

PROGRAM

Storebælt Sinatur Hotel & Konference
29-30 May 2026

DAREMUS Annual Meeting 2026

- Organized in collaboration with the Danish Multiple Sclerosis Center (DMSC)
- MS Research Talent Awards are sponsored by the Danish MS Society (Scleroseforeningen)

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DAREMUS

Friday 29 May 2026

09:00-09:30	● Registration arrival coffee/tea
09:30-09:40	Welcome (DAREMUS' Board, Tobias Sejbæk)
09:40-10:30	2026 DAREMUS Lecture (Chair: Melinda Magyari) Prof. Jiwon Oh (Canada); Novel and emerging therapies in MS
10:30-11:30	2026 MS Research Talent Awards (Chairs: Lars Hvid & Tobias Sejbæk)
10:30-10:42	Sahla El Mahdaoui; Early effects of CD20-depleting therapy on cerebrospinal fluid biomarkers in MS
10:42-10:54	Andreas Færk; Immediate and short-term effect of engaging in cognitively stimulating activities: Post hoc analyses of a randomized controlled crossover trial
10:54-11:06	Anna San Torcuato; Validation of kappa free light chain index for MS diagnosis in Danish cohort
11:06-11:18	Michelle Agathon Hansen; AT2R Activation Enhances CNS Repair in Progressive MS
11:18-11:30	Eliza Varjú; Effectiveness of Escalation vs. Early High-Efficacy Therapies on Progression Independent of Relapse Activity in MS
11:30-12:30	● Lunch
12:10-12:25	Meet the Expert (Booth GOLD sponsored by Merck) – optional participation Speaker: Jiwon Oh (Canada); Age Matters
12:30-14:00	Scientific session: Clinical & Epidemiological Research (Chair: Mads A.J. Madsen & Jesper Nørgaard)
12:30-13:00	Keynote: Tom Fuchs (Netherlands); Cognitive decline as a window into progressive clinical deterioration
13:00-13:12	Agata Beczek; Preconception Use of Disease Modifying Therapy in Women with MS: A 25-Year Danish Nationwide Study
13:12-13:24	Asta Theodorsdottir; Defining composite markers to predict EDSS progression in SPMS by artificial intelligence
13:24-13:36	Mie Reith Mahler; Age and sex specific effects of initial high-efficacy therapy versus an escalation strategy in newly diagnosed patients with MS
13:36-13:48	Sahla El Mahdaoui; Ofatumumab versus ocrelizumab in relapsing-remitting MS: a nation-wide cohort study
13:48-14:00	Elisabeth Framke; Familial risk of MS: A nationwide registry-based study

Friday 29 May 2026

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- 14:00 - 14:45** ● **Coffee break**
- 14:25 - 14:40** **Meet the Expert** (Booth GOLD sponsored by Merck) – optional participation
Speaker: Finn Sellebjerg (Denmark); MavenChats
- 14:45 - 16:15** **Scientific session: Treatment & Basic Research I** (Chair: Stephan Bramow & Reza Khorrooshi)
- 14:45 - 15:15 Keynote: Tobias Sejbæk (Denmark); Bruton Tyrosine Kinase Inhibitors in MS
- 15:15 - 15:27 Stig P Cramer; Blood-Brain Barrier Leakage in Primary Progressive MS Exceeds Relapsing-Remitting MS Independent of Age: Evidence from DCE-MRI
- 15:27 - 15:39 Birgitte Villadsen; Ceruloplasmin Deficiency Reduces CD11b+ Microglial Cell Activation in Response to Cuprizone-Induced Demyelination
- 15:39 - 15:51 Maria L Foged; Age-related de novo somatic mutations in the MS brain
- 15:51 - 16:03 Amanda ML Christiansen; CSF immune cell biomarkers enable early accurate identification and differentiation of RRMS, NMOSD, and MOGAD
- 16:03 - 16:15 Derya Tireli; Choroid plexus enlargement in MS: a global volumetric analysis of structural and disease-related drivers
- 16:15 - 16:45** ● **Coffee break**
- 16:45 - 18:15** **Poster Session** incl. refreshments (Havegangen and Udsigt)
- 19:00 - 22:00** **Dinner & DAREMUS 2026 MS Research Talent Award Ceremony**

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Saturday 30 May 2026

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- 09:00-10:00** **Scientific Session: MS Rehabilitation** (Chair: Ulrik Dalgas & Nana Folman))
- 09:00-09:30 Keynote: Roshan das Nair (Norway); Evaluating and implementing cognitive screening and rehabilitation in MS
- 09:30-09:42 Laurits Taul-Madsen (Giulia Casu); AI-based telerehabilitation for MS: feasibility and usability in a multicenter pilot study
- 09:42-09:54 Lars Hvid; Dose-response effects of supervised power-oriented resistance training in people with MS – secondary data from the NEXIMS study
- 10:00-10:20** ● **Coffee break**
- 10:20-11:10** **Scientific Session: MS Diagnosis & Cases** (Chair: Stig Cramer & Ronald Antulov)
- 10:20-10:50 Keynote: Daniel Harrison (USA); Imaging chronic active lesions and relapse-independent worsening in MS
- 10:50-11:00 Marie M Hansen; [Case] Early MS-diagnose with solitary periventricular lesion and paramagnetic rim lesion and oligoclonal bands: application of McDonald 2024 criteria
- 11:00-11:10 Nanna Mouritzen; [Case] FLAIR-Hyperintense Lesions in Anti-MOG Associated Encephalitis with Seizures (FLAMES) and Subsequent Hemiatrophy
- 11:10-11:25** ● **Coffee break**
- 11:25-12:10** **Scientific Session: Basic Research II & Cases** (Chair: Zsolt Illes & Jette Frederiksen)
- 11:25-11:55 Keynote: Simon Hametner (Austria); Complement deposition in NMOSD, MOGAD and MS: lessons from neuropathology
- 11:55-12:05 Jesper Nørregaard; [Case] Severe multifocal relapse despite b-cell depletion on Rituximab – possible rebound activity post fingolimod
- 12:05-12:15 Hacer Cetinalp; [Case] Diagnostic challenge with isolated inflammatory steroid responsive rhombencephalitis
- 12:15-13:00** ● **Lunch & see you next year**
- 13:00-13:45** **DMSG meeting**
- 13:45-14:30** **DAREMUS General assembly**
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Abstracts



2026 MS Research Talent Awards

Early effects of CD20-depleting therapy on cerebrospinal fluid biomarkers in multiple sclerosis.

