiple sclerosis (MS) underscore the importance of a multidisciplinary approach. Despite recommendations of strategies to maximize brain health in individuals with MS, there are no educational tools available to patients that summarize the main pillars of brain health. Mnemonics can improve the recall of information with a memorable word and mental visuals for retaining health information, especially in students and the public. This approach has been successfully employed for many disorders, including stroke education, with the mnemonic *BE FAST*. We posit that increasing awareness about the elements involved in brain health in MS, such as what has been done for stroke, will facilitate education at the early stage for patients and increase their proactive participation in prevention and treatment.

OBJECTIVES: Develop a mnemonic to facilitate memorization of the common pillars of brain health in MS. Improve awareness of the main pillars of brain health among patients with MS.

METHODS: We performed a literature review of educational tools for brain health in MS and found there are no such tools. Informed by recently published guidelines for brain health in MS, we devised an educational framework to facilitate memorization of the common pillars of brain health in the mnemonic *DEFEAT MS*. DEFEAT stands for (1) diet and vitamin D supplementation, highlighting the importance of healthy nutritional strategies; (2) exercise, representing a key element in promoting brain health in MS; (3) focus, with cognitive stimulation and engagement as fundamental aspects of brain health; (4) empowerment, encouraging education and emotional support for patients; (5) access, to address the need for specialized care; and (6) treatment, representing the importance of starting disease-modifying therapies early.

RESULTS: We invited health care providers within the community to review and provide feedback on the DEFEAT MS mnemonic. A total of 9 providers completed the questionnaire in its entirety. Clinicians were asked to answer a series of questions regarding the efficacy of the mnemonic using a Likert-type scale with a range of 1 to 5 ("unfavorable" to "highly favorable"). Of the respondents, 89% felt the mnemonic was relevant to brain health in MS, 66% felt the mnemonic was clear and intuitive, and 89% reported the mnemonic would be an effective tool for empowering patients and caregivers.

CONCLUSIONS: To address the need for patient-facing educational tools, we present a framework for effective learning and awareness in the mnemonic DEFEAT MS (English). We also created a visual aid, which could be adapted as an educational tool for patients and the public. This educational tool was sent to health care providers, MS experts, and other key stakeholders.

DISCLOSURES: *Jules Skoda, Julian Miravalle, Kathryn Keefer: Nothing to disclose. Augusto Miravalle: Alexion, Celgene, EMD Serono, Genentech, Genzyme, Novartis (consulting fee, speakers' bureau).*

KEYWORDS: Brain Health and MS, Comprehensive Care and MS

(QOL03) Quality-of-Life Outcomes for People With Multiple Sclerosis Participating in a Day Wellness Program Over 8 Years: Pandemic and Postpandemic Findings

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BACKGROUND: The John A. Schafer, MD Multiple Sclerosis Achievement Center conducts day wellness programs to address physical, cognitive, and social well-being. As previously reported, improvements were seen in quality-of-life measures up to 3 years. The current analysis evaluated pandemic and postpandemic outcome measures of the same cohort to assess the effects during and following the COVID-19 pandemic. During 2020 and 2021, programs were modified because of the pandemic. In 2022, prepandemic programming resumed.

OBJECTIVES: To determine, through the use of patient-reported outcomes (PROs), pre- and postpandemic effects for individuals participating in a day wellness program.

METHODS: Baseline data were collected in 2017 through PRO measures for 110 people with MS. Data were assessed for individuals who had baseline data and data collected during and following pandemic restrictions. Outcome measures include the Multiple Sclerosis Impact Scale-29 (MSIS-29), Multiple Sclerosis Self-Efficacy Scale-10 item (MSSE), Godin Leisure-Time Exercise Questionnaire, and 8 sections of the Quality of Life in Neurological Disorders instrument (Neuro-QOL). Five-year data were available for 39 people in 2022, 34 in 2023 (year 6), 32 in 2024 (year 7), and 29 in 2025 (year 8).

RESULTS: Analysis of 5-year data demonstrated statistically significant increases in Neuro-QOL Depression score (P = .02) and a significant decrease in MSSE score (P = .006) when compared with baseline. The decrease in MSSE score was not significant (P = .06) in year 6, identified as the first year post pandemic, nor year 7 (P = .11) but was in year 8 (P = .02). Significant improvements in Neuro-QOL social roles and MSIS-29 scores, seen before the pandemic, were not maintained post pandemic. Statistically significant improvements were maintained in physical activity all years (5 [P = .001], 6 [P = .03], 7 [P = .01], and 8 [P = .004]) when compared with baseline.

CONCLUSIONS: The pandemic had profound negative impacts on our members' quality of life and self-efficacy. There has been improvement in these areas since pandemic restrictions were lifted, but they have not returned to prepandemic levels. However, there were maintained positive effects on self-reported physical activity during and after pandemic restrictions were lifted.

DISCLOSURES: *Brian Hutchinson: EMD Serono (consulting fee).*

KEYWORDS: Comprehensive Care and MS, Psychological Issues and MS, Wellness

(QOL04) Social Determinants of Health Are Associated With Suffering in People With Multiple Sclerosis

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BACKGROUND: Although many symptom-oriented patient-reported outcomes have been created for people with MS (PwMS), the construct of suffering has not been as

well studied. To quantify suffering in PwMS, the Wilder Multiple Sclerosis Suffering Index (WMSSI) was developed.

OBJECTIVES: We aimed to identify demographic and clinical factors contributing to increased suffering in PwMS as measured by the WMSSI.

METHODS: We recruited PwMS from the neuroimmunology clinics at the University of California San Diego through the TRAC-MS database registry study from April 2024 to October 2024. Demographic and clinical data were collected via chart review, and the WMSSI was administered. Multiple linear regression analysis, adjusted for relevant variables, was conducted using R software to explore factors influencing suffering.

RESULTS: The analysis included 196 participants (mean age, 47 ± 14 years; 79% female; 152 with relapsing-remitting MS). As expected, progressive disease was significantly associated with worse suffering scores (β = 9.7; 95% CI, 3.4-28.9, adjusted for sex, age, and racial category; $P = .02$). Black or African American racial identity was linked to higher suffering scores compared with White, non-Hispanic participants (β = 12.1; 95% CI, 1.1-36.7, adjusted for sex, age, and type of MS; $P = .04$) and non-White, non-Black participants (β = 13.1; 95% CI, 6.0-39.6, adjusted for sex, age, and type of MS; $P = .02$). Lower income levels were associated with greater suffering compared with medium-income (β = 13.5; 95% CI, 1.5-25.6, adjusted for sex, age, and racial category; $P = .03$) and high-income levels (β = 26.5; 95% CI, 15.4-37.7, adjusted for sex, age, and racial category; $P < .01$). Participants with a graduate education reported significantly less suffering compared with those with a high school education or less (β = 16.3; 95% CI, 4.6-39.6, adjusted for sex, age, racial category; $P = .01$). In a subset of 75 participants who completed additional questionnaires on mental health support and assistive device use, both mental health service use (β = 16.8; 95% CI, 2.3-31.3, adjusted for sex, age, and racial category; $P = .02$) and assistive device use (β = 15.1; 95% CI, 4.7-39.6, adjusted for sex, age, and racial category; $P = .01$) were associated with increased suffering.

CONCLUSIONS: Findings from this study highlight that PwMS with progressive disease, Black or African American identity, lower income, or lower education level and those utilizing mental health services or assistive devices experience higher levels of suffering. These findings underscore the need for targeted interventions and additional support for these vulnerable populations in MS management.

DISCLOSURES: *Sargis Manukyan, Carolyn A. Wilder, Alice Astarita, Shauna Rosengren, Kayla Jacques, Anastasie Dunn-Pirio, Jennifer Graves: Nothing to disclose. Tamara Shabi, Emily M. Schorr: Octave Bioscience (contracted research).*

KEYWORDS: Comprehensive Care and MS, Psychological Issues and MS

(QOL05) Impact of Treatment on Mobility and Health Care Utilization in Patients With Multiple Sclerosis: A Retrospective Matched Cohort Analysis

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BACKGROUND: Multiple sclerosis (MS) is a chronic immune-mediated and neurodegenerative disease of the central nervous system. Although disease-modifying therapies (DMTs) aim to improve patient quality of life by reducing relapse rate and MRI activity, their impact on disease progression is less robust. Findings from a recent study by the New York State MS Consortium observed that patients with untreated MS had the least disease progression. The authors explained the observation by assuming that those untreated possibly had milder MS. We aimed to investigate this further in an independent cohort.

OBJECTIVES: To assess the impact of exposure to DMT on mobility status and emergency department (ED) visits and hospitalizations in matched patients with MS.

METHODS: This single-center, retrospective cohort study matched 39 DMT-naive patients with MS with 39 DMT-treated patients based on sex, race, and closest matches for age, years since diagnosis, and comparable radiological disease severity and lesion distribution at diagnosis. The primary outcome was walking status (unable to walk vs able to walk assisted/unassisted) at the patient's most recent visit. The secondary outcomes included the cumulative number of ED visits and hospitalizations since diagnosis. Logistic regression and Poisson regression were used, as appropriate, to assess the impact of treatment on mobility, ED visits, and hospitalizations, adjusting for years since diagnosis.

RESULTS: The mean age and follow-up duration in years (SD) were 61 (± 13) and 19 (± 14), respectively, and the cohort was 90% White and 82% female. There was no significant difference in walking status ($P = .6$), although it was numerically better in untreated patients. Treated patients had more ED visits (incidence rate ratio [IRR], 1.68; 95% CI, 1.39-2.03; $P < .001$) and hospitalizations (IRR, 1.71; 95% CI, 1.32-2.23; $P < .001$) compared with untreated patients.

CONCLUSIONS: DMT exposure did not affect long-term patient mobility. However, treatment was associated with increased health care utilization. These eye-opening findings call for careful consideration of the risks and benefits of DMTs.

DISCLOSURES: *Faizan Ahmed, Roberto S. Hernandez: Nothing to disclose. Ahmed Z. Obeidat: Alexion Pharmaceuticals, Amgen, AstraZeneca, Banner Life Sciences, Biogen, Bristol Myers Squibb, EMD Serono, Sanofi Genzyme, TG Therapeutics (consulting fee, speakers' bureau); BD Biosciences, Biologix Solutions, Celgene, Genentech, GW Pharmaceuticals, Horizon Therapeutics, Jazz Pharmaceuticals, Novartis, Sandoz, Viela Bio (consulting fee).*

KEYWORDS: Disease-Modifying Treatments in MS, Patient Outcomes

(QOL06) Assessing Mental Health Literacy and Its Impact on Quality of Life in People With Multiple Sclerosis: A Cross-Sectional Study

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BACKGROUND: Mental health literacy (MHL) refers to the awareness and understanding of mental health issues. Among people with multiple sclerosis (PwMS), the prevalence of mental disorders has been rising, highlighting the need for reliable tools to assess MHL specifically within this population. To date, no studies have been conducted to measure the level of MHL and its impact on quality of life (QOL) in PwMS, underscoring the importance of addressing this gap to improve mental health outcomes and overall well-being in this patient group.

OBJECTIVES: To assess the level of MHL in PwMS and evaluate its impact on their QOL.

METHODS: A cross-sectional study was conducted from January 1, 2024, to August 30, 2024. Data were collected using the Mental Health Literacy Questionnaire-Short Version for Adults (MHLq-SVa) and the 27-item Multiple Sclerosis Quality of Life Questionnaire (MS-QLQ27), supplemented with 4 items assessing satisfaction with nursing interventions. Data analysis included descriptive and inferential statistics (independent sample *t* test, Mann-Whitney *U* nonparametric test, and Pearson correlation), performed using IBM's SPSS software.

RESULTS: A total of 170 participants were enrolled; most were women (88.8%; n = 151) with a mean age of 36.46 years and a mean age of MS onset of 28.26 years. Most participants were employed (69.4%; n = 118) and diagnosed with relapsing-remitting MS (91.8%; n = 156). Treatments included natalizumab (19.4%; n = 33), ocrelizumab (13.5%; n = 23), and ofatumumab (8.2%; n = 14). The MHLq-SVa mean score was 67.08, reflecting the general awareness and understanding of mental health issues within this population. Sex differences were observed in mental health literacy, with women scoring higher in overall literacy (Total MHLq-SVa $P = .049$), showing greater knowledge of mental health issues (Factor 1; $P = .003$) and holding fewer misconceptions and stereotypes (Factor 2; $P = .048$) compared with men. No other factors demonstrated significant sex differences. Mann-Whitney *U* tests showed a significant difference in the Global MS-QLQ27 score based on educational level ($P = .001$). Pearson correlation analysis revealed several significant relationships between global MS-QLQ27 score correlated with Factor 1 ($r = 0.184$; $P = .016$), age ($r = 0.190$; $P = .013$), and education level ($r = 0.270$).

CONCLUSIONS: Findings from this study highlight that women with MS demonstrate higher MHL and fewer misconceptions compared with men. Additionally, higher education levels were associated with improved QOL outcomes, emphasizing the influence of demographic factors. Targeted educational interventions could improve MHL and enhance the QOL for PwMS.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Management of Activities of Daily Living in MS, Nursing Management in MS, Psychological Issues and MS

(QOL07) Analyzing Comorbidities in People With Multiple Sclerosis in the United States Using Administrative Health Claims Data

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OBJECTIVES: To analyze comorbidities in people with multiple sclerosis (MS) in the United States by applying a validated Komodo-derived algorithm to administrative health claims (AHC) data sets.

METHODS: An AHC data set using Komodo Healthcare Map was analyzed in Prism to provide national insights into comorbidities within the MS population. The data were measured using the *International Classification of Diseases, Ninth Revision* and *International Statistical Classification of Diseases, Tenth Revision* (*ICD-10*) code G35, the diagnosis code for MS, between January 1, 2023, and December 31, 2023. The data were stratified by common diagnoses relative to the matched sample population using *ICD-10* codes and ranked based on strength of the correlation coefficient.

RESULTS: A cohort of 623,165 patients with a confirmed MS diagnosis was generated. Results were determined by correlation coefficients and included patient count. The most relevant comorbidities include body mass index (40.0-44.9) or morbid obesity class 3 (0.34; 73,691 patients), optic neuritis (0.18; 71,651 patients), acidosis (0.16; 16,597 patients), neuromuscular dysfunction of bladder (0.16; 111,629 patients), and depression (0.12; 116,878 patients). Of 623,165 individuals, 565,936 were included within the patient journey data. The patient journey reflects 24 months before and 24 months after an MS diagnosis and follows a patient's interactions with the health care system. Results identified percentage of diagnoses and most frequent diagnosing specialty. Most notable diagnoses include hypertension (12% diagnosed 1 to 6 months before MS diagnosis; 26% diagnosed 0 to 5 months post diagnosis), long-term drug therapy (6% before MS; 19% post MS), vitamin D deficiency (5% before MS; 16% post MS), hyperlipidemia (6% before MS; 14% post MS), anxiety disorder (5% before MS; 11% post MS), and fatigue (4% before MS; 10% post MS). The most common diagnosing specialties include internal medicine, neurology, and family practice.

CONCLUSIONS: The National Multiple Sclerosis Society has used claims data to inform upstream engagement aimed at reducing the time to diagnosis, promoting early medical intervention, and advocating for increased education of MS symptoms among primary care providers. Collaboration with these providers facilitates earlier identification of MS, ensures timely referrals to an MS specialist, and fosters holistic, patient-centered care. Such partnership can enhance early detection, improve patient outcomes, and reduce delays in accessing treatment.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comorbidities in MS, Comprehensive Care and MS, Epidemiology of MS

(QOL08) What to Expect at Your Multiple Sclerosis Neurology Appointment: A Guide to Increase Veteran Engagement, Self-Efficacy, and Satisfaction

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BACKGROUND: People with multiple sclerosis (PwMS) need quality information to help manage their symptoms and disease progression. Some PwMS have anxiety related to their neurology appointments. Others may feel that they lack the procedural knowledge to ask questions about medications or symptoms, leaving them as passive participants in their care plans. The hub/spoke system of the US Veterans Administration (VA) Spinal Cord Injury and Disorders (SCI/D) centers focuses on a hub site (Tibor Rubin VA) featuring clinical expertise in care related to SCI/D. Clinical providers attend to 150 veterans with MS from a 200-mile radius. Long commutes and impaired mobility to access the neurology clinic can lead to cognitive fatigue and forgetting questions that they felt were important before the day of the visit. Memory and expression can also affect self-efficacy and self-advocacy. Providers may have limited time to answer questions during appointments, leading to a discrepancy between the needs of the PwMS and the provider's full comprehension of the complexity of these needs. The Multiple Sclerosis Support Program is a multidisciplinary online support group presented via telehealth. The departments of social work, occupational therapy, and psychology cofacilitate these meetings, which are open to veterans with MS in the SCI/D system. There is a monthly education session to review topics that the group may find helpful in navigating the disease process. One successful educational session was a presentation on how to prepare for a neurology appointment. This included what members believed were crucial questions to ask and what providers stated were most important to know about PwMS. This presentation was packaged into a preparation guide for members to reference during future appointments. Satisfaction, engagement, and self-efficacy are anticipated improvements for those PwMS who use this guide.

OBJECTIVES: (1) Participants will be able to describe how PwMS can increase satisfaction with their visit with neurology using the preparation guide. (2) Participants will be able to describe how PwMS can have better health outcomes, including medication adherence, when using a preparation guide. (3) Participants will be able to name 1 facet of the preparation guide that they can incorporate into their own practices.

METHODS: Participation guides were mailed out to veterans with upcoming MS neurology appointments to organize their thoughts and record any new or worsening symptoms. Veterans were encouraged to bring these back to their appointments to review with their neurologists. A patient experience survey was mailed to patients as a follow-up to their visit.

RESULTS: Use of guides began in January 2025. Patient experience surveys are to be mailed out to veterans upon completion of their neurology appointment. Data will be captured and collated to show effectiveness.

CONCLUSIONS: Anecdotal data are showing a higher level of engagement for those who used the guide. The survey data will be presented during the poster presentation.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Management of Activities of Daily Living in MS, Self-Advocacy in MS

(QOL09) Perceptions of Discreetness Among Female Intermittent Catheter Users With Neurogenic Lower Urinary Tract Dysfunction

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BACKGROUND: Despite intermittent self-catheterization (ISC) being the preferred bladder management method, there is a need to better understand the real-life experiences and challenges of ISC users. The Continence Care Registry collects electronic patient-reported outcomes to explore catheter preferences, such as compact or portable catheters, health care usage, and ISC's impact on quality of life (QOL).

OBJECTIVES: To examine ISC's impact on QOL, specifically the discreetness of the catheter type, for women with neurogenic lower urinary tract dysfunction (NLUTD), including those with multiple sclerosis.

METHODS: Baseline data from the United States, Canada, and the United Kingdom were collected. A subgroup of 53 women with reported NLUTD-associated diagnoses that required them to perform ISC was identified: 27 used compact catheters, and 26 used noncompact catheters. Data from the discreetness domain of the Intermittent Self-Catheterization Questionnaire were analyzed descriptively.

RESULTS: Among compact catheter users (n = 27), 89% agreed their catheter was discreet and enabled confidence while catheterizing away from home. Similarly, 89% felt they could use their catheter discreetly and 96% found it easy to carry enough catheters daily. However, only 48% found catheter disposal easy and 63% felt they could discreetly dispose of their catheter in public.

CONCLUSIONS: Females using compact catheters reported higher confidence and satisfaction in discreet use and portability compared with noncompact users. However, disposal challenges were noted across both groups, potentially affecting privacy, independence, and ISC adherence. Challenges with catheter disposal outside the home may affect perceptions of privacy and consequently have the potential to limit independence by affecting activity outside the home, becoming a barrier to ISC adherence. These findings suggest that although compact catheters may offer advantages in terms of discreetness and portability, further improvements are needed to address issues related to catheter disposal in public settings.

DISCLOSURES: *Diane K. Newman: Hollister Incorporated (consulting fee). Jessica A. Simmons, Daniel A. Gordon: Hollister Incorporated (salary).*

KEYWORDS: Management of Activities of Daily Living in MS, Nursing Management in MS, Psychological Issues and MS

(QOL10) Impact of Adverse Childhood Experiences on Long-Term Quality of Life in Pediatric-Onset Multiple Sclerosis

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BACKGROUND: People with pediatric-onset multiple sclerosis (POMS) historically take longer to reach disability milestones than their adult counterparts but do so at a younger age. Little is known about long-term health-related quality of life (HRQOL) in POMS or the factors that may modify it. Adverse childhood experiences (ACEs) are traumatic life events associated with decreased brain volumes, chronic physical/mental health diagnoses, and poorer quality of life overall. The impact of ACEs on the developing brain of patients with POMS into adulthood is unexplored.

OBJECTIVES: We aimed to evaluate the relationship between ACEs and demographic factors with long-term HRQOL, symptom severity, and disability measures in adults with POMS.

METHODS: We surveyed 98 adults with POMS recruited from the North American Research Committee on Multiple Sclerosis, Nationwide Children's Hospital, and The Ohio State University Wexner Medical Center. Questionnaires measured quality of life, symptom severity, disability (Patient-Determined Disease Steps, PDDS), resiliency, and ACEs. We used the Kruskal-Wallis test to measure the association between ACE score severity, QOL, and symptom burden.

RESULTS: Adults with higher ACE scores reported worse mental (P =.05) and physical (P <.01) HRQOL as well as more severe symptoms (P <.01). However, ACEs were not associated with disability level on PDDS (P >.9). In those with higher resiliency scores, higher ACEs burden did not significantly associate with lower mental HRQOL (P =.2) as it did for those with lower resiliency scores (P =.02). Educational attainment, income, and insurance status had significant relationships with HRQOL scores (all P <.05).

CONCLUSIONS: Childhood adversities leave a lasting mark on adults with POMS, shaping their lived experience of symptom burden and quality of life more than physical disability. Resiliency may positively modify HRQOL. Future research should evaluate whether early resiliency training could protect against the negative effects of ACEs in this population.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Pediatric-Onset MS, Psychological Issues and MS

(QOL11) Patient-Reported Outcomes from the OLIKOS Study of Patients With Relapsing Multiple Sclerosis Who Switched to Ofatumumab From Intravenous Anti-CD20 Therapies

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BACKGROUND: OLIKOS (NCT04486716) was a single-arm, prospective, multicenter phase 3b trial assessing the efficacy/safety of switch from intravenous (IV) anti-CD20 therapy, ocrelizumab (OCR)/rituximab (RTX) to subcutaneous (SC) anti-CD20 therapy ofatumumab (OMB) in people with relapsing multiple sclerosis (PwRMS). All PwRMS (n =84) with evaluable imaging assessments met the primary end point, which was no change, or a reduction in the number of gadolinium-enhancing lesions at month (M) 12; these data have been presented.

OBJECTIVES: To characterize patient-reported treatment satisfaction, convenience, and quality of life (QOL) after switching to OMB.