El Mahdaoui, Sahla¹; Hansen, Malene Bredahl¹; Hansen, Marie Mathilde¹; Sejbæk, Tobias^{2,3}; Buhelt, Sophie¹; Chow, Helene Højsgaard¹; Nørregaard, Jesper¹; Michelsen, Josephine¹; Søndergaard, Helle Bach¹; Sellebjerg, Finn^{1,4}; Romme Christensen, Jeppe¹ ¹Danish Multiple Sclerosis Center, Department of Neurology, Copenhagen University Hospital – Rigshospitalet, Glostrup, Denmark. ²Department of Neurology, Hospital Southwest Jutland, University Hospital of Southern Denmark, Esbjerg, Denmark. ³Department of Regional Health Research, University of Southern Denmark, Odense, Denmark. ⁴Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark.

BACKGROUND & AIM: Anti-CD20 monoclonal antibody therapy has demonstrated high effectiveness on disease activity in multiple sclerosis (MS). However, many patients on anti-CD20 treatment experience continued worsening of disability despite suppression of focal disease activity. Examination of cerebrospinal fluid (CSF) offers a valuable insight into immune processes and intrathecal treatment effects. The objective of the study was to investigate effects of anti-CD20 therapy on CSF biomarkers in MS.

METHODS: We investigated CSF samples from 52 participants with active MS before and six months after commencement of ocrelizumab or rituximab infusions, and 52 age-matched symptomatic controls (SC) without neurological disease. At baseline, 29 of the participants with MS were untreated (MSunt) and 23 switched from another disease-modifying therapy (MSswitch). Biomarker concentrations were measured in duplicates, and analyses were performed on log₁₀-transformed data. We used paired t-tests to analyze longitudinal differences in biomarker levels and one-way ANOVA with Tukey's correction to analyze differences between groups.

RESULTS: At month six, both the MSunt and MSswitch group demonstrated significant reductions of CSF concentrations of soluble B-cell maturation antigen (sBCMA) ($p < 0.001$ and $p = 0.028$, respectively) and neurofilament light chain (NfL) ($p < 0.001$ and $p = 0.049$, respectively) compared to baseline values. Furthermore, there was a reduction of myelin basic protein (MBP), sCD27, interleukin-12 p40 (IL-12p40), IL-8, chitinase 1 (CHIT1), and kappa free light chain (KFLC)-index in the MSunt group ($p < 0.05$), and of vascular endothelial growth factor A (VEGF-A) and glial fibrillary acidic protein (GFAP) in the MSswitch group ($p < 0.01$). The MSunt group demonstrated an increase in GFAP from baseline to month six ($p < 0.01$). The concentrations of sBCMA, sCD27, NfL, VEGF-A, and KFLC-index remained significantly higher in MSunt and MSswitch at month six compared to SC (adjusted $p < 0.05$). In addition, GFAP and CHIT1 remained higher in the MSunt group than in SC (adjusted $p < 0.01$).

DISCUSSION: We found reductions of most CSF biomarkers six months after the first infusion doses of anti-CD20 therapy in the MSunt group; treatment effects were less pronounced in the MSswitch group. Concentrations of several biomarkers remained higher in anti-CD20-treated patients than in age-matched SC, indicating residual neuroinflammation after the first infusion series.

Immediate and short-term effects of engaging in cognitively stimulating activities: Post hoc analyses of a randomized controlled crossover trial.

Færk, Andreas¹, Sellebjerg, Finn^{1,2}, Lund, Jakob Lindegaard¹, Loft, Mia¹, Højsgaard Chow, Helene ^{1*}, Marstrand, Lisbet^{1*}. ¹Danish Multiple Sclerosis Center, Department of Neurology, Copenhagen University Hospital – Rigshospitalet. ²Department of Clinical Medicine, Faculty of Health and Medical Science, University of Copenhagen. ^{*}Shared last authorship

BACKGROUND & AIM: Cognitively stimulating activities (CSAs) are associated with cognitive reserve and improved cognitive performance in people with MS (pwMS). The primary aim was to study immediate and short-term training effects of a CSA intervention on objective and subjective cognition. The secondary aim was to investigate intervention adherence.

METHOD: We performed post hoc analyses of data from 60 non-depressed, cognitively impaired pwMS (30 relapsing-remitting, 30 progressive) participating in a randomized controlled crossover trial with a waitlist control (NCT05691192). The 12-week intervention consisted of individualized CSAs. Participants were assessed at baseline, 12, and 24 weeks. Co-primary endpoints were the oral Symbol Digit Modalities Test (SDMT) and the Multiple Sclerosis Neuropsychological Questionnaire (MSNQ). Adherence was measured with the Cognitive Leisure and Activity Scale (CLAS). Statistical analyses included Bonferroni-corrected linear mixed models adjusted for age and education.

RESULTS: Compared with the control state, intervention states were significantly associated with improvements on the SDMT, both in the 12-week ($\beta = 4.7$, 95% CI [3.1, 6.3], $p < 0.0001$) and 24-week training state ($\beta = 8.0$, 95% CI [5.4, 10.7], $p < 0.0001$). There were also statistically significant differences in the 12-week ($\beta = -2.6$, 95% CI [-4.8, -0.5], $p < 0.0393$) and 24 week state ($\beta = -4.5$, 95% CI [-7.2, -1.9], $p < 0.0022$) on the MSNQ, though for the 12-week state this was driven by a

worsening in the control state. On the CLAS, scores improved significantly compared to the control state both in the 12 week ($\beta = 5.5$, 95% CI [3.8, 7.2], $p < 0.0001$) and 24-week state ($\beta = 4.5$, 95% CI [2.4, 6.7], $p < 0.0007$).