METHODS: OLIKOS enrolled PwRMS aged 18 to 60 years who were on IV OCR or RTX for 1 year or longer, were clinically stable on IV therapy, and switched for reasons other than safety/lack of efficacy. Participants received 20 mg SC OMB monthly, following loading doses on days 1, 7, and 14. Patient-reported outcomes included the 9-item Treatment Satisfaction Questionnaire for Medication (TSQM-9), the 12-item Short-Form Survey (SF-12), and the 2-item Patient Global Impression of Change questionnaire. Outcomes were assessed at baseline (BL) for TSQM-9 and SF-12 only and M1, 6, and 12 for all. Descriptive statistics assessed change from BL.

RESULTS: The full analysis set included a total of 102 patients. Mean (SD) age at BL was 43.5 (8.2) years, 67.6% were women, 76.5% were White, and 99% used OCR before switching to OMB (1 used RTX). Mean (SD) duration of MS was 9.4 (7.1) years. Mean (SD) BL scores on the TSQM-9 global satisfaction, effectiveness, and convenience domains were 62.6 (24.0), 61.1 (21.2), and 65.7 (21.6), respectively. At M12, treatment satisfaction increased for all 3 domains, with mean (SD) change from BL of 9.3 (30.7) for global satisfaction, 8.6 (22.9) for effectiveness, and 16.4 (23.1) for convenience (n=42). On the SF-12 Physical (PCS) and Mental Component Summary (MCS), mean BL scores were 43.8 (9.4) and 50.5 (10.8), respectively. Mean (SD) change from BL to M12 was 1.01 (5.4) on PCS and −1.00 (11.3) on MCS. On the PGIC, 56% (47/84) of patients with assessments reported improvement after 1 month of OMB. At M12, 49.2% (32/65) reported improvement, whereas 26.2% (17/65) remained stable and 24.6% (16/65) deteriorated.

CONCLUSIONS: In PwRMS who switched from IV anti-CD20 therapy to SC OMB, patient-reported treatment satisfaction and overall impression of current therapy at M12 were improved vs BL, with pronounced improvement in convenience, and QOL was generally maintained.

DISCLOSURES: *Le H. Hua: Alexion, EMD Serono, Genentech, Genzyme, Horizon, Novartis, TG Therapeutics (consulting fee, speakers' bureau); Genentech (contracted research). Brandon Brown, Elizabeth Camacho, Erik Houtsma: Novartis Pharmaceuticals (salary). Benjamin M. Greenberg: Alexion, Arialys, Clene, Cycle, EMD Serono, Genentech/Roche, Sanofi/Genzyme, Amgen, IQVIA, Novartis, PHAR, Sandoz, Signant Health, Syneos Health, TG Therapeutics (consulting fee); Clene, GenrAb (equity); National Institutes of Health, Regeneron (contracted research); Siegel Rare Neuroimmune Association (unpaid member of the board); UpToDate (royalty). Roland G. Henry: Atara, Boston Pharma, Genentech/Roche, MedDay, Neurona Therapeutics, Novartis, QIA Consulting, Sanofi-Genzyme (consulting fee, contracted research). Enrique Alvarez: Atara, Biogen, Bristol Myers Squibb, Genentech/Roche, National Institutes of Health, National Multiple Sclerosis Society, Novartis, Patient-Centered Outcomes Research Initiative, Rocky Mountain MS Center, Sanofi, TG Therapeutics (research support); Biogen, Celgene/Bristol Myers Squibb, Cionic, EMD Serono/Merck, Genentech/Roche, Horizon/Amgen, Novartis, Sanofi, TG Therapeutics (consulting fee).*

KEYWORDS: Disease-Modifying Treatments in MS, Treatment Satisfaction; Patient-Reported Outcomes

(QOL12) Living With Cognitive Impairment in Multiple Sclerosis: Insights from a Photovoice Pilot Study

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BACKGROUND: Although the physical impacts of multiple sclerosis (MS) are well documented with established treatment protocols, the cognitive impacts on the daily lives of the estimated 70% of people with MS affected remain less examined in clinical research. This pilot study builds on existing research on the cognitive and social impacts of acquired brain injuries, explicitly shedding light on the underexplored lived experiences of individuals navigating cognitive impairment in MS.

OBJECTIVES: This study aims to explore the lived experiences of individuals with MS-related cognitive impairment to inform future clinical research, nursing protocols, and training. By identifying patient challenges and adaptive strategies, this study seeks to lay the groundwork for expanded research and improved care practices tailored to the cognitive dimensions of MS.

METHODS: This pilot study will use photovoice, a participatory visual research method, to explore how individuals with MS experience and navigate living with cognitive impairment. Participants will take photographs to answer study questions and participate in narrative interviews about their photos. Data analysis methods will identify themes across the study participants' data (photos and interviews) and use a case study approach to delve more deeply into an individual's experiences and stories observed in their photos and text.

RESULTS: The results will be shared, including photos, text, themes, and case study findings. Implications for an expanded study, future research, and application of study learning to nursing protocols and training will be identified.

CONCLUSIONS: This study will create opportunities for participants to share their perspectives on the challenges, strengths, and adaptations associated with impairments from MS, focusing on the cognitive aspects of their experiences. Findings from this pilot study will inform the design of a larger-scale study utilizing photovoice and photo elicitation aimed at thematic evaluation of the lived experiences of cognitive impairment in MS. The findings of the more extensive follow-on study are anticipated to inform strategies to enhance nursing care, with an emphasis on practical approaches for training and for supporting nurses working with patients with MS in diverse settings.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Cognitive Impairment and MS, Comprehensive Care and MS, Psychological Issues and MS

(QOL13) The Pattern of Cognitive Fatigability Differs Between People With Multiple Sclerosis and Controls

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BACKGROUND: Cognitive impairment, including decreased processing speed, is a common and debilitating consequence of multiple sclerosis (MS). There is emerging evidence that cognitive fatigability is more pronounced in people with MS than in control populations, but little is known about its correlates.

OBJECTIVES: This study compared cognitive fatigability in people with MS and healthy controls and explored whether demographic and MS-related variables correlate with cognitive fatigability among people with MS.

METHODS: The sample included 432 participants: 392 people with MS and 40 healthy controls. Participants completed an online Zoom meeting to assess cognitive function using the Symbol Digit Modalities Test (SDMT) as well as an online REDCap survey. The number of correct symbol-digit pairs on the 90-second SDMT was

recorded every 30 seconds to understand cognitive fatigability. The data were analyzed using IBM's SPSS v27.

RESULTS: The mean number of correct responses per 30-second period differed between MS and controls (P <.05). There was a linear decline in the control group (P <.001), whereas there was a quadratic decline in the MS group (P <.001). None of the demographic variables (age, sex, race, and education level) nor the MS-related variables (disability, MS course, and disease duration) were significantly associated with cognitive fatigability in the MS sample.

CONCLUSIONS: The pattern of cognitive fatigability is quadratic and steeper in people with MS than in healthy controls. However, this pattern was not correlated with MS-related variables, nor with various demographic parameters. Researchers might consider health behaviors, including sleep, diet, and physical activity, as correlates of cognitive fatigability in MS.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Cognition, Management of Activities of Daily Living in MS

(QOL14) Real-World Comparison of Annualized Relapse Rate in Patients With Multiple Sclerosis Treated With Ofatumumab vs Ocrelizumab

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BACKGROUND: Ofatumumab (OMB) and ocrelizumab (OCR) are CD20-directed monoclonal antibodies approved for treatment of relapsing multiple sclerosis (MS). In the absence of a head-to-head trial, real-world (RW) data can inform the relative effectiveness of OMB vs OCR in a broad MS population.

OBJECTIVES: To compare annualized relapse rate (ARR) in patients with MS treated with OMB vs OCR using claims data from the United States.

METHODS: A retrospective cohort study was performed using Optum Clinformatics claims data (August 2019-July 2024) for adults with 1 or more claims for OMB or OCR on or after August 20, 2020; 1 or more inpatient (IP) or 2 or more outpatient (OP) MS diagnoses 30 or more days (d) apart; continuous enrollment for 12 or more months (M) preindex and 6 or more months post index; and persistent OMB or OCR use for 6 or more months post index. Treatment-naive subcohorts included patients without MS-specific disease-modifying therapy use 12 M preindex. Patients were matched 1:1 in overall and treatment-naive cohorts to balance demographic/disease characteristics. Relapse was defined as IP stay with primary MS diagnosis or OP or emergency department visit with MS diagnosis with a claim for high-dose oral corticosteroid, intravenous methylprednisolone (excluding ±5 d of OCR claim), corticotropin, or plasma exchange within 7 d. ARR was assessed using negative binomial regression over a variable follow-up period and compared between cohorts using incidence rate ratio (IRR).

RESULTS: Of 2604 eligible patients (mean age, 49 years; 70% female), 751 were in the OMB cohort and 1853 in OCR. Treatment-naive subcohorts included 315 OMB and 1104 OCR patients. After matching, overall cohorts and treatment-naive subcohorts were balanced except for index year. Overall mean follow-up was 1.50 years, ARR (95% CI) was 0.10 (0.08-0.13) in OMB vs 0.14 (0.12-0.17) in OCR, equating to a 31% lower relapse incidence for OMB (IRR, 0.69; 95% CI, 0.51-0.94; P <.05). The difference remained significant after index year adjustment. Overall mean follow-up was 1.37 years, ARR (95% CI) was 0.10 (0.07-0.15) in treatment-naive OMB vs 0.18 (0.13-0.25) in OCR, equating to a 41% lower relapse incidence in OMB (IRR, 0.59; 95% CI, 0.35-0.99; P <.05). After index year adjustment, ARR was numerically lower in OMB (IRR, 0.61; 95% CI, 0.36-1.02; P =.06).

CONCLUSIONS: In RW MS cohorts, OMB had significantly lower ARR vs OCR. In treatment-naive subcohorts, ARR was numerically lower in OMB. After index year adjustment, a nonsignificant trend was observed. These findings support potential benefits of OMB to reduce relapse vs OCR while warranting further investigation.

DISCLOSURES: *Ming-Hui Tai, Brandon Brown, Abhijit Gadkari: Novartis Pharmaceuticals (salary). Riley Taiji, Francis Vekeman: Novartis Pharmaceuticals (consulting fee).*

KEYWORDS: Claims Analysis; Relapse, Disease-Modifying Treatments in MS

(QOL15) Participation of Children With Multiple Sclerosis in Home, School, and Community Life: A Socioecological Approach

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BACKGROUND: Up to 75% of children and adolescents with multiple sclerosis (MS) report symptoms of depression and fatigue. Participation in different life activities has been found to be beneficial for the physical and mental health of children with chronic illnesses. However, little is known about the relationships of participation in home, school, and community activities; the environment; and health outcomes in children and adolescents with MS.

OBJECTIVES: To estimate the level of participation of children and adolescents with MS in home, school, and community activities and its associations with disease progression, mental health, quality of life, and fatigue.

METHODS: Consecutive children and adolescents with MS were recruited from the Pediatric Neuroinflammatory Disorders Clinic at the Hospital for Sick Children. After consent, participants completed questionnaires on participation, environmental barriers, depression, anxiety, fatigue, and quality of life. Descriptive and inferential analyses were conducted for differences and correlations.

RESULTS: In children and adolescents with MS (n=22, female=15, median age=16, IQR=1.75; recruitment ongoing), higher participation in home, school, and community life was associated with lower perceived environmental barriers (r_s=−0.74, P<.01), lower depression (r_s=−0.54, P<.05), and lower fatigue (r_s=0.42, P<.05); higher perceived environmental barriers were associated with higher depression (r_s=0.66, P<.01), higher anxiety (r_s=0.56, P<.01), lower quality of life (r_s=−0.56, P<.01), and higher fatigue (r_s=−0.51, P<.05).

CONCLUSIONS: In children and adolescents with MS, participation in home, school, and community life may be associated with better mental health outcomes. Environmental barriers perceived by these individuals may be associated with decreased participation and poorer mental health outcomes. Completion of recruitment and comparison with control may further clarify these associations. Future studies are needed to assess the directionality of these relationships and to investigate the potential of participation and environmental modifications in improving symptoms in this population.

DISCLOSURES: *Paul Y. Yoo, Marcia Finlayson: Nothing to disclose. E. Ann Yeh: Alexion, Hoffman-LaRoche (consulting fee); Pipeline Therapeutics (data safety board).*

KEYWORDS: Lifestyle and Environmental Factors, Psychological Issues and MS

(QOL16) The Role of Glucagon-Like Peptide-1 Agonists in Managing Obesity Among Patients With Multiple Sclerosis

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BACKGROUND: Obesity in people with multiple sclerosis (MS) is associated with worsened disease progression, increased inflammation, and reduced mobility, underscoring the importance of effective weight management. Traditional strategies, such as diet and exercise, may be less effective in MS due to individuals' physical disability and fatigue. Glucagon-like peptide-1 (GLP-1) agonists, widely used in type 2 diabetes, have shown efficacy in weight reduction and metabolic improvements, but their potential in MS populations remains unclear.

OBJECTIVES: To evaluate the efficacy, safety, and tolerability of GLP-1 agonists in managing obesity among people with MS, focusing on weight, mental health, and functional outcomes.

METHODS: We conducted a chart review of 19 people with MS who initiated GLP-1 therapy between 2023 and 2024 for weight management. Baseline and follow-up measures included body mass index (BMI), Modified Fatigue Impact Scale (MFIS-21), Timed 25-Foot Walk (T25-FW), cognitive evaluation scores, Patient Health Questionnaire (PHQ-9), and Generalized Anxiety Disorder (GAD-7). Insurance coverage, comorbidities, and reasons for therapy discontinuation were reviewed.

RESULTS: We looked at 16 patients treated for at least 3 months. Of these, 10 had a diagnosis of obstructive sleep apnea, 9 had hyperlipidemia, 7 had hypertension, 3 had prediabetes or diabetes, and 1 had idiopathic intracranial hypertension. Over that time frame, median BMI decreased from 36.1 (28.5, 32.3) to 31.5 (28.5, 33.85). Utilizing CDC obesity classes, 1 patient increased from class 2 to 3 obesity, 6 did not change, 5 dropped 1 class, and 4 dropped 2 classes. PHQ-9 improved from 6 (IQR, 3.75-9.25) to 5.5 (2-7.5), GAD-7 improved from 4 (IQR, 0.75-6.25) to 2 (0.25-6.5), MFIS-21 increased from 31.5 (24.75-56.75) to 34.5 (22.5-54.0) and T25-FW increased from 6.09 (5.1-8.4) to 6.94 (5.05-8.15). One patient discontinued treatment due to reaching target weight, 1 for gastrointestinal adverse effects, and 1 for lack of efficacy.

CONCLUSIONS: Most patients on GLP-1 agonist therapy had a reduction in BMI. We also observed improvement in mental health outcomes. Although we saw an increase in fatigue scores and the T25-FW, further exploration is needed to determine whether this may change with longer treatment duration. Of note, insurance coverage for GLP-1

medications remains a barrier to access. Of our 19 patients, only 4 were covered through insurance.

DISCLOSURES: *R. Chase Cullen: TG Therapeutics (consulting fee). Katherine Gwin, Kaelianne Newbold, Nicole Dooda, Tyler Cress, Cindy Smith: Nothing to disclose. Nina Bozinov: EMD Serono (consulting fee, speakers' bureau); Genentech (consulting fee).*

KEYWORDS: Economic Issues and MS, Symptom Management

(QOL17) Urinary Tract Infection Hospitalization Outcomes in Patients With Multiple Sclerosis and Neurogenic Bladder: A Population-Based Study

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BACKGROUND: Multiple sclerosis (MS) is the most common autoimmune demyelinating disorder that affects the central nervous system in young people. This progressive disease leads to substantial costs to both the individual and the health care system. Bladder dysfunction is a common complication of MS, often progressing to neurogenic bladder (NB). Current data are lacking on demographics and in-hospital outcomes of acute urinary tract infections (UTIs) in patients with MS and NB.

OBJECTIVES: We seek to establish the effect of acute UTIs on people with MS (PwMS), stratifying for NB, on demographics and in-hospital outcomes.

METHODS: Hospitalization data from PwMS hospitalized for acute UTI were abstracted from the 2016 to 2021 National Inpatient Sample and stratified by whether the patient had a concomitant diagnosis of NB. To assess whether NB was associated with differences in hospitalization outcomes, we estimated logistic regression and lognormal models. Multivariate models were estimated to adjust for age, comorbidity burden, type of UTI, urbanicity, and facility geographic location.

RESULTS: In our cohort, there were an estimated 31,635 hospitalizations for acute UTI where the patient had MS. Of these hospitalizations, 26% (n=8310) had an NB diagnosis. Hospitalizations of patients with NB were more frequent at urban and large bed-size facilities than hospitalizations of patients without NB (urban: 89.58% vs 87.07%, respectively; $P<.001$; large bed-size: 47.35% vs 41.78%; $P=.004$). Patient income varied between hospitalizations with and without NB (highest income quartile: 26.78% vs 22.29%; $P<.001$). Hospitalizations of patients with MS and NB were associated with 13% longer adjusted length of stay (LoS) and 4% greater adjusted cost than hospitalizations of those without NB (LoS: 95% CI, 1.07-1.19; $P<.001$; cost: 95% CI, 1.01-1.08; $P=.010$). Compared with hospitalizations without NB, hospitalizations of patients with NB were associated with 28% lower adjusted odds of routine discharge and 47% greater adjusted odds of discharge to home health care (routine: 95% CI, 0.63-0.82; $P<.001$; home health care adjusted: OR, 1.47; 95% CI, 1.30-1.66; $P<.001$).

CONCLUSIONS: Concomitant NB in hospitalizations for acute UTI in PwMS was associated with increased LoS, cost, and discharge to home health care compared with hospitalizations without NB. Notably, there were differences in patient income and facility region and size between those with and without NB. These findings highlight potential disparities in the diagnosis of NB and access to specialized NB care in the United States.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Economic Issues and MS, Epidemiology of MS

(QOL18) Development of Novel Biomechanical Outcomes Using Motion Capture to Characterize Hand Function in Multiple Sclerosis.

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BACKGROUND: Multiple sclerosis (MS) often significantly impacts upper extremity function. Currently, the most widely utilized assessment, the 9-Hole Peg Test (9HPT), is limited to a single outcome measure of total time, which can be insensitive to impairment in certain populations.

OBJECTIVES: To develop novel biomechanical outcomes that better characterize upper extremity function in people with MS (PwMS).

METHODS: For the study, 15 PwMS and 15 healthy controls (HC) completed the manual dexterity test (MDT), an iPad adaptation of the 9HPT, with their dominant hand and nondominant hand. A Kinect device captured bilateral, 3-dimensional, multijoint hand motion while performing the MDT. An advanced mathematical model, using MDT data and closure coefficients derived from motion capture analysis, was then constructed to yield novel outcomes. Cross-sectional associations between the MDT outcomes (traditional and novel) and clinical characteristics (arm spasticity, dysmetria, upper extremity weakness) were evaluated. Cohen *d* effect size was calculated to evaluate the ability of the MDT outcomes to distinguish MS and HC.

RESULTS: The study was completed by 15 PwMS (mean age, 55.91 years; disease duration, 13.90 years) and 15 HC (mean age, 40.45 years). MDT total time (traditional) and the novel measure of time-to-grab showed a consistent large effect size between dominant hand (0.92 and 1.50) and nondominant hand (1.10 and 1.10). The novel measure of movement delay showed a moderate correlation with disease duration of MS (dominant, −0.55; nondominant, −0.52), which was not consistent for total time (0.52, 0.23). Movement time and MDT total time were moderately correlated with arm spasticity for dominant and nondominant hands (0.52/0.64, 0.46/0.49).

CONCLUSIONS: MDT total time showed an excellent ability to discriminate PwMS from HCs for both dominant and nondominant hand movements, which supports the continued use of MDT total time as a conventional measure. Several novel measures were also identified that demonstrated an excellent ability to discriminate PwMS from HCs and correlated with various clinical measures. Movement delay, movement time, time to insert, and time-to-grab were moderately correlated with different clinical characteristics, suggesting unique measurement properties. Further studies are needed to evaluate the sensitivity of these measures over time to disease progression.

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KEYWORDS: Motion Capture

(QOL19) Accelerating the Translation of Multiple Sclerosis Research Into Practice With People-Powered Research Dissemination

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BACKGROUND: A significant gap exists between multiple sclerosis (MS) research discoveries and their application in clinical practice. Traditional dissemination methods, such as journal articles and conference presentations, are often inaccessible to patients and nonresearcher stakeholders. These methods lack the engagement needed for shared decision-making, delaying the practical benefits of research findings. This challenge is particularly critical in MS, where timely, actionable information can significantly impact outcomes.

OBJECTIVES: To develop a scalable, multimedia dissemination strategy cocreated with the MS community, aimed at making research findings accessible, relevant, and actionable for patients, caregivers, clinicians, and researchers.

METHODS: The iConquerMS Dissemination Capacity-Building Project employed a multiphase approach rooted in stakeholder engagement. A 13-member multistakeholder steering committee guided project development, ensuring inclusion of historically underrepresented groups. A landscape review and survey of more than 300 MS stakeholders identified diverse preferences for receiving and applying research findings. These insights shaped a multimedia dissemination plan, featuring plain language summaries, infographics, webinars, podcasts, and video abstracts to meet varying audience needs. A Patient-Centered Outcomes Research Institute–funded study served as a pilot for the approach, and stakeholder focus groups and surveys provided iterative feedback to refine the strategy.

RESULTS: Stakeholders emphasized the need for resources that cater to diverse learning styles and preferences, including short and long formats. Short-form materials, such as plain language summaries and infographics, provided concise updates, while long-form materials, including research education, webinars, and podcasts, allowed deeper engagement with highly relevant topics. This approach empowered stakeholders to choose how they interacted with research findings, enhancing accessibility and relevance.

CONCLUSIONS: People-powered dissemination models can accelerate research translation by addressing diverse stakeholder needs. The iConquerMS multimedia approach fosters accessibility, engagement, and real-world impact, providing a model for inclusive and effective dissemination. Future efforts will expand these strategies to reduce disparities in MS care and ensure equitable access to

research benefits.

DISCLOSURES: *Stephanie Buxhoeveden: Genentech (consulting fee). Robert N. McBurney: EMD Serono (consulting fee). Hollie Schmidt: EMD Serono, Novartis, Quest, Sandoz (contracted research). Sara Loud: EMD Serono, Novartis, Sandoz (contracted research). Laura Kolaczkowski, Surachat Ngorsuraches, Seth Morgan, Cassie Martin, Sara Bernstein: Nothing to disclose. Sherilyn George-Clinton: Aledade (salary).*

KEYWORDS: Translational Research

(QOL20) Experiences of COVID-19 Infection and Recovery in People With Multiple Sclerosis: A Qualitative Analysis

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BACKGROUND: Individuals with chronic medical conditions experienced delays in receiving usual care during the COVID-19 pandemic, exposing them to risk for complications and even death. People with multiple sclerosis (PwMS) constitute a vulnerable population and may have experienced a disproportionate burden during the COVID-19 pandemic. PwMS who contracted COVID-19 have experienced alterations in their disease course and/or progression and required modifications to their treatment therapies. Limited evidence is currently available about the impact of COVID-19 infection on the quality of life and experiences of PwMS.