DISCUSSION: Results lend preliminary evidence that adherence to an individualized CSA intervention is feasible and may improve objective and subjective cognition after 12 and 24 weeks. Though encouraging, these are post hoc analyses and will need replication.

Validation of kappa free light chain index for MS diagnosis in Danish cohort.

San Torcuato, Anna^{1,2} Peiris, Michella Dinithi³ Farup Revsholm, Jesper⁴ Helskov Jørgensen, Louise⁴ Illes, Zsolt⁵ Nielsen, Christian³ Sejbæk, Tobias¹ ¹Department of Neurology, Esbjerg Hospital, University Hospital of Southern Denmark, Esbjerg, Denmark. ²Nordic Bioscience A/S, Herlev, Denmark. ³Department of Immunology, Odense University Hospital, Denmark. ⁴Department of Clinical Biochemistry, Odense University Hospital, Denmark. ⁵Department of Neurology, Odense University Hospital, Denmark.

BACKGROUND & AIM: Multiple sclerosis (MS) is a critical and severe disease, emphasizing the need for accurate and accessible diagnostic tools. The kappa free light chain (kFLC) index was first included in the revised 2024 McDonald criteria alongside oligoclonal bands (OCB). The kFLC index represents a quantitative alternative to OCB reflecting intrathecal immunoglobulin synthesis. This study aimed to validate the diagnostic performance of the kFLC index in a Danish cohort and compare it to OCBs.

METHODS: A total of 196 individuals were included, with 91 MS patients (median age 36 years) and 104 patients with other neurological disorders (OND; median age 58 years). kFLC index, defined as the ratio of kFLC to albumin in CSF relative to blood, was determined using Binding Site's Freelite assay on the Optilite platform in CSF and blood. Group differences in kFLC levels were assessed using Kruskal–Wallis tests. Diagnostic performance was evaluated by receiver operating characteristic (ROC) analysis. Odds ratios and likelihood ratios were calculated, and an optimal cut-off was determined using the Youden index.

RESULTS: kFLC levels differed significantly between MS and OND groups ($p < 0.0001$) and according to OCB status ($p < 0.0001$). ROC analysis demonstrated high diagnostic accuracy of the kFLC index, with an AUC of 0.94, sensitivity of 90%, and specificity

of 95% at a cut-off value of 5.4. The overall odds ratio for MS diagnosis was 39.7 if above the cut-off. Likelihood ratio analysis showed comparable performance between kFLC and OCBs. An intermediate “grey zone” for kFLC values between 5.4 and 19.4 was identified, corresponding to sensitivity $\geq 90\%$ and specificity $\geq 99\%$. Within this range, OCB testing could resolve diagnosis in 82% of cases.

DISCUSSION: The kFLC index demonstrates high diagnostic accuracy and performs comparably to OCBs while offering the advantages of a quantitative and less labor-intensive method. Implementation of kFLC in clinical practice could improve efficiency and precision in MS diagnostics. The identification of an intermediate zone supports a complementary approach, where OCB analysis remains valuable in borderline cases. These findings support the integration of kFLC into routine diagnostic workflows for MS in Denmark.

AT2R Activation Enhances CNS Repair in Progressive Multiple Sclerosis.

Agathon Hansen, Michelle¹, Fischer Larsen, Marie¹, Ojha, Bhavya¹, Ramazani, Bitu¹, Belal, Rouhin¹, Krieger, Jonathan¹, Steckelings, Ulrike Muscha², Owens, Trevor¹, Khoroshi, Reza¹
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BACKGROUND & AIM: Progressive multiple sclerosis (PMS) is driven by chronic neuroinflammation, sustained glial activation, and demyelination, with limited therapeutic options. Central nervous system (CNS)-intrinsic mechanisms, including persistent microglial and astrocyte activation, ongoing demyelination, and impaired blood-brain barrier (BBB) integrity, underlie disease progression, particularly in aging, which reduces CNS repair capacity. The angiotensin II type 2 receptor (AT2R) exerts anti-inflammatory and reparative effects in the CNS. AT2R signalling may therefore limit neuroinflammation and enhance repair. This study investigates whether activation of AT2R with the selective non-peptide agonist Compound 21 (C21) can shift glial responses toward reparative phenotypes, reduce neuroinflammation, and support CNS recovery in aging-related PMS-like pathology.

METHODS: We used two experimental models: (1) a two-photon laser-induced cortical lesion to mimic key PMS features, including localized subpial inflammation and cortical demyelination, and (2) cuprizone-induced demyelination to examine mechanisms of myelin loss and repair. 0,3 mg/kg C21 (Vicore pharma) was administered i.p. in both models, 6 h post-irradiation (1) and during week 4 of the 6-week cuprizone feeding (2). Histological and immunofluorescent analyses were used to assess lesion size, immune cell infiltration, glial activation, BBB integrity, and microglial phenotypes.

RESULTS: C21 treatment significantly reduced cortical lesion size following laser-induced injury, accompanied by decreased immune cell infiltration, attenuated astrocyte activation, improved BBB integrity, and reduced demyelination. Notably, microglia adopted a reparative phenotype, with reduced expression of MHC-II and increased expression of anti-inflammatory and homeostatic markers CD163 and P2RY12, without changes in total IBA1+ cell numbers. Cuprizone induced white matter demyelination in the corpus callosum in both young and aged mice, with more severe pathology in young animals, highlighting age-dependent differences. Ongoing studies investigate C21's effects on Cuprizone-induced de- and remyelination to further define AT2R's reparative role.

DISCUSSION: These findings indicate that AT2R activation via C21 suppresses chronic neuroinflammation while promoting targeted immunomodulatory responses that support CNS repair. By shifting microglia toward reparative phenotypes and enhancing BBB integrity, C21 represents a promising disease-modifying strategy for PMS. Future studies will investigate the mechanisms by which AT2R signalling regulates neuroinflammation and promotes remyelination, with particular attention to age-related effects.

Effectiveness of Escalation vs. Early High-Efficacy Therapies on Progression Independent of Relapse Activity in Multiple Sclerosis.

Varjú, Eliza¹, Pontieri, Luigi¹, Mahler, Mie R^{1,2}, Magyari, Melinda^{1,2,3} ¹The Danish Multiple Sclerosis Registry, Department of Neurology, Copenhagen University Hospital – Rigshospitalet, Glostrup, Denmark. ²Danish Multiple Sclerosis Center, Department of Neurology, Copenhagen University Hospital, Rigshospitalet Glostrup. ³Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark.

INSTITUTION: The Danish Multiple Sclerosis Registry

BACKGROUND & AIM: Early use of high-efficacy therapies in multiple sclerosis reduces relapse activity, but its effect on silent disease progression, termed progression independent of relapse activity or PIRA, remains uncertain. This study aimed to compare the effectiveness against PIRA of early initiation of high-efficacy therapies with escalation from moderate-efficacy therapies in patients with relapsing-remitting multiple sclerosis.

METHODS: From the Danish MS Registry, treatment-naïve adult patients with RRMS started on high-efficacy therapies or moderate-efficacy therapies between 2012 and 2022 were included. Stabilized inverse probability of treatment weights, derived from propensity scores, were applied to balance confounders and to perform weighted Cox and negative binomial regression models. Patients were followed under an intention-to-treat framework until the latest clinical visit before the data extraction date (2025-06-02). The primary outcome was time to first PIRA while the secondary outcome was annualized relapse rate.

RESULTS: Among 3,316 patients (594 high-efficacy, 2,722 moderate-efficacy) with a median follow-up time of 7.4 years [min-max: 1.5 – 13.4], we found no statistical difference in time to first PIRA with a hazard ratio of 0.903 (95% confidence interval (CI):

0.70 – 1.11, $p = 0.45$). Early high-efficacy therapy initiation was associated with a 37% reduction in ARR (Incidence rate ratio of 0.63, 95% CI 0.54–0.74, $p < 0.001$).

DISCUSSION: In this nationwide cohort study, we found a reduction in relapse activity associated with early initiation of high-efficacy therapies, but no statistically significant difference when investigating time to first PIRA. Our findings indicate a therapeutic gap in the current treatment landscape with respect to mitigating PIRA.

Scientific Session



Clinical & Epidemiological Research

Preconception Use of Disease Modifying Therapy in Women with MS: A 25-Year Danish Nationwide Study.

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BACKGROUND & AIM: The management of multiple sclerosis (MS) has evolved substantially over the past two decades. The use of high-efficacy disease-modifying therapies (DMT) has increased, and emerging evidence supports continuation until conception. However, it remains unclear to what extent this is reflected in real-world treatment patterns among women with MS who become pregnant. Thus, the aim is to describe preconception DMT use among Danish women with MS who became pregnant.

METHODS: We conducted a nationwide register-based cohort study among women with MS who became pregnant after diagnosis between 2000 and 2025. Data were obtained from the Danish Multiple Sclerosis Registry, the Danish Medical Birth Registry, and the National Abortion Registry. The index date was defined as the first day of the last menstrual period (LMP), estimated from the delivery or abortion date minus gestational age. Preconception DMT exposure was defined as use on, or within a defined washout window prior to the index date.

RESULTS: A total of 2,365 women contributed 3,775 pregnancies. The number of pregnancies recorded in the registry increased from 490 (13.0%) in 2000 – 2004 to 1,024 (27.1%) in 2020 – 2025. Most pregnancies resulted in live birth (84.6%), while 15.4% ended in induced abortion. The median age at LMP was 32.5 years (IQR 29.3 – 35.8) overall, with minimal differences

between pregnancies with DMT exposure prior to or at LMP and those unexposed. Relapse activity one year prior to LMP was higher among pregnancies with DMT exposure prior to or at LMP (≥ 1 relapse: 19.5% vs. 10.6%). Preconception DMT use increased markedly over time. Overall, 1,993 of 3,775 pregnancies (52.8%) were exposed to any DMT at LMP during the study period. The proportion of women receiving DMT at conception increased from 25.7% in 2000–2004 to 73.7% in 2020–2025, indicating a substantial shift in treatment patterns.

DISCUSSION: Preconception DMT use among women with MS in Denmark has increased markedly over the past 25 years, reflecting a shift in clinical practice aligned with emerging evidence and ensuring a better maternal disease stability.

Defining composite markers to predict EDSS progression in SPMS by artificial intelligence.

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BACKGROUND & AIM: We hypothesized that in SPMS, 1) composite markers predict progression better than single features and 2) definition of composites depends on disability.

METHODS: By artificial intelligence (AI) and combining clinical measures, serum biomarkers, cognition, MRI features, and patients' own perception in differentially disabled SPMS patients, we aimed to identify composites that predict EDSS progression. 61 patients with SPMS were classified as stable or with EDSS worsening over 24 months. To predict progression, 29 features were evaluated by incremental feature analysis using Random Forest as AI or logistic regression (LR) with balanced class weights. Cross-validation (50×5-fold) was used for robust performance estimation. Features included upper/lower limb function (T25FWT, 9HPT, 6SST), cognition (SDMT, BVMT), serum biomarkers (NFL, GFAP), MRI metrics (volumetry, WM integrity), and PROs (fatigue, quality of life, daily function, working ability).

RESULTS: In patients with moderate disability (EDSS 3.5–4.5, n=26), AI and RF achieved up to 67% accuracy with ≤3 features. Cognitive processing speed and mental fatigue were the most important with GFAP, NFL, and hand function as top five features in the predicting composites. In patients with advanced disability (EDSS≥5.0, n=35), both models achieved 80% accuracy with 2–5 features. PROs measuring health and quality of life emerged as major predictors in composites with cognition and

walking ability as top five features. When volumetric/WM integrity MRI metrics were added, hippocampus and T1 black hole volume were strong predictors in the moderate disability group while top features still included cognition and hand function. For patients with advanced disability, walking ability and PROs still remained top features, while hippocampus and corpus callosum volume, cognitive function and GFAP were part of the predicting composites.