OBJECTIVES: To better understand how PwMS experienced the COVID-19 pandemic, we conducted a qualitative study on their perceptions and experiences from diagnosis through recovery.

METHODS: From across the United States, 8 PwMS who contracted COVID-19 (COVID-19 diagnosis duration >2 years at time of interview: 87.5%; single vs multiple infection incidences: 75% vs 25%, respectively) were invited to participate in a brief survey and 45- to 60-minute interviews. A semistructured interview asked about the participants' experiences with COVID-19 infection, recovery, and its impact on their MS. The interviews were transcribed using Otter. ai and Panopto and coded using content analysis in ATLAS.ti. Consensus between coders was reached via discussion.

RESULTS: Major themes included medical and self-management advice on infection and recovery, medical and behavioral suggestions to health care providers, the cross-interaction between COVID-19 infection and MS, changes in MS management, perceptions of health and MS, COVID-19 infection symptoms and experiences, difficulties with long-term recovery (including emotional, financial, social, physical and functional impact), lessons learned, and lingering post–COVID-19 symptoms.

CONCLUSIONS: Findings from this study enhance our general understanding of the consequences of COVID-19 infection in PwMS and suggest areas for targeted interventions to improve their experience throughout the course of MS and COVID-19 or other similar infections.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Immunology and MS, Management of Activities of Daily Living in MS

(QOL21) The Intersection of Multiple Sclerosis and Coronavirus Infection: Examining Mobility and Quality of Life Outcomes

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BACKGROUND: People with multiple sclerosis (PwMS) are at increased risk for severe complications from infections such as coronavirus disease (COVID-19) due to their pathology and immunosuppressive disease-modifying therapies. Limited evidence is currently available about the impact of COVID-19 infection on the disease course, mobility, and quality of life outcomes in PwMS.

OBJECTIVES: This pilot survey study aimed to (1) describe the impact of contracting COVID-19 infection on outcomes of mobility; disease management; and physical, emotional and financial well-being of PwMS, (2) assess the effects of COVID-19 on mobility and vaccination status, (3) determine correlations between demographic factors, MS clinical factors, and COVID-19 clinical factors in PwMS.

METHODS: An online cross-sectional survey assessed demographic factors; MS clinical factors; COVID-19 clinical factors; mobility status; and physical, emotional, and financial well-being for 22 PwMS who had had COVID-19. Descriptive (mean, percentages), comparative (x^2, Fisher exact tests), and correlation (Pearson product-moment correlation) statistics were used for data analysis.

RESULTS: A total of 22 PwMS from across the Unites States participated (M/F=7/15, mean ± SD age=44.5 ± 16.95 yrs; height: 66.32 ± 4.86 inches; weight 177.09 ± 42.43 pounds, COVID-19 diagnosis duration >2 yrs=87.5%). Relapsing-remitting MS (68%), COVID-19 vaccination status (86% vaccinated with 1-4 booster shots), and hospitalizations (82%) with the lengths of stay ranging between 2 and 42 days were reported. Common COVID-19 symptoms included vomiting/diarrhea (95%), muscle aches (91%), difficulty breathing (82%), cough (68%), and loss of smell (68%). Treatment options included clonal antibodies and Mucinex (95%). Most patients reported full recovery from the infection (86%), while 18% reported a negative change, such as their use of an assistive device (27%), a relapse (32%), and continued need for family support (59%) after the infection. Walking ability improved after recovering from COVID-19 ($P<.05$), however, vaccination status didn't change walking ability. The number of MS relapse symptoms was significantly correlated with relapse duration ($r=0.66$; $P=.033$).

CONCLUSIONS: The findings from this survey enhance our general understanding of the consequences of COVID-19 infection and recovery in PwMS and can help develop comprehensive treatment strategies.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Epidemiology of MS, Management of Activities of Daily Living in MS

(QOL22) Medical Comorbidities in Adults With New Diagnoses of Multiple Sclerosis and Clinically Isolated Syndrome: An Observational Study Exploring Risk Factors and Outcomes

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BACKGROUND: Comorbidities are common in people with multiple sclerosis (PwMS) and clinically isolated syndrome (CIS), and they have been shown to impact outcomes like pain and fatigue. However, research exploring factors associated with comorbidity and impacts on health outcomes for people with new diagnoses of MS and CIS is limited.

OBJECTIVES: This study aimed to (1) explore the relationship between comorbidity and demographic factors, (2) examine the relationship between comorbidities and outcomes 1 year following diagnosis, accounting for baseline outcomes to assess change over time, and (3) explore whether these relationships differ with comorbidity treatment.

METHODS: Secondary analysis of data collected from a longitudinal, observational study of adults newly diagnosed with MS or CIS 1 month and 12 months after diagnosis (N=230). Statistical methods included point-biserial correlation coefficient, x^2, analysis of covariance, and multivariate linear regression.

RESULTS: Age and race were associated with hypertension and heart disease, respectively. After 1 year, mental health comorbidity was associated with higher fatigue scores, musculoskeletal and neurological comorbidity with higher pain interference, and neurological comorbidity with less exercise, after accounting for baseline fatigue, pain interference, and exercise. Those with treated neurological conditions had worse pain interference compared with those with untreated conditions.

CONCLUSIONS: Assessing comorbid conditions should be a standard part of MS care at diagnosis, as it may prevent unnecessary negative outcomes. Future research should explore how early treatment of comorbidities may impact outcomes and disease progression.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comorbidity, Comprehensive Care and MS

(QOL23) Validating the Wilder Multiple Sclerosis Suffering Index: Psychometric Properties and Their Impact on Quality of Life

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BACKGROUND: Multiple sclerosis (MS) imposes multifaceted suffering on patients, profoundly impacting their physical, emotional, and social well-being. The Wilder Multiple Sclerosis Suffering Index (WMSSI) was developed to quantify suffering in people with MS.

OBJECTIVES: This phase 2, cross-sectional study aimed to validate the WMSSI by evaluating its psychometric properties and exploring its utility in capturing the lived

experiences of individuals with MS.

METHODS: The study included a diverse cohort of people with MS recruited from multiple clinical sites. Participants completed the WMSSI and additional validated tools, including the 27-item Multiple Sclerosis Quality of Life Questionnaire and the Schulz et al (2010) experience and perception of suffering scales. Psychometric analyses included assessments of internal consistency, construct validity, and concurrent validity. Regression modeling was used to examine the WMSSI's relationship with quality of life (QOL).

RESULTS: The WMSSI demonstrated excellent internal consistency (Cronbach α=0.93) and strong concurrent validity, correlating significantly with both pain (r=0.72) and psychological distress (r=0.68). Factor analysis revealed 5 distinct domains of suffering: physical, psychological, existential, social, and health care–related, which is consistent with the multidimensional construct of suffering. Regression analyses showed that both the frequency and impact subscales of the WMSSI independently contributed to QOL (P<.01 for both). Specifically, for every 1-point increase in WMSSI, QOL decreased by 0.29 (impact) or 0.32 (frequency), underscoring the tool's sensitivity in capturing the effect of suffering on well-being. Sex was also a significant predictor of QOL, while other demographic factors were not.

CONCLUSIONS: The WMSSI is a reliable and valid tool for quantifying the nuanced suffering experienced by people with MS. Its ability to predict QOL across diverse patient groups supports its use in clinical and research settings to evaluate patient-centered interventions and guide personalized treatment strategies.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Nursing Management in MS, Psychological Issues and MS, Suffering

(QOL24) Quality of Life in Multiple Sclerosis: Fundamentals of Building a Quality-of-Life Clinic at an Academic Center

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BACKGROUND: People with multiple sclerosis (PwMS) can experience a significant symptom burden that impacts activities of daily life. Chronic symptom burden can influence patient perception of quality of life (QOL), highlighting the importance of understanding and managing QOL initiatives. Current evidence supports using lifestyle interventions to improve chronic symptoms and reduce the risk of disease progression. These strategies used in conjunction with disease-modifying therapies (DMT) improve QOL metrics. Building a dedicated QOL clinic to understand symptom burden, measure QOL objectively, and inform on evidence-based intervention is critical to improving patient outcomes regarding perception of QOL.

METHODS: The first step to building an MS QOL clinic started with institutional leadership. It is necessary to present the rationale for this service based on current evidence-based practice. The next step was to discuss the service line with MS providers and other specialists who would refer patients, including neurologists, advanced practice providers, and primary care providers. Support from these providers was crucial to maintaining the flow of patients into the clinic. Third, it was important to identify clinical metrics to collect during the clinic visit, including patient-reported outcomes (PROs) that have been validated in MS. Additional clinical metrics can include objective assessments, such as optical coherence tomography (if available), bladder scan, Timed 25-Foot Walk, an estimated disability status scale, etc. PROs can be implemented in the electronic health system to be taken remotely prior to the clinical visit. We use the MS Quality of Life Inventory (MSQLI), a PRO that contains 10 verified scales, to assess different components of symptomatic burden in people with MS. These scores provide an assessment of the impact of MS and symptomatic burden of each individual PwMS. Based on outcomes from the PROs and clinical testing, individualized targeted interventions can be provided and referrals made to collaborating specialists such as urology, neuropsychology, physical therapy, psychology, etc. Additionally, PRO metrics can be reassessed periodically to assess response to target interventions. After implementing this program, a future consideration was to create an in-person education symposium where PwMS and their families and caregivers can connect with the multidisciplinary care team.

OBJECTIVES: To educate providers on the process of building an MS QOL clinic for PwMS.

RESULTS: Building a dedicated QOL clinic for PwMS allowed for the development of a platform for the objective measurement of QOL metrics utilizing validated PROs and advanced testing. Improvement in QOL metrics was tracked through interval measurements of PROs like the MSQLI. Follow-up visits can be scheduled after the initiation of recommended interventions, such as starting a DMT, starting recommended evidence-based lifestyle interventions, and completion of referrals to collaborating specialists. Interventions can be individually modified as needed, based on scores from validated PROs at interval QOL clinic visits.

CONCLUSIONS: The expected level of care at an MS center includes a comprehensive, multidisciplinary approach delivered by highly specialized professionals to improve patient outcomes. With chronic disease, it is important to assess and address symptomatic burden and the impact on the patient's well-being. QOL-targeted interventions are an important adjunct to traditional DMT to achieve the best outcomes in disease management in MS care. Building a dedicated QOL clinic for PwMS provides an organized platform for measuring QOL and initiating individualized, evidence-based interventions to improve chronic symptomatic burden.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Complementary/Alternative Therapies in MS, Comprehensive Care and MS, Quality of Life in Multiple Sclerosis

REHABILITATION

(REH01) Steps to Health: Backward Walking Predicts Physical Activity Levels in Multiple Sclerosis

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BACKGROUND: Physical activity (PA) is a key determinant of health, linked to improved physical and mental well-being. In populations with limited PA, such as people with multiple sclerosis (PwMS), mobility impairments, cognitive challenges, and fear of falling can affect daily movement. While connections between these factors and step count, a common measure of PA, are established, methods for predicting who meets recommendations remain scarce. Identifying individuals who meet activity recommendations, like step count goals, is crucial for the development of targeted interventions.

OBJECTIVES: To develop a clinically practical method for determining whether PwMS meet step count goals, integrating patient-reported outcomes with objective measures of mobility and cognition to guide strategies for enhancing PA and health outcomes.

METHODS: Participants reported demographics and completed assessments of mobility disability (Patient-Determined Disease Steps [PDDS], Multiple Sclerosis Walking Scale [MSWS-12]), fear of falling (Falls Efficiency Scale International [FES-I]), forward/backward walking (FW, BW), static/reactive balance (eyes-closed, feet-together, push-and-release test). Additionally, cognition was assessed via a comprehensive battery including the Symbol Digit Modalities Test, Brief Visuospatial Memory Test, Trail Making Test (parts A and B), and the California Verbal Learning Test. Fitbit tracked PA for 3 months, categorizing participants based on whether they met the MS daily step goal (7500 steps).

RESULTS: A total of 46 PwMS participated (age: 51.30 ± 11.05; median PDDS:1; 83% female), with 15 meeting the 3-month average daily step goal. Wear-time adherence was 90.15 ± 7.56%. Step count correlated significantly with PDDS (–.36), MSWS-12 (–.49), FES-I (–.38), FW (.46), and BW (.58). Logistic regression with backward selection identified the best predictors of meeting the daily step goal. The analysis identified a backward walking speed cutoff of 0.89 m/s as a strong predictor of meeting the step goal, with a sensitivity of 90.3%, specificity of 60.0% (area under the curve=.80; Nagelkerke R^2=.32).

CONCLUSIONS: This study identifies BW speed as a clinically feasible predictor of meeting the recommended daily step goal for PwMS. The model demonstrates good sensitivity, moderate specificity, and a significant area under the curve, providing a valuable tool for health care providers to assess PA levels. These findings emphasize the clinical significance of using objective mobility measures, such as BW, to target interventions aimed at improving PA and health outcomes for PwMS.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Complementary/Alternative Therapies in MS, Comprehensive Care and MS, Physical Activity

(REH02) Effects of High-Intensity Interval vs Moderate-Intensity Walking Training on Fatigue, Walking Speed, and Cardiovascular Fitness in Multiple Sclerosis

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BACKGROUND: Moderate-intensity, continuous training (MICT) is recommended for

people with multiple sclerosis (MS), but has had small impacts on fatigue and walking outcomes. High-intensity, interval-based walking training may yield better and/or more efficient outcomes. There have been few studies investigating the effects of high-intensity interval training in people with MS. These studies have largely focused on people with low or unspecified levels of symptomatic fatigue and walking dysfunction and have used nonwalking interventions.

OBJECTIVES: The purpose of this pilot project was to compare the effects of moderate- and high-intensity treadmill training on symptomatic fatigue and walking function in people with MS with elevated fatigue and walking dysfunction.

METHODS: Ten individuals with MS (age 49.8 [SD 7.5] years; 3 men, 7 women; 1-34 years post diagnosis, Fatigue Severity Scale Score>4; Patient-Determined Disease Steps score range, 3-6) were randomly distributed to perform high-intensity, speed-based interval treadmill training (HISTT; n=5) or moderate intensity, continuous training (MICT; n=5) walking on a treadmill. Participants performed 12 sessions of training, which were up to 40 minutes in duration. Pre- and posttests included fatigue severity, walking speed, and peak oxygen consumption.

RESULTS: Groups experienced similar reductions in fatigue severity (HISTT: −0.8 [1.4] vs MICT: −1.5 [1.3]; t=0.85, P=.42). The HISTT group had trends for greater improvements in comfortable (HISTT:+0.16 [0.26] m/s vs MICT:+0.02 [0.10] m/s; P=.29) and maximal (HISTT:+0.10 [0.17] m/s vs MICT:+0.03 [0.16] m/s; P=.09) walking speeds and peak consumption (HISTT:+2.5 [1.4] mL/kg/min vs MICT:+0.04 [2.9] mL/kg/min; P=.06).

CONCLUSIONS: Initial results from this pilot study suggest that high-intensity interval walking training has similar benefits for fatigue as moderate-intensity training, but may lead to greater improvements in walking speed and cardiorespiratory fitness. Importantly, our study focused on people with elevated fatigue and impaired walking function and used a task-specific intervention.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Treadmill Training

(REH03) Acute Effects of Cycling Exercise With Virtual Reality on Inhibitory Control in People With Multiple Sclerosis-Related Mobility Disability: Preliminary Analysis

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BACKGROUND: Aerobic exercise is a promising treatment for cognitive deficits in people with multiple sclerosis (MS). However, the strongest evidence supports walking-based interventions for people with minimal disability. While cycling exercise is more accessible to those with mobility disability, it may be less powerful and effective. Virtual reality (VR) can increase the multisensory demand during cycling to improve its potential benefit on cognition.

OBJECTIVES: This in-progress study evaluates the acute effects of aerobic cycling exercise with and without VR on cognitive outcomes in people with MS-related mobility disability (ie, Expanded Disability Status Scale score of 4-6). This study uses a within-subjects, repeated-measures design wherein participants serve as their own controls. Multisensory demand is manipulated across the bouts of cycling using the VR.

METHODS: Participants completed 3 experimental conditions, separated by about 1 week, in a random order. During each session, participants completed the modified Flanker test, which measures processing speed (ie, congruent trials) and inhibition (ie, executive function; incongruent trials), before and after 20 minutes of moderate-intensity cycling. Multisensory demand was manipulated across conditions: cycling alone (LO), cycling with VR (MED), and cycling with VR where participants were instructed to complete a perceptual task embedded in the VR (HI).

RESULTS: Preliminary data analysis was conducted on participants who completed all 3 experimental sessions to date (n=11). The anticipated final sample size will be 24 people with MS. The overall 3-way analysis of variance on modified flanker reaction time (condition × time × congruency) was significant (F[2]=4.45, P=0.03, η_p^2=0.31). Overall, the HI and LO conditions were associated with acute reductions (ie, improvements) in reaction time on incongruent trials (ie, measure of inhibitory control), while the MED condition was associated with acute increases (ie, worsening) in reaction time.

CONCLUSIONS: This preliminary analysis suggests that combining exercise with VR may impact cognition in persons with MS-related mobility disability. However, the specific characteristics of the VR may differentially affect changes in cognition. Thus, the optimal dose of multisensory demands for improving cognition using VR is not yet clear. We plan to reanalyze the data once the final cohort completes this Consortium of Multiple Sclerosis Centers-funded study.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Rehabilitation

(REH04) Music-4-MS: A Randomized Controlled Feasibility Study to Enhance Psychosocial Well-Being and Cognition in Individuals With Multiple Sclerosis

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BACKGROUND: Multiple sclerosis (MS), a chronic neuroinflammatory and neurodegenerative disease, affects over 2.8 million people globally and is associated with significant cognitive, physical, and psychosocial challenges. Up to 70% of people with MS experience cognitive impairment, often without effective interventions. Cognitive impairment is characterized by slow processing, poor memory, and impaired learning, which negatively impact emotional well-being and quality of life. Active music learning offers unique therapeutic potential as it integrates sensory, motor, and cognitive systems.

OBJECTIVES: This study evaluated the feasibility and preliminary effect of Music-4-MS, an online music-learning intervention, compared to an active control group (music-listening). Music-4-MS is a 12-week program designed to teach participants how to play the ukulele. The ukulele is affordable, relatively easy to learn, and requires less hand dexterity than larger stringed instruments. Each week, participants followed a structured ukulele protocol that included instructions on holding, tuning, and strumming the instrument, as well as learning basic chords and popular songs like *Happy Birthday*, *Don't Worry Be Happy*, and *Three Little Birds*.

METHODS: In a 2-group randomized controlled trial, 29 participants were assigned to the intervention (n=16) or control (n=13) groups. Assessments at baseline (T1), post intervention (T2), and 1-month post intervention (T3) examined anxiety, depression, self-efficacy, quality of life, fatigue, and cognitive outcomes. Semistructured interviews assessed intervention delivery, content, and perceived impact. Descriptive statistics were used for feasibility data, and content analysis was conducted for the qualitative data. Analysis of covariance was used to assess outcomes at T2 and T3, controlling for T1 scores.

RESULTS: The dropout rate was 21%; adherence to the intervention was high. At T2, the intervention group showed significantly lower anxiety and depression scores compared with controls. At T3, the intervention group demonstrated improved cognitive flexibility, with moderate to large effect sizes across all cognitive performance outcomes. Qualitative analysis revealed 6 themes related to acceptability: emotion, function, connection, motivation, navigation, and recommendations.

CONCLUSIONS: These findings suggest that Music-4-MS is a feasible, acceptable, and innovative online health intervention with strong potential to enhance psychosocial well-being and cognitive functioning in people with MS. Further studies with larger samples are warranted to confirm its efficacy.

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KEYWORDS: Cognitive Rehabilitation, Music-Based Intervention, Complementary/Alternative Therapies in MS, Psychological Issues and MS

(REH05) Evaluating Safety During Exercise Training in Adults With Multiple Sclerosis: Does Where You Exercise Matter?

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BACKGROUND: Exercise training is considered safe and effective for adults with

multiple sclerosis (MS). Nevertheless, adverse event (AE) reporting in clinical trials of exercise training in MS is often unclear or omitted.

OBJECTIVES: This abstract presents data on the safety of exercise training in supervised and unsupervised settings for people who participated in the STEP for MS comparative effectiveness trial (NCT03468868).

METHODS: We enrolled adults with MS (age 18-65 years) who had moderate disability (Expanded Disability Status Scale, 4.0-6.5) and slow walking speed (Timed 25-Foot Walk Test, 6-360 seconds). Participants engaged in 16 weeks of moderate-intensity aerobic exercise (2×/week) and resistance training (2×/week) in person with supervision at a facility (GEMS-F) or at home with remote supervision (GEMS-H). Both groups received an individualized exercise program based on evidence-based exercise guidelines, in-person or remote coaching, and education on fall prevention. The home group was provided with internet-based exercise videos for reference during the trial.

RESULTS: The sample (n=379) was mostly female (75.7%), White (64.9%) or Black (29.3%), unemployed (45.9%), and had relapsing-remitting MS (72.7%). There were no significant differences between the baseline demographics of GEMS-F and GEMS-H. During the 16-week intervention, 61 AEs deemed related to the intervention were reported (21 GEMS-F, 40 GEMS-H), affecting 52 participants (17 GEMS-F, 35 GEMS-H). There were 192 AEs deemed unrelated to the study, including 5 serious AEs (SAEs; 4 GEMS-F, 1 GEMS-H). SAEs included fall with injury (2 GEMS-F), COVID-19 (1 GEMS-F, 1 GEMS-H), and viral infection (1 GEMS-F). The most common AEs were pain (10 GEMS-F, 13 GEMS-H), fall without injury (4 GEMS-F, 9 GEMS-H), fall with injury (1 GEMS-F, 4 GEMS-H), weakness (1 GEMS-F, 4 GEMS-H), or other neurological symptoms (4 GEMS-F, 1 GEMS-H). One GEMS-H participant was withdrawn by an investigator due to an AE (low back pain); 1 GEMS-H participant voluntarily withdrew due to a fall with injury.

CONCLUSIONS: Overall, there were few SAEs, with none attributed to the intervention. Only 14% of study participants experienced AEs, none of which were serious. Participants in the home condition had twice as many AEs as participants with in-person supervision at a facility. Future research should identify those at higher risk for injury who may need closer supervision during exercise training.

DISCLOSURES: *Casey Kandilakis, Robert W. Motl, Jeffrey Hebert, Alexander V. Ng, Kevin McCully, Whitney N. Neal, Jonathan Lowman, Deborah Backus: Nothing to disclose. Francois Bethoux: Bristol Myers Squibb (consulting fee, advisory board member); MedRhythms (consulting fee, contracted research, scientific advisory board member); Qr8 (intellectual property rights). Prudence Plummer: Helius Medical (contracted research). Gary Cutter: Alexion, Antisense Therapeutics, Biogen, Clinical Trial Solutions, Entelexo Biotherapeutics, Genentech, GW Pharma, Immunic, Immunosis, Klein-Buendel, Merck/Serono, Novartis, Perception Neurosciences, Protalix Biotherapeutics, Regeneron, Roche, SAB Biotherapeutics, Sanofi (consulting/ advisory board); AI Therapeutics, AMO Pharma, Applied Therapeutics, Astra-Zeneca, AveXis, BioLineRx, Brainstorm Cell Therapeutics, Bristol Myers Squibb/Celgene, CSL Behring, Galmed, Green Valley Pharma, Horizon, Immunic, Karuna Therapeutics, Mapi Pharma, Merck, Mitsubishi Tanabe Pharma Holdings, National Heart, Lung, and Blood Institute, Novartis, Opko Biologics, Prothena Biosciences, Reata, Regeneron, Sanofi, Teva, (protocol review committee); University of Pennsylvania, University of Texas Southwestern, Visioneering Technologies (data and safety monitoring boards); Pythagoras (president); University of Alabama, Birmingham (employee).*

KEYWORDS: Comprehensive Care and MS, Exercise Training

(REH06) A Pilot Investigation of a Novel Cognitive Performance Feedback Value Training Paradigm in Individuals With Multiple Sclerosis

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BACKGROUND: Effectively learning from feedback related to performance is essential for improving cognitive function in people with multiple sclerosis (PwMS). However, the learning utility of feedback will be limited if individuals are not motivated to engage with that information. Development of tools for sustaining motivation to learn from feedback is an important, but lacking, area of research.

OBJECTIVES: We test the effectiveness of a novel Feedback Value Training (FVT) in PwMS. The FVT is designed to enhance the perceived value of feedback and improve learning from feedback. Implicit and explicit learning approaches are used to help participants recognize the value of feedback and its utility for their cognitive performance.

METHODS: Twenty-six PwMS were randomly distributed to receive either the FVT (treatment group; n=13) or a sham paradigm (control group; n=13). All participants then completed a willingness-to-pay (WTP) associative memory task, which measured the perceived value of feedback and cognitive performance. Participants decided whether they were willing to purchase performance feedback while learning word pairs, with the knowledge that they would earn a monetary bonus contingent on their performance during a future recall test phase.

RESULTS: The amount of feedback purchased during the WTP task did not differ significantly between groups. However, within-group analysis revealed that the treatment group was responsive to the implicit learning of feedback value during the FVT. Generalized logistic mixed-effects regression revealed that feedback purchased on incorrect trials during learning (ie, negative feedback) predicted significantly better performance at test [$x^2(3)=33.71$; $P<.001$; $b=0.73$; $b_{SE}=0.31$]. Importantly, this beneficial effect of negative feedback was especially pronounced in the treatment group, suggesting that the FVT may improve learning from error-related feedback [$x^2(1)=5.29$; $P=.02$; $b=0.98$; $b_{SE}=0.43$] in PwMS.

CONCLUSIONS: The results of this preliminary work align with other reports of the importance of performance feedback for learning in PwMS. We further demonstrate that the FVT can potentially serve as a tool for improving learning from error-related feedback, which can be useful in rehabilitation settings where clinicians use performance feedback to facilitate cognitive training in PwMS. We also present preliminary evidence for the possibility that the value of feedback can be implicitly learned. These findings lay a foundation for future work to refine the FVT and improve cognitive function in MS.

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KEYWORDS: Cognition and MS

(REH07) Compensatory Strategy Use Differs by Level of Self-Reported Cognitive Issues: Implications for Self-Management Program Development

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BACKGROUND: Self-management programs can help people with multiple sclerosis (PwMS) improve their quality of life and functioning. While up to 70% of PwMS experience cognitive difficulties, few self-management programs have focused on compensatory skill development. Understanding which strategies PwMS are frequently using, and whether their usage differs by level of self-reported cognitive issues, can help guide the process of developing a new self-management program.

OBJECTIVES: To explore (1) which compensatory cognitive strategies are used the most (often or all the time) by PwMS and (2) whether their usage differs by level of self-reported cognitive issues.

METHODS: Participants (N=1075) were a national sample of PwMS recruited through the National Multiple Sclerosis Society, Mandell MS Center, and the University of Washington who reported mild (n=549), moderate (n=320), or severe (n=206) cognitive issues on the SymptoMScreen. The Compensatory Cognitive Strategies Scale was used to measure how often participants used each of the 20 different strategies, with responses aggregated into 3 categories (*Never/Rarely*, *Sometimes*, and *Often/All the Time*) for analyses. x^2 were used to compare frequency of usage among the 3 groups, followed by individual logistic regressions that adjusted for sex, race, education, disability level, and MS type.

RESULTS: Establishing a routine for placing items (79.3%-89.3%) and using electronic reminders (77.6%-80.3%) were the 2 most frequently used strategies for all 3 groups. The severe group had higher usage on 17 strategies compared with the mild group, with their odds of using these strategies *Often/All the Time* being 56% to 372% greater. Differences in the frequency of use were also noted between the mild and moderate groups on

15 strategies, with the odds of the latter using any of these strategies *Often/All the Time* being 43% to 182% higher. In addition, 3 strategies (slowing down/avoiding situations with fast reaction times, requesting accommodations, and slowing the pace of communication) were more likely to be used by the severe group compared with the moderate group. No impact was found for demographic and disease-related factors.

CONCLUSIONS: People with MS-related cognitive issues report using compensatory strategies, and this occurs independently of demographic and disease-related factors. These results support the use of a cognition-focused self-management program early in the disease process, as well as therapeutic intervention across the MS continuum.

DISCLOSURES: *Elizabeth S. Gromisch, Dawn M. Ehde, Lindsay O. Neto, Sarah A. Raskin, Swapna S. Gokhale, Jodie K. Haselkorn, Thomas Agresta, Rachel M. Nicholson, Aaron P. Turner: Nothing to disclose. Jaime Imitola: Genentech (contracted research).*

KEYWORDS: Cognitive Functioning, Management of Activities of Daily Living in MS, Psychological Issues and MS

(REH08) Pilot of a Multiple Sclerosis Curriculum for Occupational Therapy Practitioners to Increase Confidence With Service Delivery and Improve Patient Care

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BACKGROUND: Occupational therapy (OT) program accreditation standards require that curricula address varied foundational conceptual areas and skills necessary for entry-level practice including screening, evaluation, intervention planning, and intervention implementation (Accreditation Council for Occupational Therapy Education. *2023 Accreditation Council for Occupational Therapy Education Standards and Interpretive Guide*. Updated April 7, 2025. Accessed April 15, 2025. https://acoteonline.org/accreditation-explained/standards). While neuroscience is included as a foundational content area, there are no criteria regarding specific diagnoses to address (ACOTE 2023). As such, OT practitioners (OTPs) have varied exposure to and knowledge of working with people with multiple sclerosis (PwMS), which can impact their confidence with service delivery and quality of patient care.

OBJECTIVES: Describe the delivery of an MS-specific curriculum for newly hired OTPs in an outpatient setting with pre- and postsurvey results to demonstrate the benefit of additional training in the overall confidence and preparedness of OTPs to treat PwMS.

METHODS: The OTP participated in a 15-hour curriculum delivered over 5 weeks; it focused on MS pathophysiology and symptoms, lived experience, social disparities, and evidenced-based and best practices for rehabilitation treatment in varied health management occupations (Occupational therapy practice framework: domain and process-fourth edition. *Am J Occup Ther*. 2020;74(suppl 2):7412410010p1-7412410010p87. doi:10.5014/ajot.2020.74S2001). Symptom and condition management was expanded to include self-management of fatigue, pain, bowel and bladder, and cognitive symptoms. A 16-question survey with a 5-point Likert scale was administered before and after the curriculum to gauge knowledge and confidence in each topic and in treating PwMS.

RESULTS: The OTP demonstrated a 20-point overall score increase on the postcurriculum survey. Most notably, the OTP's score for overall confidence and ability to provide care for and treat an individual living with MS increased from 3 of 5 to 5 of 5.

CONCLUSIONS: This highlights the benefit of adding MS-specific training for OTPs and contributes to the literature supporting the need for additional education to increase confidence with service delivery and to improve treatment for individuals living with MS.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Rehabilitation in MS

(REH09) A Pro-Bono Group Exercise and Wellness Program for Individuals With Multiple Sclerosis in Underserved Communities: Preliminary Results

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BACKGROUND: Individuals with multiple sclerosis (MS) experience significant barriers to regular exercise participation, particularly in socioeconomically disadvantaged areas. Despite the well-documented benefits of exercise in MS, many lack access to adapted exercise programs and do not know how to safely exercise with their disability.

OBJECTIVES: To evaluate the effects of a 6-month community-based group exercise and wellness program on (1) physical activity levels, (2) energy expenditure, and (3) exercise adherence in underserved individuals with MS, as part of a larger cohort study that included participants with various neurologic conditions.

METHODS: This prospective observational study enrolled participants with various neurologic conditions from the Cleveland Clinic. For this preliminary analysis, we focused on participants with MS (n = 3, with 2 additional participants pending final assessments). The intervention consisted of supervised group exercise sessions (60-75 minutes, 3 times/week) combining aerobic, strengthening, and stretching exercises with biweekly wellness education. Physical activity was measured using ActiGraph monitors at baseline, 3 months, and 6 months.

RESULTS: Initial data from 3 participants with MS demonstrated progressive increases in both physical activity and energy expenditure. Average daily steps increased from 7364 at baseline to 10,266 at 3 months and 11,184 at 6 months. Daily caloric expenditure showed substantial improvement, increasing from 1328 calories at baseline to 2028 calories at 3 months and 2298 calories at 6 months, representing a 73% increase over the intervention period. No adverse events were reported.

CONCLUSIONS: Preliminary results show promising increases in physical activity levels and energy expenditure in persons with MS from underserved communities. While complete analysis awaits final assessments from additional participants, these initial findings suggest that supervised group exercise programs can effectively promote sustainable physical activity behavior change in this population. The broader study outcomes, including participants with other neurologic conditions, will provide further insights into the program's effectiveness.

DISCLOSURES: *Jared Telecky, Susan M. Linder, Donayja Harris, Andrea Bischof-Bockbrader, Kate Balthaser, Chase Holmes, Jessica Ruff, Courtney Miller, Bradley Heiss, Hailey Mekruit, Matthew Kempert: Nothing to disclose. Francois Bethoux: Bristol Myers Squibb (consulting fee, advisory board member); MedRhythms (consulting fee, contracted research, scientific advisory board member); Qr8 (intellectual property rights).*

KEYWORDS: Physical Activity and MS

(REH10) Understanding Compensatory Cognitive Strategy Use in People With Multiple Sclerosis

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BACKGROUND: Cognitive impairment is highly prevalent among individuals with multiple sclerosis (MS), affecting up to 65% of those with the condition and significantly impacting daily functioning. To counter these challenges, cognitive rehabilitation interventions emphasizing compensatory strategies have shown promise in enhancing functional independence and quality of life. However, research on naturalistic (not resulting from intervention) compensatory strategy use among individuals with MS is limited and restricted by consideration of a narrow range of compensatory strategies.

OBJECTIVES: This study aimed to explore whether demographic/clinical factors, self-reported symptoms, or objective measures of cognitive function predict the use of cognitive compensatory strategies.

METHODS: This secondary analysis used baseline data from a longitudinal observational study. Participants completed a web-based survey battery of demographics and self-reported measures, including the Compensatory Cognitive Strategy Scale, a 24-item survey of the frequency of strategy use related to processing speed, attention, memory, and executive function, and the Patient-Reported Outcomes Measurement Information System Fatigue Short Form 7a. Cognitive function was assessed with the National Institutes of Health Toolbox (NIH-TB) Cognitive Battery. Hierarchical linear regression identified predictors of compensatory strategy use.

RESULTS: A total of 272 individuals with MS participated (mean age: 50.99 years; 77.6% female; 72.1% White). Nearly half (46.3%) reported walking disability per their Patient-Determined Disease Steps (PDDS) score. No significant differences in Compensatory Cognitive Strategy use were associated with demographic factors, including age, education, sex, marital status, employment, or MS subtype. Hierarchical linear regressions revealed that the final model including greater walking disability (PDDS 0-2 vs 3+; $\beta = 0.143$; $P = .026$) and higher fatigue ($\beta = 0.340$; $P < .001$) were associated with more frequent use of strategies, and accounted for 21.7% of the variance in strategy use. Separate regression analyses showed lower cognitive test scores, particularly on the NIH-TB Total Composite Score ($B = -0.199$; $P = 0.040$), NIH-TB Flanker Inhibitory Control and Attention Test ($B = -0.236$; $P = .034$), and NIH-TB Pattern Comparison Processing Speed Test ($B = -0.131$; $P = .019$) were associated with greater strategy use.

CONCLUSIONS: The findings demonstrate that people with MS experiencing greater walking disability, fatigue, and objective cognitive dysfunction employ cognitive compensatory strategies more frequently. Future research is needed to evaluate the efficacy of these strategies in maintaining both daily and longitudinal functioning and improving overall quality of life.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Management of Activities of Daily Living in MS, Nursing Management in MS

(REH11) Identifying Pseudo-Progression for Rehabilitation

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BACKGROUND: Rehabilitation increases one's ability to engage in meaningful life tasks. Individuals with multiple sclerosis (MS) who reported needing to see a rehabilitation provider but lacked access were found to have lower health-related quality of life than those with access. Despite the growing evidence for MS rehab and symptomatic care, there is suboptimal uptake and access to care in practice.

OBJECTIVES: The multidisciplinary Canadian MS Rehab Knowledge Mobilization Network was established in 2024 to address gaps in MS rehabilitation. An initial priority for the network is to describe situations warranting bouts of rehabilitation care.

METHODS: A working group was established from the larger network to draft clinical scenarios representative of clinical patterns at MS onset and over the disease course that may benefit from rehabilitation intervention. This working group met in person once and virtually 4 times to create, refine, and achieve consensus on the scenarios. They were then presented to the larger network group for real-time discussion; further feedback was also sought via email.

RESULTS: A number of clinical scenarios describing symptom and functional changes occurring at onset and over the disease course appropriate for rehab interventions were created. The concept of *pseudo-progression* emerged as a clinical scenario occurring uniquely or in association with MS relapse, pseudo-relapse, MS disease progression, or advanced MS scenarios. Pseudo-progression is seen when a more chronic stressor is the primary driver of worsening function (ie, knee osteoarthritis limiting mobility, spinal stenosis, social stressors, etc), while pseudo-relapse occurs with an acute stressor (ie, urinary tract infection [UTI]). Deconditioning or maladaptive coping may occur rapidly in both scenarios. Duration of rehabilitation and goals of care differ across scenarios. A return to baseline at the impairment and function levels would occur faster for treatable pseudo-relapses vs pseudo-progression. A return to baseline at the impairment level is not anticipated with true isolated MS progression. Pseudo-relapse and pseudo-progression are not exclusive to each other or to the other scenarios. For example, a person can have a life event (eg, grieving loss of spouse) with pseudo-progression (functional decline over months since loss of spouse), and then a UTI at the same time as a true new relapse.

CONCLUSIONS: Recognizing different scenarios, including pseudo-progression, may help with timely access to rehabilitation interventions and goal setting to optimize function.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Management of Activities of Daily Living in MS, Natural History of MS

(REH12) Walking Path Length Affects 6-Minute Walk Test Scores in People With Multiple Sclerosis: A Comparison of 2 Recommended Methodologies

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BACKGROUND: The 6-minute walk test (6MWT) is a widely used assessment of functional endurance and a recommended core outcome measure in neurologic physical therapy practice. It measures the distance covered during 6 minutes of continuous walking and was originally validated using a 30-meter (m) path. Administration of the 6MWT using the 30-m path may not be feasible at clinics or research sites with limited space. As an alternative, the Academy of Neurologic Physical Therapy clinical practice guideline recommends using a 12-m path. The distance walked on a 12-m path may differ from that on the original 30-m path in people with multiple sclerosis (PwMS), potentially due to the increased number of turns required on the shorter path.

OBJECTIVES: To compare the effect of different walking path lengths on 6MWT scores in PwMS.

METHODS: Two 6MWT trials were conducted: one on a 12-m path and the other on a 30-m path. Both trials were performed on noncarpeted flooring, and participants could use assistive walking devices if necessary. Verbal cues and measurement procedures followed American Thoracic Society guidelines. Trials were completed on separate days, with at least 3 days between them to avoid fatigue effects. A paired samples *t* test was used to compare the distances walked on the 2 path lengths ($\alpha = .05$). Cohen *d* was calculated to assess effect size. Data are presented as mean ± SD or frequency (%).

RESULTS: Twenty-one PwMS performed both trials. Participant demographics were age 60.81 ± 8.56 years (range, 46.00-82.00); 13 (61.9%) women and 8 (38.1%) men; Patient-Determined Disease Steps (PDDS) mean score 2.62 ± 1.66 (range, 0-6); and disease duration 22.00 ± 12.05 years (range, 1.33-44.00). Mean walking distances were greater on the 30-m path. Mean distance walked using the 12-m path was 405.62 ± 138.32m, and on the 30-m path was 454.62 ± 159.10 ($P < .001$, $d = 0.989$).

CONCLUSIONS: PwMS walked farther on the 30-m path compared with the 12-m path, with a large and clinically significant effect. The mean difference exceeded the published value for minimal important change in PwMS. These findings suggest that using a 12-m path for the 6MWT may underestimate functional endurance capacity in PwMS compared to the 30-m path. This underestimation could lead to inaccurate clinical judgments. Clinicians and researchers should be cautious when interpreting scores obtained using a 12-m path, particularly when comparing them to previously published normative data.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Management of Activities of Daily Living in MS, Nursing Management in MS, Rehabilitation

(REH13) Developing a Cognitive Rehabilitation Service for People With Multiple Sclerosis

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BACKGROUND: Cognitive dysfunction affects up to 80% of people with multiple sclerosis (PwMS) in their lifetime, depending on disease course. With an insidious onset, cognitive challenges often present prior to diagnosis but frequently go unrecognized until deficits affect participation in daily activities. Emerging evidence suggests cognitive rehabilitation can mitigate these deficits. Among available interventions, RehaCom is a widely used computerized cognitive training program using repetitive practice and gradual progression to target an impaired cognitive domain. Another promising approach is Goal Management Training (GMT), a therapist-guided metacognitive intervention designed to improve goal-directed behavior and executive functioning. Both programs have been shown to improve cognitive outcomes.

OBJECTIVES: To develop a protocol for routine cognitive rehabilitation tailored to the needs of a large multiple sclerosis (MS) clinic.

METHODS: Eligibility criteria included a confirmed MS diagnosis, over 18 years of age, and a cognitive score below average in 1 or more domains in the Minimal Assessment of Cognitive Function in MS. Participants completed 9 weeks of cognitive rehabilitation using RehaCom or GMT. Program selection was guided by area(s) of deficit and treatment goals identified in a screening interview. Follow-up assessments included the Brief International Cognitive Assessment for MS. The Canadian Occupational Performance Measure, patient-reported outcomes, and a satisfaction questionnaire were administered to evaluate program effectiveness.

RESULTS: Comparative effectiveness data for RehaCom and GMT are pending. The process of initiating cognitive rehabilitation will be presented. Preliminary feedback highlights benefits and challenges of integrating the program into routine care, including implementation (establishing a structured cognitive rehabilitation service within a high-demand clinic), evaluation (measuring intervention benefits systematically), and access (establishing eligibility criteria and triage strategies to identify those most likely to benefit from the program).

CONCLUSIONS: To our knowledge, this is the first program in Canada to offer routine cognitive rehabilitation for PwMS. It marks a significant step forward in addressing cognitive dysfunction in this population. By evaluating the outcomes of RehaCom and GMT, we aim to establish evidence-based guidelines for triaging referrals and delivering targeted cognitive rehabilitation to enhance patient care.

DISCLOSURES: *Kelly F. Hennessy, Marta Pogacar, Robin Lui, Cecilia Meza, Anne Kever, Michelle Williams: Nothing to disclose. Jiwon Oh: Biogen Idec, Roche (consulting fee, contracted research, speakers' bureau); Eli Lilly, EMD Serono, Novartis, Sanofi Genzyme (consulting fee, speakers' bureau). Anthony Feinstein: Amadeus Press, Cambridge University Press, Glitterati Editions, Johns Hopkins University Press (royalty); Multiple Sclerosis Society of Canada (grant); Novartis (speakers' bureau).*

KEYWORDS: Cognitive Rehabilitation, Complementary/Alternative Therapies in MS, Comprehensive Care and MS

(REH14) Understanding Who We Serve: A Retrospective Chart Review of People With Multiple Sclerosis Referred to Occupational and Physical Therapy Services

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BACKGROUND: Relapsing and progressive neurological deficits associated with multiple sclerosis (MS) can adversely impact the functioning in a range of physical, cognitive, and psychological components, with large variation in disease presentation. With ongoing medical advancements in MS, people with MS (PwMS) are being diagnosed earlier and living longer. However, symptoms and comorbidities are often present even in mild cases of MS. These symptoms and comorbidities significantly impact quality of life for PwMS, as their participation or engagement in productivity, self-care, and leisure activities can become disrupted. Occupational therapists (OT) and physical therapists (PT) may assess and collaborate to mitigate functional implications of symptom burden; however, referrals to these services are not always consistent. To our current knowledge, there are no best-practice guidelines for OT or PT practice in MS care, which may contribute to ambiguity in physician referrals.

OBJECTIVES: To identify the most common medical, social, and demographic characteristics in PwMS at the BARLO MS Centre referred to OT and/or PT services, compared with PwMS who are not referred.

METHODS: A retrospective chart review from March 2023 to February 2024 identified patients at a large tertiary clinic in Toronto, ON, of whom 200 were referred to OT and/or PT and 200 were not referred to OT and/or PT. Demographic (eg, age, sex, gender), clinical (eg, diagnosis, medications, symptoms, relapse date and type), and social (eg, living arrangements, work status) information will be extracted and analyzed using descriptive statistics and correlation analyses.

RESULTS: Data will be available at the annual meeting.

CONCLUSIONS: This research will have implications for equitable service provision for PwMS by informing the optimization of referrals and service coordination for PwMS. This will be driven by exploring potential facilitators and barriers to accessing services at a large MS center in Canada. Further, this research will benefit MS clinics and community services by providing a deeper understanding of services PwMS require through the lens of medical, social, and demographic characteristics. Through an in-depth examination into the characteristics and symptom profiles of those referred and not referred to OT and/or PT at a large MS center in Canada, a better understanding of the reasons for, and omission of, referrals and referral patterns is anticipated to emerge.