DISCUSSION: Simple composites with robust performance predicted EDSS progression in SPMS over 24 months better than single features. Cognitive processing speed, hand function, and biomarkers were important for moderate disability, while PROs measuring fatigue, walking ability, and cognition were key predictors in more disabled patients. Volumetric MRI features provided additional value, particularly for patients with moderate disability. While simple composites can be effective in predicting SPMS progression, it is important to consider the level of disability.
Supported by Sanofi

Age and sex specific effects of initial high-efficacy therapy versus an escalation strategy in newly diagnosed patients with multiple sclerosis.

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BACKGROUND & AIM: On a group level, initial high-efficacy therapy (HET) is now widely recognized for its superiority in suppressing relapses and MRI activity compared to an escalation strategy also termed initial moderate-efficacy therapy (MET). However, whether this is true for all ages and both sexes remains uncertain. We therefore sought to estimate the conditional average treatment effect of initial HET vs MET on disease activity and the average treatment specific absolute risks across age groups and sexes.

METHODS: We conducted a cohort study using the Danish Multiple Sclerosis Registry and included patients with relapsing-remitting multiple sclerosis initiating MET (fumarates or teriflunomide) or HET (natalizumab or anti-CD20 therapies) from 2014 to 2022. The primary outcome was disease activity within 2 years (relapses or MRI activity). Data from 2014–2020 were used to train prediction models based on logistic regression models with an elastic net penalty and multiple imputation (25 imputed datasets). We then predicted the outcome in data from 2021–2022 for each person with HET and with MET, respectively.

RESULTS: We included 3,905 patients (MET n=3,121; HET n=784). In 2021–2022 data, females and males aged 18–24 years on

average had a 54.9% [95% CI: 52.7–57.2] and 54.5% [50.8–58.1] predicted risk of disease activity within 2 years on MET compared to 38.2% [37.1–39.3] and 35.7% [34.2–37.1] on HET, respectively. The average predicted risks decreased in older age groups, with females and males aged 45–54 years having a 35.0% [33.4–36.7] and 32.5% [30.8–34.2] risk on MET, respectively, compared to 22.3% [21.6–23.0] and 19.5% [18.6–20.5] on HET. The conditional average risk difference between HET and MET was highest among males aged 18–24 years (18.8 percent [15.8–21.8]) and decreased slightly in older age groups to 12.7 percent [11.3–14.2] in females aged 45–54 years.

DISCUSSION: We found a superior effect of HET in all age groups and both sexes; however, the average absolute risk of disease activity within 2 years for patients aged 45–54 years on MET was lower than that of younger patients on HET. This evidence can support clinicians and patients in individualised risk-benefit discussions regarding an initial HET or escalation treatment approach.

Ofatumumab versus ocrelizumab in relapsing–remitting multiple sclerosis: a nation-wide cohort study.

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BACKGROUND & AIM: B cell depleting therapy with anti-CD20 monoclonal antibodies is a highly effective and increasingly used treatment strategy for multiple sclerosis (MS), however, comparative effectiveness of anti-CD20 therapies is unclear. In this study, we aimed to evaluate the effectiveness of ofatumumab compared to ocrelizumab in relapsing–remitting MS (RRMS).

METHODS: This was an observational cohort study based on data extracted from the

Danish Multiple Sclerosis Registry. Patients with RRMS initiating ofatumumab or ocrelizumab treatment were included between January 2022 and November 2025. Primary outcomes were annualized relapse rate (ARR) rate ratio between the ofatumumab and ocrelizumab group, and hazard ratio (HR) for time to first relapse. Secondary outcomes were time to first 24-weeks confirmed disability worsening (CDW), progression independent of relapse activity (PIRA), and brain MRI lesion activity. We used the inverse-probability of treatment weighting based on propensity scores to estimate the average treatment effects adjusted for baseline confounders. The main analysis followed an intention-to-treat (ITT) principle, with an additional per-protocol (PP) analysis performed.

RESULTS: A total of 1870 patients were included in the study, of whom 485 started ocrelizumab treatment at baseline, and 1385 started ofatumumab. In the ITT analysis, the mean ARR was 0.05 [95% CI 0.04–0.06] for the ofatumumab group, and 0.03 [0.02–0.04] for the ocrelizumab group, with a rate ratio of 1.65 [1.09–2.50] ($p = 0.018$). The median follow-up time was 2.0 years for the ofatumumab group and 2.5 years for the ocrelizumab group. No significant differences were found in the time to first relapse (HR 1.50 [95% CI 0.99 – 2.29]), CDW (HR 0.83 [0.58 – 1.2]), PIRA (HR 0.78 [0.53 – 1.15]), or brain MRI lesion activity (HR 1.72 [0.95 – 3.13]). PP analyses yielded consistent results.

DISCUSSION: The study indicates that ofatumumab treatment is associated with a marginally increased relapse rate compared to ocrelizumab treatment in patients with RRMS. However, the ARR was very low with both anti-CD20 therapies, and the difference is of limited clinical relevance. Important limitations include the observational and retrospective nature of the study, and the risk of residual indication bias. Moreover, the study does not address adverse effects and longer-term effectiveness.

Familial risk of multiple sclerosis: A nationwide registry-based study.

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BACKGROUND & AIM: Multiple sclerosis (MS) is a chronic disabling disease of the central nervous system involving progressive disability accrual affecting physical and cognitive capacity and quality of life. MS is known to aggregate within families; however, the magnitude of the familial risk differs across previous studies. We aimed to provide an updated estimate of MS risk in first-degree relatives.

METHODS: All persons diagnosed with MS in The Danish Multiple Sclerosis Registry by 5 March 2023 who were alive on 1 January 1973 or later were identified. Based on information from the Danish Medical Birth Register and the Danish Civil Registration System, we identified children and parents of persons with MS. The proband was defined as the individual in a familial first-degree relationship first diagnosed with MS. We followed first-degree relatives for incident MS from the latest of 1 January 1973, the MS diagnosis date of the proband, or date of birth until the first of MS diagnosis, death, or 5 March 2023. Standardized incidence rates (SIR) and 95% confidence intervals (CI) of MS comparing first-degree relatives with the background population were calculated overall and stratified according to sex of the proband, and by parents versus children and by sex of parents and children. Absolute lifetime risk and 95% CI was also calculated overall and in all subgroups.

RESULTS: Children (n=653 diagnosed with MS) of persons with MS have a more than fivefold increased risk of MS compared with the background population (SIR: 5.23; 95% CI

4.85–5.65). The estimate for parents (n=64; SIR: 5.09; 95% CI 3.99–6.51) was similar. SIR in subgroups ranged from 4.30 (95% CI 1.61–11.45; father of male proband) to 6.89 (95% CI 4.08–11.64; father of female proband). Absolute lifetime risk in children and parents were 3.7% and 3.6%, respectively.

DISCUSSION: Using nationwide information during 50 years of follow-up, we found a five times higher risk of MS in first-degree relatives compared to the background population.

Scientific Session



Treatment & Basic Research I

Blood-Brain Barrier Leakage in Primary Progressive MS Exceeds Relapsing-Remitting MS Independent of Age: Evidence from DCE-MRI.

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BACKGROUND & AIM: Blood-brain barrier (BBB) permeability in normal-appearing white matter (NAWM) is elevated in relapsing-remitting MS (RRMS) relative to healthy controls (HC). Whether primary progressive MS (PPMS) also exhibits BBB leakage in normal-appearing tissue has not been investigated. Critically, PPMS patients are typically older than RRMS patients, and BBB permeability increases with age even in healthy individuals, most prominently in higher-order cortical regions and white matter, so any cross-subtype comparison must account for age. In MS accelerated brain atrophy is observed despite stable disease, suggesting microvascular mechanisms beyond acute inflammation. We therefore examined whether capillary transit time heterogeneity (CTH) and cerebral metabolic rate of oxygen (CMRO₂) differ across HC, RRMS, and PPMS, and whether age-related microvascular trajectories diverge between groups.

METHODS: 184 participants (77 HC, 82 RRMS, 25 PPMS) underwent DCE-MRI at 3T. Ki was quantified by Patlak modelling across seven regions (lesions excluded). CTH was estimated from gamma-variate transit time distributions. Global cerebral blood flow (CBF) was measured by phase-contrast MRI; CMRO₂ via Fick's principle

with susceptibility-weighted oximetry. Multiple linear regression (age and sex as covariates), age×group interaction testing, FDR correction, and three-group ANCOVAs were applied.

RESULTS: Age independently predicted Ki (standardised β : SD change per SD increase in age) in white matter ($\beta=.377$), NAWM ($\beta=.329$), thalamus ($\beta=.283$), and tertiary regions ($\beta=.272$; all $p<.001$), but not primary regions ($\beta=.063$, $p=.594$). After age adjustment, MS patients showed elevated Ki in NAWM and thalamus (both $p\sim\text{FDR}<.001$), with a stepwise ANCOVA pattern in NAWM (HC<RRMS<PPMS, all pairwise $p<.05$) and markedly elevated thalamic Ki in PPMS ($p<.001$). CTH showed age×group interactions in NAWM ($p=.038$) and thalamus ($p=.001$), with age-related increases specific to MS. CMRO₂ was reduced in both MS subtypes versus HC ($p=.001$) but was not predicted by Ki or CTH after controlling for group.

DISCUSSION: PPMS patients exhibit elevated BBB permeability in NAWM and thalamus, exceeding both RRMS and HC even after stringent age correction. Divergent CTH trajectories suggest disease-specific capillary dysregulation beyond normal ageing. The dissociation between microvascular measures and CMRO₂ suggests that reduced oxygen metabolism in MS reflects neuronal loss rather than vascular dysfunction alone, potentially explaining accelerated atrophy in clinically stable patients.

Ceruloplasmin Deficiency Reduces CD11b+ Microglial Cell Activation in Response to Cuprizone-Induced Demyelination.

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BACKGROUND & AIM: Iron handling and microglial activation are integrated components in the pathogenesis of multiple sclerosis (MS). Ceruloplasmin (Cp), a multicopper ferroxidase expressed in glial cells, regulates cellular iron export and reduced Cp activity has been associated with increased vulnerability to iron-mediated oxidative stress in MS. However, the impact of Cp deficiency on de- and remyelination and on the microglial response to demyelination remains unknown. This study aimed to determine whether Cp deficiency affects (1) the extent of cuprizone (CPZ)-induced de- and remyelination and (2) the microglial activation state assessed by CD11b expression.

METHODS: Three- to four-month-old Cp wildtype (WT), heterozygous (Cp^{+/-}), and knockout (Cp^{-/-}) mice were fed 0.3% CPZ for six weeks to induce demyelination, followed by two weeks on normal chow. Myelin integrity was assessed using luxol fast blue (LFB) staining and Mbp immunofluorescence. Microglial activation was assessed by CD11b immunohistochemistry, while the other glial cell responses were evaluated using Olig2 and Gfap immunohistochemistry.

RESULTS: The three genotypes showed comparable and extensive demyelination in the corpus callosum after six weeks of CPZ, with LFB and Mbp intensity reduced relative to naïve mice. Following two weeks of recovery, remyelination resulted in an increased Mbp+ area across groups, while LFB intensity was less sensitive to early

repair. In contrast, microglial activation differed by genotype. During demyelination CD11b expression in the corpus callosum increased strongly in WT mice, whereas Cp^{+/-} and Cp^{-/-} mice showed a 30–40 % lower CD11b response. Although cellularity increased during demyelination, the increase was substantially smaller in Cp-deficient mice than in WT, indicating blunted glial accumulation. The association between CD11b expression and nuclear fraction was also reduced in Cp-deficient mice. Cp protein expression increased in CPZ-treated WT mice. Cp-deficient mice showed no compensatory upregulation of the ferroxidase hephaestin.

DISCUSSION: Ceruloplasmin deficiency does not affect the extent of cuprizone-induced de- or remyelination. However, Cp-deficient mice attenuate microglial CD11b response during demyelination, indicating impaired microglial activation despite comparable myelin loss. These findings point at ceruloplasmin as a regulator of microglial activation during demyelinating stress and suggest that disrupted iron handling may affect microglial responsiveness in MS-related pathology.