DISCLOSURES: *Marta Pogacar, Kelly F. Hennessy, Suzanne Ezekiel, Michelle Williams: Nothing to disclose. Robert Simpson: Associated Medical Services, Canadian Institutes of Health Research, Multiple Sclerosis Canada (funding/grant).*

KEYWORDS: Allied Health, Comprehensive Care and MS, Management of Activities of Daily Living in MS

(REH15) IMPACT-MS: A Novel Cognitive Remediation Program to Enhance Functional Outcomes in Veterans With Multiple Sclerosis

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BACKGROUND: Cognitive changes are common in people with multiple sclerosis (PwMS) with estimates reaching 34% to 65% and occurring across phenotypes. Despite the heterogenous nature of the disease, neurocognitive profile patterns suggest a preferential decline in mental processing speed, complex attention, memory, and executive functions. Cognitive change has been associated with diminished functional status, community engagement, and quality of life. Although targeted cognitive remediation offers a minimal-risk solution to mitigate the negative effects of cognitive change in PwMS, few programs offer a standardized protocol that may be scaled for widespread use.

OBJECTIVES: The IMPACT-MS study is an integrated MS prospective and retrospective assessment of a novel, standardized cognitive therapy protocol and the associated outcomes in PwMS. This study examines the patient-reported functional outcomes following a 6-module (7 weeks) cognitive remediation intervention in veterans with MS.

METHODS: Veterans with both relapsing and progressive phenotypes of MS completedcomprehensive cognitive assessment, followed by participation in cognitive remediation with a rehabilitation neuropsychologist using our novel, standardized protocol. Within this frame, treatment was tailored to address patients objectively identified cognitive deficiencies and subjectively reported functional concerns. Patients' values and goals, determined at the outset of therapy, were utilized to drive treatment and promote optimal engagement. This brief, comprehensive treatment protocol also addressed the complex relations among mood, fatigue, and cognition. Patient-reported outcomes, quality of life, and fatigue impact were assessed at the following intervals: before treatment initiation, immediately following treatment, and 6 months after treatment.

RESULTS: As of December 2024, 5 PwMS have completed the protocol. Preliminary data show that all participants reported meeting their identified short-term goals and progressing toward their long-term goals. While patients continued to acknowledge cognitive difficulty and MS-related fatigue, they reported improved ability to manage these symptoms. Patients also reported improved task efficiency and increased participation in values-driven behavior.

CONCLUSIONS: This novel, standardized yet adaptable cognitive remediation protocol shows promise as a minimal-risk, low-cost intervention. Patients reported a diminished impact of MS-related symptoms and an increased ability to engage in personally meaningful activities and meet self-identified goals. Patients are being actively recruited and followed longitudinally for reassessment at successive 6-month intervals following treatment.

DISCLOSURES: *Kyrstina Mariouw, Nora E. Fritz, Sara Omar: Nothing to disclose. Anza B. Memon: Connected Research & Consulting, Inlightened (consulting fee).*

KEYWORDS: Cognition and MS, Rehabilitation, Symptom management and MS, Fatigue, Psychological Issues and MS, Comprehensive Care and MS, Psychological Issues and MS

(REH16) Maximizing Functional Outcomes in Multiple Sclerosis: Insights From a Cognitive Remediation Protocol for Veterans

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BACKGROUND: Cognitive changes are common in multiple sclerosis (MS), seen in an estimated 34% to 65% of patients across disease phenotypes. Neurocognitive profiles indicate an impact on mental processing speed, memory, and executive functions. These changes are associated with diminished functional independence, community engagement, and quality of life. Cognitive remediation strategies are minimal risk, cost-effective interventions that can mitigate the effects of cognitive decline. Yet, there remains a need for a standardized, accessible, and adaptable protocol tailored to veterans with MS that is scalable to all persons with MS.

OBJECTIVES: This program aimed to develop a standardized, accessible, and adaptive cognitive remediation protocol to address cognitive decline in veterans with MS, with a focus on enhancing functional independence and promoting effective symptom management strategies in MS-related cognitive difficulties and fatigue.

METHODS: This integrated program involves both prospective and retrospective evaluation of functional outcomes in veterans with MS following participation in a 6-module (7 weeks) cognitive remediation protocol. After comprehensive neuropsychological assessments, treatment is tailored to address objectively identified cognitive impairments and subjectively reported functional challenges. Veterans' values and goals, determined at the outset, drive the intervention to promote engagement and meaningful progress. The protocol also examines the interplay among mood, fatigue, and cognition. Functional outcomes, quality of life, and fatigue impact are assessed before treatment, immediately post treatment, and at a 6-month follow-up. Annual cognitive screening is conducted to detect changes requiring additional resources.

RESULTS: Preliminary findings from 5 veterans completing the protocol demonstrate progress toward both short- and long-term goals, with patients reporting improved

symptom management, task efficiency, and engagement in personally meaningful activities. Enhanced functional ability, quality of life, and community engagement were also noted.

CONCLUSIONS: This program highlights the potential of a novel cognitive remediation protocol to address MS-related cognitive challenges in veterans with MS. By combining standardized treatment with personalized goals, this intervention supports functional independence and symptom management, offering a scalable, low-risk approach to improve outcomes in this patient population that experiences cognitive and physical fatigue.

DISCLOSURES: *Kyrstina Mariouw, Nora E. Fritz, Sara Omar: Nothing to disclose. Anza B. Memon: Inlightened, Connected Research & Consulting (consulting fee).*

KEYWORDS: Cognition and MS, Rehabilitation, Symptom Management and MS, Fatigue, Psychological Issues and MS, Comprehensive Care and MS, Psychological Issues and MS

(REH17) Efficacy of Transcranial Magnetic Stimulation on Processing Speed in People With Multiple Sclerosis

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BACKGROUND: Multiple sclerosis (MS) causes various cognitive symptoms. Transcranial magnetic stimulation (TMS) is a resource used for rehabilitation.

OBJECTIVES: To evaluate the effects of TMS on the processing speed of people with MS.

METHODS: A double-blind crossover study was carried out in people diagnosed with MS through a convenience sampling. The active group received 10 TMS interventions (primary motor cortex [Cz]: 10Hz, 50 pulses per time, 30 trains, 20 seconds apart, totaling 1500 pulses at 90% of the resting motor threshold; pre–left dorsolateral front [F3]: 10Hz, 50 pulses per train, 40 trains, 20-second intervals, totaling 2000 pulses at 110% of resting threshold) for 10 consecutive working days. The sham group received the inactive TMS. Both groups participated in simple physical activities 3 times a week (gait and balance training and motor activities in virtual game). After 30 days, there was an inversion of the active and sham groups for a new sequence of 10 days. For evaluation, an interview was conducted for data collection, and the Five Digit Test (FDT) was applied at the beginning and end of the stimulations; x^2 tests were used for statistical analysis.

RESULTS: The sample included 29 people diagnosed with MS (18 relapsing-remitting, 6 primary progressive, and 5 secondary progressive), aged 29 to 68 years (mean=47.2; SD=10.9 years). There were 9 men (31%) and 20 women (69%), with Expanded Disability Status Scale scores from 0 to 6.5 (median=4.5; mean=4.3; SD=1.85) and time since diagnosis between 1 and 24 years (mean =9.5; SD=6.57 years). The FDT results showed 66.1% of people who received active TMS improved in terms of processing speed (ie, they were quicker to perform the task) compared with 34.5% of people who received the sham TMS. This difference was significant (P=.0355). The active TMS group had an average improvement in processing speed of 18.4%.

CONCLUSIONS: TMS appears to be an important resource for treating the processing speed of people with MS. This result may encourage further research.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Cognition, Transcranial Magnetic Stimulation

(REH18) Factors Influencing Multiple Sclerosis Rehabilitation Care Decisions in Canada: Perspectives of Rehabilitation Providers

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BACKGROUND: Evidence supports the inclusion of rehabilitation services to improve health, functioning, and well-being of people with multiple sclerosis (MS) regardless of setting, disability level, or age. Yet limited knowledge about the features, variability, and processes of MS rehabilitation in Canada raises questions about care decisions, such as where, when, and what rehabilitation services are provided, why, to whom, and under what models of care.

OBJECTIVES: Describe the factors that influence MS rehabilitation care decisions from the perspective of rehabilitation providers from different disciplines.

METHODS: Rehabilitation providers were recruited through advertisement to participate in virtual in-depth qualitative interviews. Interviews were recorded and transcribed. A combination of content and thematic analysis was used to describe where, when, why, how, and what rehabilitation services were delivered to people with MS and the factors that influenced these care decisions.

RESULTS: Twenty providers from 4 provinces participated. Providers worked in hospitals, MS clinics, outpatient rehabilitation programs, home care, and private practice clinics. They represented the disciplines of occupational therapy, physiotherapy, speech language pathology, physiatry, social work, and pastoral care. Across all disciplines, 4 broad categories of factors influenced MS rehabilitation care decisions: system-level factors (eg, setting), service-level factors (eg, program eligibility), provider characteristics (eg, experience), and patient needs and goals. Together, system constraints, geography, and interactions among the other categories influenced what, how, when, and where rehabilitation was provided.

CONCLUSIONS: Participants reported that system and service level factors play a large role in MS rehabilitation care decisions in Canada. At times, these factors limit the ability of rehabilitation providers to implement patient-centered, goal-directed, evidence-based care to individual patients.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Delivery of Care, Management of Activities of Daily Living in MS

(REH19) Transcutaneous Spinal Cord Stimulation for Recovery of Hand/Arm Function in Multiple Sclerosis: A Preliminary Study

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BACKGROUND: Current disease-modifying therapies aim to prevent new lesions in people with multiple sclerosis (MS); unfortunately, there are no current Food and Drug Administration–approved therapies to promote central nervous system (CNS) repair. Thus, strategies to promote functional recovery are needed, and upper extremity function has been specifically identified as a high research priority. Electrical spinal cord stimulation is a neuromodulation technique used to amplify sensorimotor recovery after a wide variety of CNS disorders but has been limited by the need for surgical implantation. However, new technologies have emerged, allowing for stimulation via adhesive electrodes placed on the skin over the vertebrae.

OBJECTIVES: Test the feasibility and tolerability of transcutaneous cervical spinal cord stimulation in people with MS. Preliminary efficacy on recovery of arm and hand function was also explored.

METHODS: This is an open-label pilot crossover clinical trial of transcutaneous cervical spinal cord stimulation combined with occupational therapy compared with occupational therapy alone in adults with MS in whom upper extremity impairment is underway. After enrollment, participants are randomly assigned to either 6 weeks of therapy alone or 6 weeks of therapy combined with transcutaneous spinal stimulation as their first intervention arm. Next, participants undergo a 6-week washout period, after which they will complete the alternate 6-week intervention arm.

RESULTS: Four participants (Expanded Disability Status Scale score range, 5.5-8) have been enrolled in this preliminary study. Two have completed 6 weeks of transcutaneous cervical spinal cord stimulation combined with therapy (3 times per week) with 100% treatment adherence. Transcutaneous cervical spinal cord stimulation was well-tolerated, with global improvements in pinch and grip force (increase in force in the affected hand after completing the 6-week intervention; range, 53%-200%). Both participants demonstrated improvement in other upper extremity functional outcome measures, such as the Action Reach Arm Test, Box and Blocks Test, Quality of Life in Neurological Disorders upper extremity function questionnaire, and 1 of the participants demonstrated improvement in the 9-Hole Peg Test.

CONCLUSIONS: Preliminary data from the first 2 participants suggest that transcutaneous spinal cord stimulation is safe and well-tolerated in people with MS, supporting the need for further clinical trials to determine the efficacy of transcutaneous spinal cord stimulation on recovery of upper extremity function.

DISCLOSURES: *Sarah B. Simmons, Shawn Luke, Annie Yang, Fatma Inanici: Nothing to disclose. Chet T. Moritz: SpineX (SpineX has licensed intellectual property from the University of Washington that was invented by author and collaborators.).*

KEYWORDS: CNS Repair

(REH20) The Relationship Between Disability Status and Walking Speed in Adults With Multiple Sclerosis

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BACKGROUND: The timed 25-Foot Walk (T25FW) and Patient Determined Disease Steps (PDDS) are measures commonly used for adults with multiple sclerosis (MS). However, there is limited knowledge about the utility of using the measures to customize interventions for people with MS (PwMS).
OBJECTIVES: This exploratory study aimed to assess the correlation between T25FW and PDDS in participants with MS enrolled in the Tele-Exercise and Multiple Sclerosis (TEAMS) study conducted from 2017 to 2020.
METHODS: This exploratory analysis utilized retrospective baseline from 756 individuals (mean age, 50.1 years; 89% women, 11% men; 73% White, 24% Black, 3% other) to evaluate the correlation between the T25FW (in seconds[s]) and self-reported PDDS scores using Spearman ρ. An additional Spearman correlation assessed the relationship between T25FW baseline benchmarks (‹6 s, 6-7.99 s, ›8 s, unable to complete) and PDDS modified ranges (0-2, 3-4, 5-6, 7), which were used for intervention assignment. A x^2 test with Monte Carlo simulations was employed to examine the association between TEAMS intervention levels and PDDS-modified ranges.
RESULTS: The results of Spearman ρ showed a strong significant positive correlation between the PDDS and the T25FWT (ρ = .72; P < .001). An additional Spearman ρ found a strong significant positive correlation between the T25FW baseline benchmarks and the modified PDDS ranges established for TEAMS level intervention assignment (ρ = .73, P < .001). A x^2 test with Monte Carlo simulations showed a significant association between the TEAMS intervention level and PDDS-modified ranges (P = .005).
CONCLUSIONS: The T25FW can be used with the PDDS to guide clinicians to customize interventions for PwMS from both the participant's perspective and objective data.
DISCLOSURES: *Nothing to disclose.*
KEYWORDS: Complementary/Alternative Therapies in MS, Comprehensive Care and MS, Management of Activities of Daily Living in MS

(REH21) Dropout, Adherence, and Compliance Rates for the Targeted Exercise for African Americans With Multiple Sclerosis Project

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BACKGROUND: There is increasing interest in documenting rates of dropout, adherence, and compliance within randomized controlled trials (RCTs) of exercise training in multiple sclerosis (MS). Understanding exercise behavior in RCTs is important, as adherence and compliance might be particularly salient for identifying the dose necessary for benefits.
OBJECTIVES: We report dropout, adherence, and compliance rates of the 16-week Targeted Exercise for African Americans With MS (TEAAMS) project.
METHODS: We recruited African American individuals with MS from the southeastern portions of the United States, and participants were screened for walking dysfunction as a primary inclusion criterion. Participants were randomly assigned into 1 of 2 conditions delivered over 16 weeks—aerobic and resistance exercise training (ET) or flexibility control group (FT)—using a random numbers sequence with concealed allocation. Adherence and compliance were obtained from participant logbooks, video chats with the behavioral coach, and coaching logs. Adherence was defined as the overall number or frequency of sessions completed, regardless of prescribed intensity and duration, and compliance was defined as the overall number of sessions completed that align with 75% prescribed intensity and duration. Data were maintained in Microsoft Excel, and descriptive statistics (mean, SD, percentages, and frequency counts) were used to describe each adherence and compliance metric within and across the ET and FT conditions.
RESULTS: Of the 87 participants enrolled in the TEAAMS intervention (ET: n=42; FT: n=45), 73 completed the program (ET: n=34; FT: n=39), yielding a 16% dropout rate. Adherence in the ET group averaged 31.4 of 48 (65%) possible aerobic sessions, and 28.3 of 48 (59%) possible resistance sessions. Adherence in the FT group averaged 35.1 of 48 (73%) possible flexibility sessions. Compliance rates for prescribed aerobic minutes and number of resistance exercises in the ET group averaged 74%, whereas it was 74% for the FT group.
CONCLUSIONS: We provide the first evidence of rates of dropout, adherence, and compliance of an exercise training RCT of African Americans with MS who have walking dysfunction.
DISCLOSURES: *Victoria A. Flores, Robert W. Motl, Edson Flores, Whitney N. Neal, Dominique Kinnett-Hopkins, Dorothy Pekmezi: Nothing to disclose. Mitzi J. Williams: Alexion, Biogen, Bristol Myers Squibb, Novartis (consulting fee); Amgen, EMD Serono, Genentech, Sanofi, TG Therapeutics (consulting fee, speakers' bureau).*
KEYWORDS: African American, Comprehensive Care and MS

RELAPSE THERAPY

(REL01) Exploring Treatment Approaches in Myelin Oligodendrocyte Glycoprotein Antibody–Associated Disease: A Survey of Neurologists

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BACKGROUND: Diagnostic criteria for antimyelin oligodendrocyte glycoprotein antibody disorders (MOGAD) were published in 2023, but debate continues regarding optimal therapeutic strategies for pediatric MOGAD.
OBJECTIVES: To investigate treatment approaches and preferred diagnostic investigations for pediatric MOGAD among neurologists.
METHODS: A survey questionnaire focused on pediatric MOGAD treatment was launched through the Practice Current section of *Neurology*: *Clinical Practice* from April 2024 to October 2024. Responses from neurologists were solicited through advertisements on American Academy of Neurology (AAN) social media platforms, the AAN website, in print editions of *Neurology*, and through QR codes shared at professional neurological meetings. The questionnaire included 12 questions evaluating clinical decision-making after the first and second neuroinflammatory episodes in a child testing positive for MOG-immunoglobulin G (MOG-IgG) antibody. Demographic questions were included. Responses were evaluated using descriptive statistics.
RESULTS: The survey was completed by 346 neurologists (52.3% general neurologists, 32.1% neuroimmunologists [NIs], and 15.6% those in other neurology fields). Of the respondents, 90.5% chose to send for serum MOG-IgG antibody testing after the first event (59.7% serum, 36.4% cerebrospinal fluid plus serum). For acute treatment, 84.1% chose to give a 3- to 5-day course of high-dose intravenous steroids. Approaches to steroid tapering varied, with 33.0% choosing a 2- to 4-week taper, 27.2% a 7- to 12-week taper, and 21% not offering a steroid taper. Although only 18.9% of NIs chose to do so, 56.6% of all respondents chose to initiate maintenance therapy after the first episode. After the second episode, 98.3% of all respondents recommended starting maintenance therapy, with rituximab (37.1%) being the most frequently chosen agent, followed by monthly intravenous immunoglobulin (IVIg) (25.6%) and azathioprine (17.1%). NIs selected monthly IVIg (50%) over rituximab (27.3%). The duration of treatment in relapsing cases varied: 42.9% would maintain treatment for 2 years or less, 35.3 % would maintain treatment for more than 2 years, and 21.8% chose to continue treatment indefinitely.
CONCLUSIONS: The survey results demonstrated substantial variability in the treatment of MOGAD among neurologists, reflecting current gaps in knowledge about therapies for MOGAD. Future work should focus on identifying optimal therapeutic approaches to this disorder.
DISCLOSURES: *Nothing to disclose.*
KEYWORDS: MOGAD

SELF-CARE

(SEL01) Health Issues in Patients With Multiple Sclerosis: A Focus on Oral Health

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BACKGROUND: People with multiple sclerosis (PwMS) often experience neurological deficits that can impair their ability to maintain proper daily oral hygiene routines. These deficits, coupled with systemic inflammation and potential medication adverse effects, may contribute to a higher prevalence of oral health complications.
OBJECTIVES: This study aimed to investigate the prevalence of dental problems and limitations in oral hygiene practices among PwMS and to evaluate the impact of MS phenotypes, disability levels, and disease duration on oral health outcomes.
METHODS: PwMS attending the private outpatient MS clinic in Baku, Azerbaijan, were recruited to the study. They were interviewed about their oral hygiene habits through surveys and referred for a dental examination conducted by a qualified dentist. Dental x-rays were excluded from the study to limit unnecessary exposure. Data collected included MS phenotype (relapsing-remitting [RRMS] vs progressive [SPMS/PPMS]), disease duration, symptoms, and Expanded Disability Status Scale (EDSS) scores.
RESULTS: A total of 50 patients with mean age of 35±7 years were assessed; of these, 73.5% had RRMS. Our study revealed that dry mouth (40.2%) and gum bleeding (26.1%) were the most frequent oral health concerns reported. These issues were significantly more prevalent among patients with progressive MS compared with those with RRMS (P=.02). Association was observed between increased oral health problems and higher EDSS scores (mean, 4.5±0.5), and longer disease duration (mean, 6±0.5 years; P<.05). Individuals who reported irregular tooth brushing and experienced oral health issues more frequently also exhibited greater motor deficits, such as muscle weakness and imbalance. Conversely, visual problems and mood instability were not significantly associated with these oral health complaints (P>.05). Furthermore, our findings indicate that regular dental visits were significantly less common among patients with progressive MS compared with those with RRMS (P=.01).
CONCLUSIONS: Oral health issues, particularly dry mouth and gum bleeding, are significantly more prevalent in individuals with progressive MS, especially those with higher disability and longer disease duration. This emphasizes the critical need for routine dental care as part of comprehensive MS management.
DISCLOSURES: *Nothing to disclose.*
KEYWORDS: Comprehensive Care and MS, Management of Activities of Daily Living in MS, Oral Health

SYMPTOM MANAGEMENT

(SYM01) Subjective Cognitive Performance Is Driven by Invisible Symptoms of Multiple Sclerosis

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BACKGROUND: Multiple studies have highlighted the intricate and ambiguous relationship between subjective self-evaluations and objective assessments of cognitive performance.
OBJECTIVES: This study probed the relationship between subjective and objective cognitive impairment, their cooccurrence, and their relationship with important covariates in people with early multiple sclerosis (MS). Patients were asked about their experiences with cognition in their care and their opinions about the preservation of cognition as a therapeutic goal.
METHODS: In this cross-sectional study, 205 people with MS (PwMS) used the icompanion app for self-assessments of cognitive function (Quality of Life in Neurological Disorders), objective cognitive testing (icompanion symbol test), patient-reported outcomes on disability, depression, fatigue, and MS symptoms. Correlations between subjective and objective cognitive impairment across pwMS with different Expanded Disability Status Scale (EDSS) levels were evaluated, along with various other covariates. Of the 205 participants, 52 had a brain MRI in the past 6 months, from which volumetric biomarkers were calculated using icobrain.
RESULTS: A significant but weak correlation was observed between subjective and objective cognition (ρ=.21; P=.002). Subjective and objective cognitive impairment (a score at least 1.5 SD lower than a healthy normative population) showed low cooccurrence (2.0%). Subjective cognition was associated with symptoms such as pain, fatigue, and depression, whereas objective cognition was more related to physical functions. Objective performance correlated positively with thalamus volume (ρ=.49; P=.023). The survey results highlighted that preservation of cognition is a high or top priority for 81.9% of patients across all EDSS levels and that patients with more severe disability worry more about their cognitive deterioration.
CONCLUSIONS: The study suggests that PwMS may not accurately recognize their cognitive status and that subjective and objective impairment seldom cooccur. Both concepts were shown to correlate with different covariates, illustrating their complex relationship and challenging the assumption that subjective reports can act as proxies for objective cognitive decline. The study survey results indicated that patients found the preservation of cognition a high priority in their MS care, with an increased concern in patients with higher disability levels.
DISCLOSURES: *Augusto Miravalle: Alexion, Celgene, EMD Serono, Genzyme, Genentech, Novartis (consulting fee, speakers' bureau). Lars Costers, Rebecca Bartz, Diana M. Sima, Dirk Smeets: icometrix (salary). Guy Nagels: icometrix (ownership interest). Enrique Alvarez: Atara, Biogen, Bristol Myers Squibb, Genentech/Roche, National Institutes of Health, National Multiple Sclerosis Society, Novartis, Patient-Centered Outcomes Research Institute, Rocky Mountain MS Center, Sanofi, TG Therapeutics (research support); Biogen, Celgene/Bristol Myers Squibb, Cionic, EMD Serono/Merck, Genentech/Roche, Horizon/Amgen, Novartis, Sanofi, TG Therapeutics (consulting fee). Wissam Elmalik, Hanan Al Halawani, Maarten Dewil, Melissa Cambron, Matthias Grothe, Delphine Van Laethem, Stijn Denissen: Nothing to disclose. Aaron L. Boster: Amgen, Sanofi, Serono (speaking); Amgen, Biogen, Novartis Roche, Sanofi, Serono (research support).*
KEYWORDS: Cognition, Comprehensive Care and MS, Psychological Issues and MS

(SYM02) Study Design of Phase 2, Randomized, Double-Blind, Placebo-Controlled Trial of BMS-986368, a Fatty Acid Amide Hydrolase/Monoacylglycerol Lipase Inhibitor, for Treatment of Spasticity in Multiple Sclerosis

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BACKGROUND: Spasticity is a debilitating symptom of multiple sclerosis (MS). Recently, exogenous cannabis-based products have been proposed to manage MS-related spasticity (MSS). BMS-986368 is a first-in-class irreversible inhibitor of fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL), with activity that leads to increased levels of endocannabinoids anandamide (AEA) and 2-arachidonoylglycerol (2-AG), which are produced by postsynaptic neurons. AEA and 2-AG bind to cannabinoid receptors CB1 and CB2. CB1 binding reduces neurotransmitter release at presynaptic terminals, causing an antiexcitatory effect on motor neurons that may relieve MSS.
OBJECTIVES: Describe design of the phase 2 BALANCE-MSS-1 efficacy and safety study of BMS-986368 for MSS treatment.
METHODS: BALANCE-MSS-1 (NCT06782490) is a randomized, double-blind, placebo-controlled trial of BMS-986368 in adults with MS, MSS for 6 months or more, Modified Ashworth Scale (MAS) score 2 or greater in 2 muscle groups (at least 1 in the leg), and Expanded Disability Status Scale score from 3.0 to 6.5. Exclusion criteria include other conditions that can cause spasticity or interfere with study assessments. Participants must stop other antispasticity medications and cannabinoid product use prior to being randomly assigned. Participants were randomly assigned to placebo or 1 of 3 oral doses of BMS-986368 for 6 weeks. The primary end point is change from baseline (BL) to week 6 (W6) on the Total Numeric-transformed MAS–Most Affected Lower Limb. Secondary efficacy end points are change from BL to W6 on the Numeric Rating Scale of Spasticity, the Multiple Sclerosis Spasticity Scale-88, the Timed 25-Foot Walk, and W6 Clinical Global Impression-Severity. Pharmacokinetics and safety/tolerability are evaluated. Changes from BL for active treatment vs placebo are analyzed using mixed models for repeated measures with BL score, treatment, visit, treatment by visit, and BL by visit as covariates. The main estimand for primary end points uses a treatment policy strategy for intercurrent events such as treatment discontinuation and use of prohibited and restricted treatments. In an optional 6-week double-blind extension, those on BMS-986368 continue their assigned dose; the placebo group is rerandomized to an active dose.
RESULTS: BALANCE-MSS-1 begins enrollment in March 2025 and aims to randomly assign approximately 200 participants globally.
CONCLUSIONS: If safe and efficacious, BMS-986368 could offer a new first-in-class treatment of MSS, an indication with few available or developing therapies.
FUNDING: Bristol Myers Squibb

DISCLOSURES: *Francois Bethoux: Bristol Myers Squibb (consulting fee, advisory board member); MedRhythms (consulting fee, contracted research, scientific advisory board member); Qr8 Health (intellectual property rights). Brielle Carramusa, Walter Heine, Rosa Miceli, Guangyi Gao, Richard Leigh-Pemberton: Bristol Myers Squibb (employee and/or shareholder).*

KEYWORDS: Comprehensive Care and MS, Spasticity

(SYM03) Initial Symptoms and Most Prevalent Sequelae in Patients With Multiple Sclerosis: A Retrospective Study

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BACKGROUND: Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system that typically begins around the age of 20. This condition can lead to significant physical and cognitive disabilities, substantially impairing quality of life. MS is characterized by a diverse range of signs and symptoms, including spasticity, fatigue, pain, bladder dysfunction, sexual dysfunction, depression, and anxiety, as well as cognitive dysfunction stemming from progressive neuronal damage.

OBJECTIVES: The objective of this study was to determine the initial symptoms and most prevalent sequelae among patients enrolled in an MS patient association in São Paulo, Brazil.

METHODS: A total of 295 individuals participating in an MS patient association in São Paulo, Brazil, were interviewed. Data were collected between April 2023 and December 2024 during an inclusion interview conducted by the Brazilian Multiple Sclerosis Association (ABEM).

RESULTS: The initial symptoms and sequelae experienced by patients with MS are diverse and can vary significantly among individuals. Among the interviewees, 72.5% (214 individuals) were women; 27.5% (81 individuals) were men. The majority identified as White (64.4%), with a mean age range from 30 to 45 years. The most reported initial symptoms included tingling or paresthesia (65.1%), followed by changes in limb strength (56.9%) and imbalance (55.3%). Additional initial symptoms reported included changes in speech (13.6%), emotional disturbances (22.7%), cognitive changes (16.3%), as well as bladder and bowel disorders (24.1%). Among those who knew their Expanded Disability Status Scale (EDSS) score, most reported a current EDSS of 3.5 or lower. In terms of sequelae, patients reported complaints of fatigue (n=204), changes in strength (n=134), and cognitive changes primarily affecting attention, concentration, and memory (n=185). Studies by Ashtari et al and Barkhof et al indicated a higher prevalence of optic neuritis (29.3% vs 54%, respectively) and cerebellar symptoms (18.7% vs 16%).

CONCLUSIONS: The clinical manifestations at onset and the sequelae of MS exhibit considerable heterogeneity. Recognizing the range of symptoms can contribute to the improvement of the functional disability status scales currently employed. The impact of cognitive sequelae in these patients, which is often overlooked in rehabilitation therapies, is significant. Nonmotor symptoms warrant further exploration and study to facilitate the implementation of more effective interventional therapies.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Epidemiology of MS, Management of Activities of Daily Living in MS, Natural History of MS

(SYM04) A Pilot, Double-Blind Crossover Study of Intravenous, Subanesthetic Dose of Ketamine vs Placebo for Multiple Sclerosis–Related Fatigue

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BACKGROUND: Fatigue is a common and disabling symptom of multiple sclerosis (MS). No US Food and Drug Administration–approved pharmacologic treatments exist. Management of MS-related fatigue remains a significant unmet need. Ketamine, a glutamatergic *N*-methyl-D-aspartate receptor antagonist, has been shown to improve fatigue among patients with mood disorders. Findings from one small, randomized trial showed a trend for efficacy of ketamine in MS fatigue.

OBJECTIVES: We are conducting a placebo-controlled, double-blind crossover study of 20 patients to investigate the efficacy of ketamine in reducing MS-related fatigue. Secondary outcomes are depression, health-related quality of life, and global health.

METHODS: People aged 18 to 65 years with clinically definite MS and significant fatigue are being recruited for this study. Participants must be on a stable disease-modifying therapy regimen for at least 3 months prior to their first study treatment visit. Exclusion criteria include pregnancy, breastfeeding, current substance use disorder, MS relapse or serious infection in the past 30 days, or comorbid condition posing undue risk to the patient per physician discretion. Participants will first complete a screening visit to assess study eligibility. When eligibility is confirmed, they will be randomly assigned to receive an infusion of ketamine 0.5 mg/kg or normal intravenous saline over 40 minutes. Eight weeks later, patients will receive the opposite intervention. Seven days and 28 days after each infusion, patients will complete the Modified Fatigue Impact Scale-5 to assess fatigue, the Patient Health Questionnaire-9 to assess depression, and the Functional Index for Living with Multiple Sclerosis to assess health-related quality of life. A clinician also completes clinical global impression measures to assess the patient's global health. Adverse events and concomitant therapies are assessed at all study visits.

RESULTS: This study is ongoing.

CONCLUSIONS: Two primary observations have emerged as we conduct this study. First, the acute effects of ketamine compared with normal saline complicated successful blinding in this study. Insufficient blinding may cause expectancy biases and overestimation of treatment effects. In other double-blinded trials of ketamine, midazolam has been used as placebo, which we may consider in future studies. However, the acute effects of ketamine and midazolam may be distinguishable; although both are used for anesthesia, midazolam is more likely to attenuate anxiety and induce amnesia whereas ketamine is more likely to cause dissociation and analgesia. Second, we noticed an anecdotal association between positive emotions (eg, mild euphoria) during an infusion and improved clinical status over the subsequent weeks. Conversely, patients who reported negative emotions (eg, anxiety) during an infusion tended to report no change or worsened clinical status over the subsequent weeks. Psychological factors that may mediate ketamine's therapeutic effect should be studied.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Complementary/Alternative Therapies in MS

(SYM05) Cardiovascular Comorbidities Are Independently Associated With Longitudinal Measures of Multiple Sclerosis Fatigue

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BACKGROUND: People with multiple sclerosis (PwMS) experience a wide range of physical comorbidities. Cardiovascular comorbidities have emerged as important contributors to worsening disability in affected cases.

OBJECTIVES: To analyze the association between baseline cardiovascular comorbidities and longitudinal fatigue experience in a large cohort of PwMS.

METHODS: We examined the relationship between baseline cardiovascular comorbidities (self-reported cardiac disease, diabetes, or dyslipidemia) and longitudinal fatigue in 5507 PwMS. Data were collected from the MS PATHS (supported by Biogen) cohort at 10 centers in the United States and Europe. Fatigue was measured using the Quality of Life in Neurological Disorders (Neuro-QoL) fatigue *t* score.

RESULTS: Participant mean age was 54.3 ± 12.3 years at the first visit, and 73.7% of participants were women. Most participants had relapsing forms of MS (66.3%). At baseline, cardiovascular comorbidities were present in 53.6% of participants and the mean (SD) Neuro-QoL fatigue *t* score was 50.1 (9.7). In the mutually adjusted, generalized estimating equations model, several factors were independently associated with longitudinal fatigue *t* scores. Cardiometabolic comorbidity was significantly associated with higher longitudinal fatigue levels (β=0.62; 95% CI, 0.30-0.94; $P<.001$). Other significant contributors to higher longitudinal fatigue included depression *t* score, anxiety *t* score, sleep *t* score, progressive MS type, and higher Patient-Determined Disease Steps scores. Conversely, male sex, higher education, and older age at diagnosis were associated with lower fatigue scores over time. In this model, performance measures (processing speed test, manual dexterity test, and walking speed test *z* scores) and body mass index were not significantly associated with longitudinal fatigue levels.

CONCLUSIONS: This finding supports the role of cardiovascular comorbidity as a contributing factor to fatigue in people with MS and suggests that addressing these comorbidities may help mitigate a common and disabling MS symptom.

DISCLOSURES: *Mahsa Ghajarzadeh, Bardia Nourbakhsh, Kathryn C. Fitzgerald: Nothing to disclose. Ellen M. Mowry: Biogen, Genzyme (research funding); Teva (medication for a clinical trial); UpToDate (royalty).*

KEYWORDS: Management of Activities of Daily Living in MS

(SYM06) Botulinum Toxin for the Treatment of Multiple Sclerosis–Related Spasticity: A Retrospective, Single-Center Study

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BACKGROUND: Spasticity is defined as involuntary muscle overactivity resulting in increased muscle tone and exaggerated tendon reflexes. Spasticity related to multiple sclerosis (MS) is common and often debilitating. It affects 60% to 84% of people with MS, contributing to disability by causing gait disorders, falls, fatigue, spasms, sleep disturbance, pain, and potential hastening of the time to wheelchair dependence. Oral antispasmodics are widely used to treat spasticity, with only partial benefit and potential for worsening fatigue, which is already a very common symptom of MS. Botulinum toxin is effective in the treatment of focal or regional spasticity; however, its administration requires specialized training and the cost is often prohibitory.

OBJECTIVES: To assess the efficacy and safety of botulinum toxin in the management of MS-related spasticity.

METHODS: Chart review of patients receiving botulinum toxin at our MS clinic from 2022 to 2024.

RESULTS: A total of 56 patients received botulinum toxin. The average age was 54 years. Of these patients, 85% received onabotulinumtoxinA and 15% received abobotulinumtoxinA. Treatment benefits were reported by 87%, and 84% continued treatment for up to 11 treatments. Only 7 patients stopped treatment due to weakness, with no other adverse effects reported. Of these patients, 6 were ambulatory and remained ambulatory despite weakness. Two patients were lost for follow-up, and 2 patients stopped treatment due to insurance denials.

CONCLUSIONS: Botulinum toxin is an important tool in the management of MS-related spasticity, with a low rate of adverse effects, which were transient.

DISCLOSURES: *Tania Reyna: Alexion, Biogen, EMD Serono, TG Therapeutics (consulting fee); Biogen, EMD Serono, Novartis, TG Therapeutics, UCB (research support). Vinutha Ganapathy, Lyndsey Hale: Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Spasticity

LATE-BREAKERS

(LBA01) Efficacy and Safety of a Body Weight–Adjusted Higher Dose of Ocrelizumab vs the Standard Dose in Relapsing Multiple Sclerosis: Primary Results of the Phase 3b MUSETTE Study

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BACKGROUND: Ocrelizumab (OCR) is a recombinant, humanized anti-CD20 monoclonal antibody approved at 600 mg every 6 months for people with relapsing multiple sclerosis (PwRMS) or primary progressive MS (PPMS). In findings from phase 3 randomized controlled trials (RCTs) for RMS (OPERA I/II; NCT01247324/NCT01412333) and PPMS (ORATORIO; NCT01194570), higher OCR exposure was associated with greater B-cell depletion and lower risk for confirmed disability progression (CDP) and composite CDP (cCDP) without increased frequency and severity of adverse events. Prospective RCTs assessing efficacy and safety outcomes associated with higher OCR doses will help establish benefits to patients in delaying disease progression.

OBJECTIVES: MUSETTE (NCT04544436) is a phase 3b, multicenter, randomized, double-blind, parallel-group study evaluating the efficacy and safety of higher OCR doses than those approved in PwRMS.

METHODS: PwRMS were randomly assigned 2:1 to receive the higher dose (1200 mg or 1800 mg for baseline body weight< 75 kg or ≥ 75 kg, respectively) to achieve at least the highest exposure quartile of the OPERA trials or the approved 600-mg intravenous OCR dose every 24 weeks. Eligibility criteria included age between 18 and 55 years, RMS diagnosis (2017 revised McDonald criteria), Expanded Disability Status Scale (EDSS) score less than or equal to 5.5 at screening, and 1 or more documented relapses in the year or 2 or more documented relapses in the 2 years prior to screening. The primary end point is time to onset of cCDP, defined as a 12-week confirmed increase in scores for EDSS, Timed 25-Foot Walk Test (≥ 20% from baseline), or 9-Hole Peg Test (≥ 20% from baseline).

RESULTS: Of 864 PwRMS, 860 received 1 or more infusions (safety-evaluable population). Mean (SD) age at baseline was 35.8 (8.9) years, 63% of participants were women, and 88% of participants were White. Mean (SD) times since MS symptom onset and diagnosis were 7.5 (6.9) years and 5.1 (5.8) years, respectively, and mean (SD) baseline EDSS score was 2.9 (1.4). Half of participants were MS disease-modifying therapy naive. Mean time since last reported relapse was 5.6 (3.8) months. At baseline, 39% of PwRMS had contrast-enhancing lesions (CELs). Mean (SD) number of CELs was 1.6 (4.2), and median (range) volume of T2 lesions was 11.3 cm^3 (0.1-113.7).

CONCLUSIONS: MUSETTE baseline characteristics are consistent with prior clinical populations of PwRMS in the OPERA trials regarding demographics and recent disease activity. Primary efficacy and safety results for the MUSETTE population will be available and presented at the annual meeting.

DISCLOSURES: *Stephen L. Hauser: Accure, Alector, Annexon, Hinge Bio (serves on scientific advisory board); BD, Gilead, Moderna, NGM Bio, Nurix Therapeutics, Pheno Therapeutics (consulting fee); Neurona (previous board of directors, current advisor). Amit Bar-Or: Abata, Accure, Atara Biotherapeutics, Bristol Myers Squibb/Celgene/Receptos, GSK, Gossamer, Horizon Therapeutics, Immunic, Janssen/Actelion, MedImmune, Novartis, Sangamo, Sanofi-Genzyme, Viracta (consulting fee, advisory board participation); Biogen Idec, F. Hoffmann-La Roche, Genentech, Merck/EMD Serono (contracted research, consulting fee, advisory board participation). Gavin Giovannoni: Biogen Idec, Celgene/Bristol Myers Squibb, EMD Serono/Merck, F. Hoffmann-La Roche, Genentech, GSK, Janssen/J&J, Japan Tobacco International, Moderna, Novartis, Sandoz (speaker, consulting fee, contracted research); Sanofi (research support, speaker, consulting fee). Maria Pia Sormani: Alexion, Biogen Idec, EMD Serono/Merck, F. Hoffmann-La Roche, Immunic, Novartis, Sanofi (consulting fee). Jiwon Oh: Biogen Idec, Roche (consulting fee, contracted research, speaking); Bristol Myers Squibb, Eli Lilly, EMD Serono, Novartis, Sanofi Genzyme (consulting fee, speaking). Sharon Stoll: Alexion Pharmaceuticals, Biogen, Bristol Myers Squibb, EMD Serono, F. Hoffmann-La Roche, Genentech, Horizon Therapeutics, Novartis, Sanofi Genzyme, TG Therapeutics (consulting fee, speaking, advisory board, steering committees). Martin S. Weber: Bayer, Genzyme (travel funding and/or speaker honoraria); Biogen Idec, EMD Serono/Merck, F. Hoffmann-La Roche, Novartis, Teva (contracted research, travel funding and/or speaker honoraria); Deutsche Forschungsgemeinschaft (WE3547/5-1), Pro Futura Programme of the Universitätsmedizin Göttingen (contracted research); PLOS One (editor). Xavier Montalban: AbbVie, Actelion, Alexion, BIAL, Biogen, Bristol Myers Squibb/Celgene, EMD Serono, European Committee for Treatment and Research in Multiple Sclerosis, Excemed, F. Hoffmann-La Roche, Genzyme, Immunic Therapeutics, Janssen Pharmaceuticals, MedDay, Medscape, Merck, Multiple Sclerosis International Federation, Mylan, National Multiple Sclerosis Society, NervGen, Neuraxpharm, Novartis, PeerVoice, Samsung-Biosys, Sandoz, Sanofi-Genzyme, Teva Pharmaceutical, TG Therapeutics (lecture honoraria, travel expenses, scientific meetings, trial steering committee, and/or clinical advisory board). Krzysztof Selmaj: AstraZeneca (lecture honoraria, consulting fee); Biogen, Ipsen (lecture honoraria); Bristol Myers Squibb, Merck, Novartis, TG Therapeutics (consulting fee, lecture honoraria, advisory boards); F. Hoffmann-La Roche (consulting fee, lecture honoraria); Teva (travel support). Maciej Maciejowski: Amgen (consulting fee); Biogen, Bristol Myers Squibb, Novartis (honoraria). Jacqueline A. Nicholas: Biogen, Patient-Centered Outcomes Research Institute, University at Buffalo (contracted research); Bristol Myers Squibb, Horizon (speaking honoraria); EMD Serono, TG Therapeutics (consulting fee, speaking honoraria); Genentech, Novartis (consulting fee, contracted research); Greenwich Biosciences, Sanofi (consulting fee). Dusanka Zecevic, Ulrike Bonati, Qing Wang, Anastasiia Raievska, Hans-Martin Schneble: F. Hoffmann-La Roche (royalty, salary). Ludwig Kappos: Bayer, Biogen, Bristol Myers Squibb, Celltrion, Clene Nanomedicine, Eli Lilly (Suisse) SA, EMD Serono Research and Development, F. Hoffmann-La Roche, Galapagos NV, Genentech, Immunic AG, Janssen, Kiniksa Pharmaceuticals, Merck Healthcare AG, Minoryx Therapeutics S.L., MSD Merck Sharp & Dohme AG, Neurostatus-UHB AG, Novartis, Sanofi, Shionogi BV, Wellmera AG, Zai Lab (steering committee, advisory and data safety monitoring board, educational activities, consulting fee); Innosuisse (contracted research); University Hospital Basel/Stiftung Neuroimmunology and Neuroscience Basel (consulting fee, steering committee, advisory and data safety monitoring board, educational activities).*

KEYWORDS: Disease-Modifying Treatments in MS

(LBA02) Quantitative Survey of Burnout Among Neurology Advanced Practice Providers (Physician Assistants and Nurse Practitioners) and Clinical Pharmacists in the United States

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BACKGROUND: Burnout among advanced practice providers (APPs), including physician assistants (PAs) and nurse practitioners (NPs), and clinical pharmacists (CPs) is a well-recognized crisis across various disciplines as encountered by the United States health care system. Given that the prevalence of burnout among PAs, NPs, and CPs is reported as 35%, 37%, and 60% or greater, respectively, their respective American associations have issued a call for action. To the best of our knowledge, data on the burnout rate among neurology APPs and CPs in the US have not been published. Understanding the prevalence and potential risks associated with burnout may facilitate changes to support these groups in providing best patient care.

OBJECTIVES: To establish the prevalence of burnout (long-term job-related stress leading to exhaustion and detachment from job responsibilities) among neurology APPs and CPs in the US and identify potential risks associated with burnout.

METHODS: A 25-question survey was sent to neurology APPs and CPs, which included a validated 10-question Mini Z inventory v3.0 assessing work life and wellness. Information on demographics, professional data, work environment, and level of support was also collected, and all data were analyzed descriptively.

RESULTS: Overall, 83% (101 of 121) of responders completed the survey (PAs, 19%; NPs, 40%; CPs, 39%). Of these, 57% responded that they had burnout or were starting to experience burnout and 51% of respondents experienced great job stress. Per the Mini Z inventory v3.0 scoring system, 45% of respondents cited electronic medical records (EMRs) as a source of frustration, with 23% of respondents reporting a high degree of EMR-related stress. A total of 28% of respondents work more than 50 hours

per week, and 8% of respondents work more than 60 hours per week. Although 73% of respondents said they were satisfied with their current job, 57% of respondents had considered changing their career or leaving the field due to burnout or related issues in the past year. Most of these (43.1%) were from academic medical centers.

CONCLUSIONS: Despite a relatively small sample size, results from this survey provide key insights into the high prevalence of burnout among neurology APPs and CPs in the US. EMR-related stress and long work hours were the most common reasons for job stress. Although job satisfaction remained high, more than 50% of respondents were planning a change in field due to burnout or related issues. These results can guide further research to improve the quality of life in neurology APPs and CPs and further enhance patient care.