Age-related de novo somatic mutations in the MS brain.

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BACKGROUND & AIM: Progressive multiple sclerosis (PMS) affects 20–25% of patients and is characterized by worsening disability and reduced life expectancy. Secondary progression is age-related and immune cells exhibit accelerated biological aging in MS. PMS is characterized by chronically expanding brain lesions with rim enriched in both activated CNS resident cells and blood-derived macrophages and lymphocytes. We have previously identified distinct tissue- and single-cell gene signatures at the lesion rim, and we propose that lesion expansion is driven by immune cells with enhanced proliferative and pro-inflammatory capacity arising from the age-related somatic mutations.

METHODS: We performed deep exome sequencing on 96 brain tissues from ten progressive MS patients and five non-MS controls using the Twist exome panel on an Illumina NovaSeq 6000 platform (mean depth: x1000). Normal-appearing white matter, active, chronic active, remyelinating, and inactive lesions from each PMS brain, as well white matter from each control were pooled, respectively. Somatic variants were identified using a tumor-only Mutect2 algorithm, a read depth of 50 and a variant allele frequency 0.35. Statistical analyses included KEGG Pathway Enrichment Analysis, multiple-linear regression model and

correlation analyses using Spearman and multi-variate regression models.

RESULTS: Somatic mutations were identified in the aging brain in both controls and MS patients. PMS brains with the highest percentage of chronic active lesions showed the highest mutational burden. This was confirmed by a significant positive correlation between percentage of chronic active lesions and somatic mutational burden ($p=0.015$). The mutated genes in MS brains showed to be involved in regulation of inflammation in contrast to controls. We also found a trend towards higher mutational burden in MS patients compared to controls, although non-significant ($p=0.13$).

DISCUSSION: Our results indicate that chronic active lesions in PMS brains are associated with increased somatic mutation burden. As these mutations were involved in inflammation-related genes, these findings highlight the potential biological relevance of somatic mutagenesis contributing to inflammatory cellular phenotype and driving MS progression.

CSF immune cell biomarkers enable early accurate identification and differentiation of RRMS, NMOSD, and MOGAD.

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BACKGROUND & AIM: Early and accurate identification of relapsing-remitting multiple sclerosis (RRMS), neuromyelitis optica spectrum disorder (NMOSD), and MOG antibody-associated disease (MOGAD) is essential for guiding treatment. However, current routine analyses have limited sensitivity and specificity. Soluble biomarkers reflecting disease-specific immune cell subsets have shown potential for implementation for clinical diagnosis. We evaluated the diagnostic potential of soluble CD27 (sCD27), B-cell maturation antigen (sBCMA), CD163 (sCD163), and neutrophil gelatinase-associated lipocalin (NGAL), and hypothesized that sCD27 is sensitive for neuroinflammation in RRMS, NMOSD and MOGAD, while innate (NGAL and sCD163) and adaptive (sBCMA) biomarkers may help differentiate RRMS from NMOSD and MOGAD.

METHODS: Concentrations of sCD27, sBCMA, sCD163 and NGAL were measured in cerebrospinal fluid (CSF) and serum from 35 RRMS, 11 NMOSD, 22 MOGAD patients and 35 symptomatic controls (SC) using electrochemiluminescence-immunoassay.

RESULTS: CSF sCD27 was elevated in all patient groups compared to SC ($p < 0.05$) and discriminated RRMS, NMOSD and MOGAD from SC with an area under the curve (AUC) of 0.99, 0.91 and 1.00. CSF sBCMA was increased in RRMS ($p < 0.001$), while sCD163 and NGAL were elevated in NMOSD ($p = 0.001$, $p = 0.011$) and MOGAD ($p = 0.001$, $p < 0.001$). CSF biomarker

ratios (sCD27/sCD163, sCD27/NGAL, sBCMA/sCD163 and sBCMA/NGAL) showed the highest ability to discriminate RRMS from NMOSD/MOGAD with AUCs between 0.94 and 0.95. Serum levels and calculation of biomarker indices did not improve differentiation.

DISCUSSION: In this study, we demonstrate that CSF sCD27 is a sensitive marker of neuroinflammation in RRMS, NMOSD, and MOGAD. These findings strengthen the evidence that sCD27 is a highly sensitive marker of neuroinflammation, consistent with previous studies reporting elevated levels of CSF CD27 across a broad spectrum of neuroinflammatory disorders. Furthermore, our results indicate that applying CSF biomarker ratios integrating elements from the adaptive and the innate immune response may enable accurate differentiation between RRMS and NMOSD/MOGAD. Future studies should involve validation of these findings in independent cohorts and development of robust assays with short turn-around time.

Choroid plexus enlargement in multiple sclerosis: a global volumetric analysis of structural and disease-related drivers.

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BACKGROUND & AIM: Choroid plexus (CP) volume enlargement has consistently been linked to MS across several studies and has been associated with disease progression and brain atrophy. This study aimed to identify which structural and disease-related factors are associated with choroid plexus volume enlargement in MS, and specifically to test whether ventricular enlargement alone accounts for increased CP volumes.

METHODS: Seventy-nine patients with MS (16 PPMS, 28 RRMS, 35 SPMS) and 52 healthy controls (HC) underwent 3T MRI. CP volume within lateral ventricles was manually segmented on 3D T1w images using FSLeves v1.5.0 and normalized by cranial size. Brain parenchyma was automatically segmented using Freesurfer 7.4.0. Brain parenchymal fraction (BPF) was calculated as brain parenchymal volume normalized to cranial size. WM lesion volume was quantified using the Automatic Identification of MS lesions (AIMS) model.