DISCLOSURES: *Bryan Walker, Denise Bruen, Erica Zeplin-Pratt: EMD Serono (salary).*

KEYWORDS: Advanced Practice Providers, Clinical Pharmacist, Neurology, Burnout

(LBA03) Assessing the Role of Patient Portal Messaging in Multiple Sclerosis Care: Patient Preferences, Usage, and Potential Implications for Clinician Burnout

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BACKGROUND: It is presumed that health care patient portals serve as asynchronous tools that can enhance shared decision-making, optimize care time, and reduce gaps in health care information communication. Research suggests that patient portals and messaging can be particularly beneficial for care coordination in managing chronic complex diseases. However, concerns are emerging about the potential link between clinician burnout and the increasing adoption of electronic medical records technology and patient portal messaging.

OBJECTIVES: To contribute to understanding the role of patient portal messaging in multiple sclerosis (MS) care by evaluating its perceived value and usage among patients and clinicians, with the goal of identifying opportunities to enhance communication, improve care coordination, and better understand potential contributions to clinician burnout.

METHODS: Cross-stakeholder input informed the design of a set of questionnaires to be distributed to people with MS and clinicians, including nurse practitioners, to assess value and usage of patient portal messaging. The 18-question patient-facing survey was distributed through the Multiple Sclerosis Association of America's database. Data from clinician surveys, once available, will be used in addition to patient responses to identify disparities in understanding between the contributing stakeholders and potential areas for intervention.

RESULTS: Diversity of our respondents was representative of the prevalence of the MS population in the United States, with 83% identifying as White, 10% as Black, and 6% reporting Hispanic, Latino, or Spanish ethnicity. Portal messaging (43.37%) was ranked as the most preferred tool among respondents for communication with their health care team, followed closely by phone call (31.22%) and then email (8.56%). The most frequently reported use for messaging was medication refills (66.94%), requesting medical advice (52.89%), scheduling appointments (42.15%), urgent concerns (38.57%), clarifying recent visit questions (37.74%), and time-sensitive medication questions (36.91%). Predominantly, respondents felt they used portal messaging only when critically necessary (57.85%).

CONCLUSIONS: Respondent comments highlighted an appreciation for patient portal messaging, particularly among those who travel long distances for care or have limited in-person visits. However, given the prioritized reasons usage reported, there may be opportunities for targeted education on appropriate portal usage, which could help streamline communication and address a key factor in clinician burnout.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Comprehensive Care and MS, Management of Activities of Daily Living in MS, Nursing Management in MS

(LBA04) Impact of Early Treatment Modification on Long-Term Outcomes in Treatment-Naive People With Multiple Sclerosis

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BACKGROUND: Multiple sclerosis (MS) is an autoimmune demyelinating and neurodegenerative disease of the central nervous system. Early initiation and continuous adherence to treatment are recognized as crucial in mitigating disability progression in individuals with MS.

OBJECTIVES: Evaluation of 5-year outcomes of treatment-naive people with MS who discontinued disease-modifying drugs (DMDs) due to adverse effects or nonadherence within the first year.

METHODS: Patients were categorized into 2 groups: those who discontinued the drug within the first year due to adverse effects or incompatibility and those who used it continuously for 5 years. There were no significant differences between the groups in terms of age and sex. Both groups included treatment-naive patients. Outcome evaluation included the number of attacks, Expanded Disability Status Scale (EDSS) scores, and conversion to secondary progression after an average of 5 years in both groups.

RESULTS: The first group (discontinuers) had 72 people with MS, and the second group (continuers) had 37 people with MS. In the first group, 66.7% (n = 48) were women and 33.3% (n = 24) were men. In the second group, 67.57% (n = 25) were women and 32.43% (n = 12) were men. At the end of 5 years, the EDSS score (mean difference, 1.625; 95% CI, 0.887-2.363; $P < .001$) and relapse frequency (mean difference, 1.217; 95% CI, 0.715-1.719; $P < .001$) were significantly lower in patients who used medication for 5 years compared with those who stopped taking medication within 1 year. In the first group, the percentage of patients who transitioned to the secondary progressive phase was 22% (n = 16). No transition to the secondary progressive phase was observed in the second group.

CONCLUSIONS: Early discontinuation of treatment due to adverse effects or nonadherence may lead to unfavorable clinical outcomes, including disease progression and increased relapse frequency. Therefore, clinicians should prioritize the selection of DMDs with favorable tolerability profiles and engage in proactive patient education and monitoring to optimize treatment adherence and long-term outcomes in individuals with MS. Further research is warranted to elucidate the underlying factors contributing to treatment discontinuation and to develop strategies to mitigate this challenge in clinical practice.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Disease-Modifying Treatments in MS, Naive Multiple Sclerosis

(LBA05) Examining Classical Cerebrospinal Fluid Biomarkers in Primary Progressive Multiple Sclerosis

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BACKGROUND: Primary progressive multiple sclerosis (PPMS) presents unique challenges in diagnosis and prognosis assessment. Oligoclonal bands (OCB), immunoglobulin (Ig) G index, and IgM index are pivotal cerebrospinal fluid (CSF) biomarkers for PPMS diagnosis, yet their prognostic value remains underexplored.

OBJECTIVES: This study aims to comprehensively investigate the prevalence and clinical significance of classical CSF biomarkers, including OCB, IgG index, and IgM index, in individuals with PPMS. Additionally, we aim to compare these biomarker profiles between PPMS and relapsing-remitting multiple sclerosis (RRMS) cohorts to discern any distinctive features that may inform prognosis and guide personalized treatment strategies.

METHODS: We conducted a retrospective analysis of people with PPMS diagnosed according to the 2017 McDonald criteria. Demographic data, follow-up duration, Expanded Disability Status Scale (EDSS) scores at baseline and follow-up, OCB, IgG index positivity, IgM index positivity, initial symptom localizations, and T1 black hole presence on MRI were collected. OCB positivity was defined as type 2 or 3 OCB result, IgG index positivity as 0.7 or greater, and IgM index positivity as 0.1 or greater. Patients were categorized into OCB positive/negative(+/−), IgM+/−, and IgG+/− groups.

RESULTS: OF the patients with PPMS, 73.1% had OCB+ status, 29% had IgM+ status, and 50% had IgG+ status. OCB and IgG index positivity resembled CSF characteristics of people with RRMS (70% OCB positivity, 47% IgG index positivity). However, IgM index positivity was slightly lower in PPMS compared with RRMS (29% vs 38%). Median follow-up duration was 3.55 years, with no significant differences between OCB+/−, IgM+/−, and IgG+/− groups. No variations were observed in sex, diagnosis age, duration between first symptom and diagnosis, initial symptom localizations, and EDSS score worsening among the groups. The OCB+ group exhibited more T1 black holes on MRI compared with the OCB− group ($P = .032$).

CONCLUSIONS: People with PPMS exhibit higher IgM index positivity compared with those with RRMS, suggesting potential differences in disease pathogenesis. Further, the presence of oligoclonal bands may indicate more severe MRI findings, emphasizing its relevance in PPMS prognosis assessment. Further research is warranted to elucidate the prognostic implications of these classical biomarkers in the management of PPMS.

DISCLOSURES: *Nothing to disclose.*
KEYWORDS: Biomarkers

(LBA06) Efficacy and Safety of Cladribine Tablets in a Large, Real-World, Multicenter United States Population

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BACKGROUND: Cladribine tablets (CladTs) are approved for relapsing forms of multiple sclerosis (RMS) and active secondary progressive MS in the United States; CladTs are hypothesized to act as an immune reconstitution therapy.[1,2] Since the approval of CladTs, real-world evidence has complemented data from randomized controlled trials to enrich and improve the understanding of this therapeutic approach.
METHODS: This real-world, multicenter, retrospective study evaluated people with RMS 18 years or older who received 1 or more courses of CladTs from 2019 to 2024 across 4 US centers. This analysis included demographics, treatment history, efficacy, and safety outcomes.
RESULTS: The combined cohort included 342 patients with a mean age of 52 years (SD, 11.2); 72.8% were women (n = 249). Patients had a mean disease duration of 15.2 years (SD, 8.7) and an annualized relapse rate (ARR) for the prior 2 years of 0.6 (SD, 0.7). The mean number of prior disease-modifying therapies was 2.5 (range, 0-9). In the combined cohort, 7.6% (n = 26) were in year 1 of follow-up, 10.8% (n = 37) were in year 2, 15.5% (n = 53) were in year 3, 14.9% (n = 51) were in year 4, and 51.2% (n = 175) were in year 5. ARR for years 1 through 5 was 0.11 (SD, 0.34), 0.07 (SD, 0.26), 0.07 (SD, 0.29), 0.02 (SD, 0.15), and 0.02 (SD, 0.15), respectively. In each year of follow-up, 92% or more of patients were free from MRI activity. Across all years of follow-up, 4.1% (n = 7) discontinued CladTs due to an adverse event (AE), 0.6% (n = 1) discontinued due to lymphopenia, and 13.7% (n = 13) discontinued due to disease activity. The most commonly reported AEs (≥ 5%) were headache (14.3%; n = 49), COVID-19 (10.5%; n = 36), fatigue (8.5%; n = 29), upper respiratory infection (7%; n = 24), and urinary tract infection (5.8%; n = 20). Serious AEs or malignancies were reported in 1.5% (n = 5) of patients, and 6 deaths were reported. Lymphopenia was observed in 85.5% (n = 195) of patients, with 28.9% (n = 66) experiencing grade 3 and 2.2% (n = 5) experiencing grade 4. Effectiveness and safety outcomes in 5 patients who were retreated with CladTs in year 5 will be reported as data become available.
CONCLUSIONS: The data reported for the combined cohort demonstrated sustained efficacy into year 5 in a real-world setting, with no new safety concerns.

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DISCLOSURES: *Ravi Dukkipati: Allergan, Bristol Myers Squibb, EMD Serono, Genentech, Genzyme, Merck KGaA, Novartis, TG Therapeutics (speaker/consultant). Braulimar Marchand Colón, Viviana Martínez-Maldonado: Nothing to disclose. Donald Negroski: Adamas, Alexion, Alkermes, Bayer, Biogen, Celgene/Bristol Myers Squibb, EMD Serono, Janssen, Novartis, Roche-Genentech, Sanofi-Genzyme (consulting fee, speakers' bureau). Amparo Gutierrez: Biogen (contracted research). Angel R. Chinea: Allergan (speakers' bureau); Biogen, EMD Serono, Genentech, Novartis, Sanofi (consulting fee, speakers' bureau).*
KEYWORDS: Disease-Modifying Treatments in MS, Imaging and MS, Immunology and MS

(LBA07) Efficacy and Safety of Ofatumumab According to Age: A Subgroup Analysis of Data From the ASCLEPIOS I/II and the ALITHIOS Extension Study

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BACKGROUND: Ofatumumab (OMB) showed superior efficacy to teriflunomide (TER) in findings from the phase 3 ASCLEPIOS I/II trials in people with relapsing multiple sclerosis (PwRMS) and sustained efficacy and safety for up to 6 years in findings from the ALITHIOS extension.
OBJECTIVES: To assess the efficacy and safety of OMB across different age groups of PwRMS.
METHODS: Efficacy analyses included those randomly assigned to OMB or TER in ASCLEPIOS I/II stratified by age: less than 40 years, 40 to 49 years, and 50 years or older. Efficacy outcomes included annualized relapse rate (ARR), gadolinium-enhancing (Gd+) lesions, new or enlarging T2 (neT2) lesions, no evidence of disease activity-3 (NEDA-3), and 6-month confirmed disability worsening (6mCDW). Safety analyses (immunoglobulin [IgG, IgM] levels and infection rates with up to 6 years of OMB treatment) included those who received 1 or more doses of OMB in ASCLEPIOS I/II or ALITHIOS (data cutoff: September 25, 2023).
RESULTS Overall, 1882 participants (age ≤ 55 years) were randomly assigned in ASCLEPIOS I/II (< 40 years: OMB n = 496, TER n = 539; 40-49 years: OMB n = 332, TER n = 271; ≥ 50 years: OMB n = 118, TER n = 126). Safety analysis included 1028, 607, and 247 participants younger than 40 years, 40 to 49 years, and 50 years or older, respectively. Baseline disease characteristics were similar between treatment groups across ages, but the age group of 50 years or older had a longer disease duration, higher proportion of active secondary progressive MS, fewer Gd+ lesions, higher EDSS score, and lower normalized brain volume. ARR was lower for OMB vs TER across age groups (rate ratios: < 40,0.420; 40-49 years, 0.499; ≥ 50 years, 0.590). Gd+ T1 and neT2 lesion rate was reduced for OMB vs TER for all age groups as well (Gd+ T1: 0.036, 0.083, 0.000; neT2: 0.146, 0.164, 0.239). More participants achieved NEDA-3 in Year 2 of ASCLEPIOS I/II with OMB vs TER across all age groups (86.2% vs 26.9%, 81.8% vs 43.9%, and 82.2% vs 61.7% for ages <40, 40–49, and ≥50 years). OMB vs TER reduced 6mCDW risk in all age groups (HRs: 0.656, 0.629, and 0.843, respectively). Mean IgG/IgM profiles were similar between age groups: IgG remained stable, whereas IgM was reduced but remained above the lower limit of normal with OMB in all age groups at all visits. Annualized rates of serious infection (including COVID-19) with OMB were low (range, 0-0.031) across age groups.
CONCLUSIONS: OMB efficacy was observed in all age groups. Across all age categories, IgG/IgM levels up to 6 years were consistent with results reported for the overall population, with low levels of serious infection.

DISCLOSURES: *Enrique Alvarez: Atara, National Institutes of Health, National Multiple Sclerosis Society, Patient-Centered Outcomes Research Institute, Rocky Mountain Multiple Sclerosis Center (contracted research); Biogen, Celgene/Bristol Myers Squibb, Genentech/Roche, Novartis, Sanofi, TG Therapeutics (consulting fee, contracted research); CIONIC, EMD Serono/Merck, Horizon/Amgen (consulting fee). Stephen L. Hauser: Accure, Alector, Annexon, Hinge Bio (scientific advisory board); BD, Moderna, NGM Bio, Pheno Therapeutics (consulted); F. Hoffmann-La Roche, Novartis AG (travel reimbursement, writing support); Neurona (board of directors). Patricia K. Coyle: Accordant, Amgen, Eli Lilly, EMD Serono, GSK, Horizon Therapeutics, Novartis, TG Therapeutics, Viatris (consulting, nonbranded speaker fees); Celgene, Cleveland Clinic, CorEvitas, Genentech/Roche, National Institute for Neurological Diseases and Stroke (research support); Sanofi Genzyme (consulting, nonbranded speaker fees, research support). Shiv Saidha: Amgen, Horizon Therapeutics, ImmPACT Bio, Rewind Therapeutics (advisory board); Biogen, Genentech, Novartis, SetPoint Medical (consulting fee, contracted research); Clene (contracted research, advisory board); InnoCare Pharma, Kiniksa, Medical Logix (consulting fee); JuneBrain (consulting fee, ownership interest); LAPIX Therapeutics (consulting fee, contracted research, ownership interest); MedDay (contracted research). Gabriel Pardo: Amgen, Biogen, EMD Serono, Horizon Therapeutics, Novartis, Roche/Genentech, Sanofi-Genzyme, TG Therapeutics (consulting fee); Biogen, Bristol Myers Squibb, EMD Serono, Horizon Therapeutics, Novartis, Roche/Genentech, Sanofi-Genzyme, TG Therapeutics (speakers' bureau). Jun Li: Novartis Pharma AG (salary). Min Wu: Novartis Pharmaceuticals (salary). Anil Abeyewickreme: Novartis Pharmaceuticals (salary). Annette F. Okai: Alexion, Biogen, Bristol Myers Squibb, EMD Serono, Roche Genentech, Sanofi-Genzyme (consulting fee); Alexion, Biogen, Novartis, Roche/Genentech, Sanofi-Genzyme, TG Therapeutics (research support).*
KEYWORDS: Disease-Modifying Treatments in MS, Ofatumumab

(LBA08) The Effects of Cognitive Behavioral Therapy on Fatigue Impact and Severity in People With Multiple Sclerosis: A Systematic Review and Meta-Analysis

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BACKGROUND: Fatigue in individuals with multiple sclerosis (MS) is severe and disabling. One of the nonpharmacological treatments is cognitive behavioral therapy (CBT).

OBJECTIVES: To estimate the pooled effects of CBT on fatigue impact and severity in people with MS.

METHODS: Two trained researchers searched PubMed, Scopus, Embase, Web of Science, and Google Scholar on November 1, 2024. They also searched the references of identified articles and conference abstracts. We calculated mean change for Modified Fatigue Impact Scale (MFIS) and Fatigue Severity Scale (FSS) and standardized mean difference (SMD) for mean change difference of 2 groups.

RESULTS: A literature search yielded 12,731 records. A total of 141 full texts were evaluated, and 24 studies were included in the systematic review. The pooled mean change of MFIS in the CBT group was estimated at −7.77 (95% CI, −10.7 to −4.48; $I^2 = 90\%$; $P < .001$). The pooled mean change of MFIS in the CBT group was estimated at −3.87 (95% CI, −7.52 to −0.22; $I^2 = 94\%$; $P < .001$). The pooled SMD of mean change in CBT control groups was estimated at −3.72 (95% CI, −6.41 to −1.04; $I^2 = 66\%$; $P < .01$). The pooled mean change of FSS in the CBT group was estimated at −3.47 (95% CI, −6.12 to −0.81; $I^2 = 87\%$; $P < .01$). The pooled mean change of FSS in the control group was estimated at 2.76 (95% CI, −2.55 to 8.07; $I^2 = 93\%$; $P < .001$). The pooled SMD for mean change of FSS comparing 2 groups was estimated at −5.63 (95% CI, −9.59 to −1.66; $I^2 = 90\%$; $P < .001$).

CONCLUSIONS: The result of this systematic review and meta-analysis showed that all types of CBT are not effective to improve fatigue impact and severity in people with MS, and interventions such as consultation with an expert nurse could help improve fatigue impact and severity.

DISCLOSURES: *Nothing to disclose.*

KEYWORDS: Management of Activities of Daily Living in MS, Psychological Issues and MS

(LBA09) Infection Rates in People With Multiple Sclerosis Treated Long-Term With Fumarates vs Anti-CD20 Monoclonal Antibodies

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BACKGROUND: Disease-modifying therapies (DMTs) have reduced multiple sclerosis (MS) burden for people with MS (PwMS); however, the risk of infection with long-term DMT treatment is a concern, especially for immunodepleting therapies. Prior studies have shown that anti-CD20 monoclonal antibodies have a higher risk for infections vs other therapies, such as fumarates (FUM); however, there are limited studies comparing infection rates with long-term treatment beyond 2 years.

OBJECTIVES: To compare annualized infection incidence, infection-related health care resource utilization (HCRU), and relapse outcomes in PwMS on long-term FUM vs anti-CD20s treatment.

METHODS: PwMS between the ages of 18 and 64 were identified from January 1, 2016, through May 31, 2022, in the Komodo Health claims database. Baseline characteristics, including age, sex, region, infection rates, MS severity, relapse rates, medication use, comorbidities, and index date, were used to propensity score (PS) match FUM PwMS 1:2 to anti-CD20s PwMS. Infection events were identified by codes from the tenth revision of the *International Classification of Diseases*. MS relapses were identified based on a previously published algorithm.

RESULTS: The study included 1956 PS-matched PwMS, either initiated with FUM (n=652) or anti-CD20s (n=1304). The FUM cohort received dimethyl fumarate (n=614) or diroximel fumarate (n=38), while the anti-CD20s cohort received ocrelizumab (n=1296) or ofatumumab (n=8). Baseline characteristics were well balanced (standardized mean differences ≤ 0.10) following PS matching. The annualized infection-related health care encounter rate per-patient-per-year (PPPY) was significantly lower for FUM compared with anti-CD20s (1.75 vs 2.22; $P<.001$). Mean infection events PPPY were lower for FUM compared with anti-CD20s from year 2 (2.31 vs 2.75, $P=.016$) to year 4+(2.54 vs 3.64; $P=.021$). MS-related HCRU was lower for FUM vs anti-CD20s at year 4 (7.90 vs 11.48; $P=.019$). Annualized relapse rate (ARR) and time to first relapse were similar between FUM and anti-CD20s (ARR, 0.08 vs 0.09; $P=.575$).

CONCLUSIONS: Compared with those on anti-CD20s, PwMS on FUM experienced significantly lower long-term infection–related HCRU with similar relapse outcomes. The difference in infection risk between FUM and anti-CD20 therapies increased with treatment duration, consistent with prior evidence that infection risk rises with long-term B-cell depletion. These findings underscore the importance of long-term risk-benefit considerations when selecting DMTs in MS management.

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KEYWORDS: Disease-Modifying Treatments in MS, Fumarates

(LBA10) Prospective Ascertainment of Peri-Childbirth Depression and Its Relationship With Postpartum Inflammatory Activity in Women With Multiple Sclerosis

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BACKGROUND: Women with multiple sclerosis (WwMS) are at elevated risk for depression, including peripartum depression (PPD). The interplay between MS-specific risk factors (radiological and clinical activity) and general risk factors for PPD (eg, prior depression, older age, low support) requires a prospective, detailed investigation.

OBJECTIVES: To prospectively ascertain prevalence of PPD in WwMS, and evaluate its association with risk factors and with other dimensions of maternal well-being.

METHODS: Adult women with a clinical diagnosis of MS or clinically isolated syndrome (CIS) enrolled across 2 sites starting at gestational week 36 and were followed serially until 12 months (M) postpartum. PPD was measured using Edinburgh Postnatal Depression Scale (EPDS; threshold›9 of 30), structured assessments (Mini International Neuropsychiatric Interview [MINI] and Structured Clinical Interview for DSM Disorders [SCID]), Hospital Anxiety and Depression Scale (HADS-D, threshold›8), and clinician's note of PPD. Covariates included demographic and MS-specific factors; other surveys were collected.

RESULTS: Among the 121 WwMS (95% relapsing onset) enrolled, 20.7% met criteria by EPDS, 18.2% by MINI/SCID, and 40.5% by any measure. PPD by any measure was associated with Black/Hispanic ancestry (OR 1.24; 95% CI, 0.09-2.40; $P=.03$), prepregnancy depression/anxiety (OR 2.15; 95% CI, 1.12-2.91), and absence of exclusive breastfeeding (OR 3.28; 95% CI, 0.19-2.18; $P=.01$). EPDS was most commonly elevated 1M postpartum (19%). It correlated highly with HADS-D ($r=0.79$, $P<.05$), and moderately with fatigue (MFIS), lower social support (Medical Outcomes Study-Social Support), and worse mother-infant bonding (Mother-to-Infant Bonding Scale; $|r|>0.37$, $P<.05$ for all measures). PPD was associated with higher preconception Expanded Disability Status Scale score (OR 2.01; 95% CI, 1.21-3.33; $P=.006$) and with gestational clinical relapses (in 17% overall; OR 5.65; 95% CI, 1.12-28.61; $P=.03$).

CONCLUSIONS: Prospective, detailed ascertainment revealed higher levels of PPD (20%-40%) than reports in both general (12%) and MS (14%) populations, underscoring the importance of screening for PPD from late gestation until 12M postpartum. The association of PPD not only with established risk factors but also with prepregnancy disability and inadequate disease control during pregnancy suggests that active management of MS inflammatory activity could reduce the impact of PPD on WwMS and their families.

DISCLOSURES: *Min Ji Kim, Ayushi Balan, Melika Arab Bafrani, Annika Anderson, Saumya Gupta, Gabriel Najarian, Stephanie Hsu, William Rowles: Nothing to*

disclose. Hemali Patel, Jennifer Smrtka, James B. Lewin, Sarah M England: Biogen (employee). Maria Houtchens: Biogen, Consortium of Multiple Sclerosis Centers, National Multiple Sclerosis Society (funding); Novartis (consulting fee, funding); Roche Genentech (consulting fee); Sanofi, Serono (consulting fee). Riley Bove: Alexion, Amgen, Cadenza, EMD Serono, Genzyme Sanofi, TG Therapeutics (consulting fee); Biogen, Eli Lily, National Institutes of Health and Department of Defense, National Multiple Sclerosis Society Harry Weaver Award, National Science Foundation, Novartis, Roche Genentech (funding).

KEYWORDS: Comprehensive Care and MS, MS and the Caregiver/Family, Psychological Issues and MS

(LBA11) When Shingles Strike the Spinal Cord: A Case of Varicella Zoster Virus–Triggered Neuromyelitis Optica

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BACKGROUND: An 83-year-old man was diagnosed with infiltrating high-grade urothelial carcinoma involving the bladder neck and prostate. Pathology revealed involvement of the muscularis propria, multifocal lymphovascular invasion, and perineural invasion. The patient declined radical cystoprostatectomy; therefore, a treatment plan consisting of concurrent chemoradiation with gemcitabine was initiated. Following treatment, he developed progressive right-lower-extremity weakness, which led to a fall and subsequent hospital admission.

OBJECTIVES: This case presents a rare and compelling intersection of myelitis in a patient with urothelial bladder cancer, accompanied by aquaporin-4 (AQP4) immunoglobulin G (IgG) seropositivity and varicella zoster virus (VZV) meningoencephalitis. Such a constellation of findings is exceptionally uncommon. Only a few reported cases suggest that VZV may trigger or worsen Neuromyelitis Optica Spectrum Disorder (NMOSD), and the literature on paraneoplastic neurological syndromes linked to urothelial carcinoma remains sparse. This case underscores the diagnostic and therapeutic challenges at the crossroads of neuroimmunology and oncology.

METHODS: We performed a comprehensive neurological examination, supplemented by advanced imaging— including brain and full spinal MRI—along with cerebrospinal fluid analysis via lumbar puncture.

RESULTS: Spinal MRI demonstrated an intramedullary T2/STIR hyperintensity at the T9 level. Cerebrospinal fluid analysis was positive for VZV DNA and revealed an AQP4-IgG antibody titer of 9.9, an IgG synthesis rate of 19.4, and an albumin quotient of 24. Additionally, the patient tested positive for VZV IgG, consistent with viral reactivation.

CONCLUSIONS: VZV myelitis is an uncommon complication, typically seen in immunocompromised individuals, and may occur without a preceding rash or IgM elevation. Viral infections—including VZV—have been proposed as potential triggers for NMOSD flares or initial onset, though mechanistic understanding remains limited. Concurrently, emerging evidence suggests an association between paraneoplastic syndromes and urothelial carcinoma. In this case, whether the patient's AQP4-IgG seropositivity represents a paraneoplastic manifestation or an autoimmune demyelinating process initiated by VZV reactivation remains uncertain.

DISCLOSURES: *Nazanin Kiapour, Maarib Hassan, Anuradha Singh: Nothing to disclose.*

KEYWORDS: NMOSD, VZV, Cancer, AQP4

(LBA12) Pregnancy and Natalizumab: 58 Pregnancies in a Single United States Center

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BACKGROUND: Family planning for women treated with natalizumab (NTZ) has evolved over the last 2 decades. Research has shown that clinicians need to consider not only the impacts on the fetus but also on the mother. While observational studies have assessed maternal and neonatal outcomes in women treated with natalizumab (NTZ) during pregnancy, they are largely limited to Europe, where health care differs from that in the United States.

OBJECTIVES: To evaluate the impact of NTZ exposure on maternal multiple sclerosis (MS) disease activity and neonatal outcomes at a US clinic

METHODS: From 2008 to 2024, all pregnant women on NTZ at the Rocky Mountain Multiple Sclerosis Clinic were followed.

RESULTS: Forty-three women with MS, representing 58 pregnancies, were included. Age at onset of pregnancy ranged from 21 to 41 years (mean 29.8 years). The number of NTZ doses prior to pregnancy ranged from 0 to 163 (mean 39.8). Pregnancy exposures to NTZ varied from 1 to 8 doses (mean 2.37 doses). Participants were stratified into 2 groups based on their NTZ use during pregnancy: women who remained on NTZ until 34 weeks gestation or delivery (n=20), and women who discontinued NTZ at the time of a positive pregnancy test or within 8 weeks of conception (n=38). Among the 20 pregnancies where NTZ was continued, no MRI activity or relapses were reported. Of the 38 pregnancies where NTZ was discontinued, 17 women showed MRI activity, 13 of whom also had a clinical relapse. Eight of these women restarted NTZ treatment during pregnancy. Eighteen relapses occurred within 3 months postpartum, with 17 of these relapses observed in women who discontinued NTZ. Among the 31 women who restarted NTZ within 3 months postpartum, the average time to restart was 2 weeks (range: 1 day to 12 weeks). Of the 58 pregnancies, outcomes are known for 52, including 36 healthy live births, 10 miscarriages, and 6 abnormal neonatal outcomes. Hematologic outcomes were not captured. Twenty-six women breastfed, while 13 opted not to breastfeed, with the remainder unknown.

CONCLUSIONS: NTZ continuation during pregnancy was associated with an absence of MS disease activity in 20 women. In contrast, discontinuation of NTZ during pregnancy resulted in clinical and/or MRI activity in approximately one-third of the patients. Further research is needed to extend these findings, particularly with respect to neonatal/infant outcomes.

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KEYWORDS: Disease-Modifying Treatments in MS

(LBA13) Role of Disease-Modifying Therapy in the Aging Multiple Sclerosis Population: Neurologist Survey

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BACKGROUND: The management of multiple sclerosis (MS) in older patients is currently controversial, and the data supporting discontinuation of disease-modifying therapies (DMTs) is inconclusive. Observatoire Français de la Sclérose en Plaques and the DOT-MS trial (NCT04260711) demonstrated higher MS activity in people who discontinued DMT, and despite the DISCOMS trial's focus on a carefully selected population enriched for those less likely to have activity, results showed an increase in disease activity, which was downplayed in the conclusions. The risk of these data being used by payors to support DMT discontinuation places older people with MS (PwMS) at risk for worsening disease activity.

OBJECTIVES: To assess neurologists' perspectives on DMT use and discontinuation in older PwMS.

METHODS: Members of the Medical Partnership 4 MS+(MP4MS+), a group of more than 1300 neurologists, were surveyed anonymously from June 2024 to February 2025 to explore attitudes toward DMT in older patients, disability influence on treatment, risk of relapse after discontinuation, and criteria for considering discontinuation.

RESULTS: A majority (87.1%) of the 341 respondents indicated that there is "really no [age] rule because patients are different." Because the "goal of treatment is preservation of function for as long as possible," 64.51% felt that having high disability does not play a role in discontinuation. This is in line with the clear agreement among prescribers that disability level should not be used by payors as a reason for discontinuation. As found in the literature, 87.1% agreed with scientific evidence that older PwMS relapse, even after long-term stability. In contrast to the 5 years of stability studied in recent trials, 50% felt that discontinuation should only be considered after 10 years of disease stability. Of survey respondents, 77.7% do not tell their stable patients to discontinue, and 25% of those discuss it only after the topic is raised by the patient/care partner, consistent with patient-centered decision-making.

CONCLUSIONS: Consistent with the lack of evidence from DMT discontinuation trials, a majority of the neurologists surveyed support individualized assessment rather than age-based rules in considering DMT discontinuation after long-term stability. Neurologists agree that disability, age, and ambulation should not preclude DMT use. Avoiding disease activity in patients remains a principal goal, including in those who are

older. Most importantly, disability level should not be used by payors as a reason for DMT discontinuation.

DISCLOSURES: *Flavia Nelson: EMD Serono, Horizon, Novartis, Sanofi (consulting fee); Genentech (consulting fee, speakers' bureau); Imcyse (contracted research). Amy Perrin Ross: Alexion, Amgen, Bristol Myers Squibb, EMD Serono, Roche, Sandoz, TG Therapeutics, UCB (consulting fee). Regina Berkovich: Alexion, Biogen, Bristol Myers Squibb, EMD Serono, Horizon, Johnson & Johnson, Mallinckrodt, Novartis, Sanofi (consulting fee). Samuel F. Hunter: Bristol Myers Squibb, Sanofi (contracted research); Vanda (speakers' bureau). Daniel S. Bandari: Amgen, Biogen, EMD Serono, Genentech, TG Therapeutics (consulting fee, contracted research, speakers' bureau); Sanofi (consulting fee, contracted research, salary). Daniel Kantor: CorEvitas (consulting fee, founding scientific director, co-scientific director); Vanda, Viatris (speakers' bureau).*

KEYWORDS: Disease-Modifying Treatments in MS, Economic Issues and MS, Immunology and MS

(LBA14) Pregnancy and Infant Outcomes for Women With Relapsing Multiple Sclerosis Following Exposure to Ofatumumab: Update From the PRIM Study

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BACKGROUND: Ofatumumab, a fully human anti-CD20 monoclonal antibody with a 20-mg subcutaneous monthly dosing regimen, is approved for the treatment of relapsing multiple sclerosis (MS) in adults. Current labeling indicates that women of childbearing potential should use effective contraception during treatment with ofatumumab and for at least 6 months after treatment discontinuation. However, pregnancies may occur during this interval.

OBJECTIVES: To report the cumulative pregnancy and infant outcomes data in women with MS treated with ofatumumab during pregnancy.

METHODS: The Novartis global safety database includes cases from clinical trials and the postmarketing setting collected via the noninterventional PRegnancy outcomes Intensive Monitoring (PRIM) program. Pregnancy and infant outcomes were analyzed in women with MS who were administered ofatumumab during pregnancy or up to 180 days prior to their last menstrual period (LMP) (data cutoff: September 25, 2024). Prevalences (%) are estimated in cases reported prior to September 25, 2023, providing at least 1 year post initial reporting to allow any pregnancy outcomes to occur, ie, to account for detection bias.

RESULTS: Cumulatively, until September 25, 2024, 669 prospective pregnancy cases were identified in the safety database. Among the 275 cases with at least 1 year since initial reporting (ie, reported until September 25, 2023), exposure information was available for 221, including 12% with a maternal ofatumumab administration within 180 days before their LMP, 87% in the first trimester, and 0.5% only after the first trimester. The outcome was known in 103 cases. These included 73 (70.9%) live births, 13 (12.6%) induced terminations (including 1 termination due to chromosomal anomaly), 13 (12.6%) spontaneous abortions, 1 (1.0%) spontaneous abortion NOS (not otherwise specified), 1 (1.0%) still birth, and 2 (1.9%) ectopic pregnancies. Two infants with minor congenital anomalies (hemangioma and hydronephrosis) were reported. One further major congenital malformation case involving persistent truncus arteriosus was reported since September 25, 2023.

CONCLUSIONS: While the number of cases remains limited and further effort is required to gain more data, findings suggest that prevalence estimates for pregnancy outcomes in cases of maternal ofatumumab administration during pregnancy or up to 180 days prior to LMP are in line with expected background rates in the general population.

DISCLOSURES: *Riley Bove: Alexion, Amgen, Cadenza, EMD Serono, Sanofi, TG Therapeutics (consulting fee); Biogen, Eli Lilly, F. Hoffman La Roche, Novartis (research support). Sharon Stoll: Alexion, Biogen, EMD Serono, Novartis, Sanofi Genzyme (consulting fee); BeCare MS Link, MedDay (research support); Bristol Myers Squibb (consulting fee, advisory boards); F. Hoffman La Roche, Forepont Capital Partners, TG Therapeutics (advisory boards); Global Consultant MD (chief executive officer); Horizon Therapeutics (consulting fee, steering committees, advisory boards); Roche/Genentech (consulting fee, steering committees). Ruth Dobson: Association of British Neurologists MS Advisory Group (member); Barts Charity, Celgene, Home Family Foundation, Multiple Sclerosis Society UK (contracted research); Biogen, Novartis (consulting fee, contracted research, lectures, speaking, meetings/travel); F. Hoffmann-La Roche (consulting fee, lectures, speaking); Janssen (contracted research, lectures, speaking, meetings/travel); Merck (contracted research, lectures, speaking); National Health Service England Clinical Reference Group (member); Sandoz (consulting fee); Sanofi-Genzyme, Teva Pharmaceuticals (lectures, speaking). Maria Pia Amato: Biogen, Bristol Myers Squibb, Celgene, Janssen, Merck, Novartis, Roche, Sandoz, Sanofi Genzyme (lectures, presentations, speakers' bureau, manuscript writing, educational events, data safety monitoring board, advisory board, support for attending meetings, and/or travel). Vineetkumar Kharat, Bita Rezaallah, Valentine Jehl: Novartis (salary). Anil Abeyewickreme: Novartis Pharmaceuticals UK Ltd, London, UK (salary). Bassem Yamout: Bayer, Biogen, Merck-Serono, Novartis, Roche, Sanofi (consulting fee, grants). Kristen Krysko: Biogen, Bristol Myers Squibb, EMD Serono, Novartis (consulting fee); Multiple Sclerosis Canada (research support); Roche (consulting fee, clinical trial site). Sandra Vukusic: Biogen, F. Hoffmann-La Roche, Merck-Serono, Novartis, Sanofi-Genzyme (consulting fee, contracted research, lectures, or speaking); Bristol Myers Squibb/Celgene, Sandoz, Teva Pharmaceuticals (consulting fee, lectures or speaking); Janssen (consulting fee). Kerstin Hellwig: Bayer, Biogen, Merck, Roche, Sanofi-Genzyme, Teva (research support, support for congress participation, scientific advisory boards); Novartis (research support, scientific advisory boards).*

KEYWORDS: Disease-Modifying Treatments in MS, Family Planning, Pregnancy

(LBA15) Retrospective Analysis of Efficacy, Safety, and Tolerability Outcomes After CD20-Directed Cytolytic Antibody Treatment Switches to Ozanimod in People With Relapsing Multiple Sclerosis

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BACKGROUND: The decision to switch disease-modifying therapies may be driven by convenience, safety, efficacy, tolerability, and insurance coverage. Increased understanding of what drives these decisions and how to implement therapy transition is needed to identify best clinical practices.

OBJECTIVES: This study aims to collect and analyze retrospective data from neurology health care providers (HCPs) to determine the efficacy, safety, tolerability, and treatment satisfaction after their patients with multiple sclerosis switched from a CD20-directed cytolytic antibody therapy to ozanimod.

METHODS: A retrospective study of patients who were treated with a CD20-directed cytolytic antibody and later switched to ozanimod was conducted using an electronic survey sent to 450 neurology HCPs. Data were deidentified at the time of collection.

RESULTS: Each representing a unique treatment switch to ozanimod, 251 surveys were collected and analyzed. Patients within the cohort were 66% White and 34% were from racial and ethnic minority populations; they transitioned from ocrelizumab (48%), ofatumumab (31%), rituximab (12%), or ublituxumab (10%). The top reasons for discontinuation of these therapies were patient preference (29%), provider preference (10%), and recurrent infections (10%). Since switching to ozanimod, 97% of patients experienced no disease activity, including no relapses, disability progression, or MRI activity. No adverse events were reported in 74% of patients, and HCPs reported their patients' conditions as well or extremely well in 64% of cases.

CONCLUSIONS: Switching from a CD20-directed cytolytic antibody to ozanimod was largely driven by patient and provider preference. The majority of patients on ozanimod experienced no disease activity and infrequent adverse events.

DISCLOSURES: *Christen Kutz: Bristol Myers Squibb (consulting fee, contracted research). James Appio, Michael Gatza, Corey Cusack: Nothing to disclose.*

KEYWORDS: Disease-Modifying Treatments in MS

(LBA16) The Wearing-Off Effect of Ofatumumab and Ocrelizumab—2 Anti-CD20 Therapies—in People With Multiple Sclerosis

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BACKGROUND: Anti-CD20 therapies are the standard of care for people with relapsing forms of multiple sclerosis (PwRMS). Of PwMS on ocrelizumab (OCR; administered

via biannual infusions), 61% experienced symptom worsening between 2 consecutive infusions (Toorop AA, van Lierop ZYGJ, Strijbis EMM, et al. The wearing-off phenomenon of ocrelizumab in patients with multiple sclerosis. *Mult Scler Relat Disord*. 2022;57:103364. doi:10.1016/j.msard.2021.103364).

OBJECTIVES: To quantify MS symptom worsening over a treatment (tx) cycle with ofatumumab (OMB; administered via monthly injections) and OCR using validated scales.

METHODS: This was a noninterventional primary data collection study among adults with MS treated with OMB (n=75) or OCR (n=60) in real-world practices across the United States. Data were collected by the Accelerated Cure Project, a patient-founded national MS nonprofit organization. Adults treated with OCR (for ≥ 1 year [yr]) or OMB (for ≥ 6 months [mo]) were surveyed at recruitment (baseline) and the beginning (≥ 7 days after tx was administered) and end (≤ 10 days before next dose) of their next tx cycle. Proportions of patients experiencing worsening of MS symptoms from the beginning to the end of a tx cycle were evaluated using the fatigue, mobility, cognition, depression domains of the Quality of Life in Neurological Disorders measurement system (Neuro-QOL).

RESULTS: Demographics were similar between OMB and OCR cohorts (mean age, 47 vs 49 yrs; women, 73% vs 82%; mean body mass index [BMI], 29.2 vs 28.6, respectively). Median duration of MS and tx were shorter for OMB (10 vs 14 yrs and 2 vs 5 yrs, respectively), and fewer of those on OMB used other tx to manage MS symptoms (68% vs 83%). Of OMB-treated patients, 37% were previously treated with OCR. At baseline, fewer patients on OMB vs OCR reported *usually* or *always* experiencing MS symptom worsening during *previous* cycles in their tx history (11% vs 22%, respectively; *P*=.13). Among those reporting symptom worsening *usually* or *always* during previous cycles, 25% vs 100% of those on OMB and OCR, respectively, reported the symptom worsening started more than 1 week prior to the next scheduled dose; 23% on OCR reported worsening more than 4 weeks prior to the next scheduled dose. During the tx cycle investigated, fewer OMB patients than OCR patients experienced worsening MS symptoms across the Neuro-QOL: fatigue (23% vs 42%, respectively; *P*=.019), mobility (4% vs 23%, respectively; *P*=.003), cognition (9% vs 30%, respectively; *P*=.003), depression (13% vs 18%, respectively; *P*>.05). Differences in symptom worsening remained significant after adjusting for BMI, suggesting wearing off was independent of BMI.

CONCLUSIONS: This study suggests significantly higher numbers of patients on OCR experience wearing-off-related symptom worsening than those on OMB.

DISCLOSURES: *Karishma Thakkar, Brandon Brown, Abhijit Gadkari: Novartis Pharmaceuticals Corporation (salary). Hollie Schmidt: EMD Serono, Novartis Pharmaceuticals, Quest Diagnostics, Sandoz (contracted research). Julien St-Pierre, Raluca Ionescu-Ittu: STATLOG Inc (consultancy company that received funds from Novartis for current study.). Mark Gilliland: Accelerated Cure Project (collaboration funding from Novartis for current study; grants collaboration funding, payments for use of assets, and/or in-kind contributions from Novartis and other MS biopharmaceutical companies). Francis Vekeman: Novartis Pharmaceuticals Corporation (consulting fee).*

KEYWORDS: Disease-Modifying Treatments in MS

(LBA17) Ponesimod in Relapsing Forms of Multiple Sclerosis: Long-Term Safety and Efficacy Results From the Optimum Open-Label Extension Study (OPTIMUM-LT)

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BACKGROUND: Ponesimod is a selective sphingosine-1-phosphate receptor modulator approved for the treatment of relapsing multiple sclerosis (RMS) in multiple countries.

OBJECTIVES: Characterize long-term safety, tolerability, and control of disease in people with RMS receiving ponesimod, 20 mg, once daily.

METHODS: People with RMS completing the OPTIMUM phase 3 core study (NCT02425644) comparing ponesimod with teriflunomide were eligible to enroll in the OPTIMUM-LT open-label extension trial (NCT03232073). Following completion of the core study and a posttreatment follow-up period, patients enrolling in OPTIMUM-LT were (re)initiated on ponesimod and treated for up to 240 weeks. Efficacy outcomes evaluated from randomization in the core study to the end of the extension study (combined analysis period) included annualized relapse rate (ARR), time to confirmed relapse, confirmed disability progression (CDP), and new/enlarging T2- and gadolinium-enhancing (Gd+) T1 lesions. Safety and tolerability were assessed from the start of the extension study and included monitoring of treatment-emergent adverse events (TEAEs) and serious TEAEs (SAEs).

RESULTS: A total of 877 patients entered the extension study. Of the 439 patients receiving ponesimod in both the core and extension study, 352 completed the study. Within this treatment group, ARR was 0.143 (95% CI, 0.123-0.167). At the end of the combined analysis period (up to 8.2 years), 56.7% of patients were relapse-free. Median time to relapse was 402.71 weeks. Due to the low number of events, 3- and 6-month CDP were not estimable. The mean number of new/enlarging T2 lesions per year was 1.352 (95% CI, 1.152-1.586) and mean number of Gd+T1 lesions at the end-of-treatment visit was 0.211 (95% CI, 0.131-0.341). Of the 877 patients in OPTIMUM-LT, 821 (93.6%) had any TEAE, 113 (12.9%) had an SAE, and 75 (8.5%) discontinued due to a TEAE. Similar rates occurred when assessed by core study treatment. The most common TEAEs were COVID-19 infection (25.4%), alanine aminotransferase increase (19.5%), nasopharyngitis (17.8%), lymphopenia (14.8%), and headache (13.8%).

CONCLUSIONS: The OPTIMUM-LT study confirmed the sustained efficacy of ponesimod in terms of relapses, MRI lesions, and low disability accumulation. Further, the safety profile of ponesimod during long-term treatment was consistent with prior research.

DISCLOSURES: *Mallery G. Mayo, Christos M. Polymeropoulos: Vanda Pharmaceuticals (salary). Gunther Birznieks: Vanda Pharmaceuticals (royalty). Mihael H. Polymeropoulos: Vanda Pharmaceuticals (ownership interest, salary).*

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