RESULTS: CP volume was significantly increased in all MS subgroups versus HC (Welch's t-test with Holm adjustment, all $p < 0.008$), with no significant differences

between MS subgroups (all $p > 0.129$). In unadjusted linear regression analysis, lower BPF was associated with a higher CP volume in the pooled MS cohort ($\beta = -0.002$, $p = 0.028$) and in HC ($\beta = -0.002$, $p = 0.013$). Log transformed ventricular volume (VV) showed a strong positive association with CP volume across the pooled MS cohort ($\beta = 0.00002$, $p = 3.09 \times 10^{-7}$) and in all four groups ($p \leq 0.034$), with no significant interaction ($p = 0.144$). White matter lesion volume (WMLV) was positively associated with CP in the pooled MS cohort ($p = 1.09 \times 10^{-5}$), SPMS ($p = 0.008$), and PPMS ($p = 0.002$). Multiple linear regression showed that VV and WMLV remained independently associated with CP volume, while age and BPF did not. The model explained 29.9% of the variance.

DISCUSSION: CP volume was increased across MS subtypes but does not distinguish between them. Its strong association with ventricular size in both MS and HC, suggests a structural scaling relationship, while its independent association with WMLV points to additional disease-driven mechanisms. However, it is still unclear whether CP adds information beyond established measures such as lesion burden and atrophy.

Scientific Session



MS Rehabilitation

AI-based telerehabilitation for multiple sclerosis: feasibility and usability in a multicenter pilot study.

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BACKGROUND & AIM: Telerehabilitation has emerged as a promising approach to improve access to exercise-based rehabilitation for people with multiple sclerosis (pwMS). However, many existing systems remain limited by their complexity, reliance on additional hardware, and lack of real-time feedback on exercise performance. Artificial intelligence (AI)-based platforms may help overcome these barriers by enabling accurate movement tracking and feedback using standard consumer devices. This prospective, multicenter, single-arm pilot study aimed to evaluate the feasibility and usability of an AI-based telerehabilitation system in pwMS across multiple international sites.

METHODS: Thirty-four pwMS were enrolled in a 4-week telerehabilitation program comprising 8 sessions, including both standard and AI-supported (MoveAI)

exercises. Primary outcomes included recruitment, retention, adherence, and compliance. Usability was assessed using the Telehealth Usability Questionnaire (TUQ) and semi-structured interviews. Exploratory mobility outcomes were assessed at baseline and post-intervention.

RESULTS: Retention was high, with a low drop-out rate (5.8%). Adherence was greater for MoveAI exercises (68.3% with a compliance of 70.7%) compared with standard exercises (48.4%). Usability was rated positively (mean TUQ score: 86.8), supported by qualitative findings indicating good acceptability, perceived benefits, and ease of use. Reported challenges included technical issues related to camera positioning and movement recognition. Exploratory analyses demonstrated significant improvements in mobility outcomes, including gait performance (T25FW), balance (Mini-BESTest), and patient-reported walking ability (MSWS-12).

DISCUSSION: The AI-based telerehabilitation system showed good feasibility and usability in pwMS, with higher adherence to AI-supported exercises. These findings highlight its potential to improve engagement and accessibility in rehabilitation, warranting further evaluation in a multicenter randomized controlled trial.

Dose-response effects of supervised power-oriented resistance training in people with multiple sclerosis – secondary data from the NEXIMS study.

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BACKGROUND & AIM: Muscle power is a key determinant of physical function and health in people with multiple sclerosis (pwMS), with most pwMS experiencing substantial deterioration in muscle power. However, no power-oriented resistance training (PowRT) studies have yet investigated the dose-response relationship between weekly session frequency and improvements in muscle power as well as walking capacity and ability. To address this, we conducted a 10-week randomized controlled trial.

METHODS: Sixty pwMS (72% female, age = 54±12 years, PDDS = 2.3±1.9, disease duration = 12±10 years, 70% relapsing-remitting) were enrolled, baseline tested, and randomized (1:1:1) to high-dose PowRT (HD-PowRT; 2.5 sessions/wk), low-dose PowRT (LD-PowRT; 1 session/wk) or control (CTRL; continuation of habitual living). Outcomes included 5 x sit-to-stand muscle power (5STS_power), 9-step stair ascend muscle power (9SSA_power), 6-minute walk test (6MWT), and 12-item MS walking scale (MSWS12).

RESULTS: Following the 10-week intervention period, improvements followed a dose-response pattern (HD-PowRT > LD-PowRT > CTRL). Specifically, substantial between-group differences (p<0.01) were observed for 5STS_power (0.99 [0.68;1.30] vs 0.36 [0.02;0.70] vs 0.22 [-0.10;0.54] W/kg; corresponding to 24 vs 6 vs 6 %), 9SSA_power (0.52 [0.32;0.71] vs 0.21 [0.00;0.43] vs

-0.17 [-0.37;0.04] W/kg; 15 vs 2 vs -4 %), and 6MWT (39 [24;54] vs 10 [-6;26] vs 3 [-12;18] m; 9 vs 4 vs 1 %), alongside reductions in MSWS12 (-11 [-17;-4] vs -6 [-13;2] vs -2 [-10;5] points; -40 vs -23 vs -14 %).

DISCUSSION: In the first PowRT study in pwMS, we demonstrated a dose-response relationship between weekly training frequency and improvements in lower extremity muscle power, walking capacity, and walking ability. These findings emphasize PowRT and training dosage importance, providing valuable insights for developing future exercise guidelines for pwMS.

Scientific Session



MS diagnosis & cases

Early MS-diagnose with solitary periventricular lesion and paramagnetic rim lesion and oligoclonal bands: application of McDonald 2024 criteria.

Marie Mathilde Hansen

Superviseret af overlæge Annika Langkilde og overlæge Stephan Bramow

INTRODUKTION: De reviderede 2024 McDonald-kriterier muliggør tidligere og mere specifik diagnosticering af MS ved inddragelse af MR-biomarkørerne paramagnetic rim lesions (PRL) og central vein sign (CVS). Disse biomarkører har vist høj specificitet for MS og re-præsenterer patofysiologiske kendetegn ved MS. Endvidere er nervus opticus inkluderet som en femte anatomisk lokalisation.[1] En væsentlig ændring er muligheden for at diagnosticere MS hos patienter, som tidligere ville have fået diagnosen klinisk isoleret syndrom (CIS), når specifikke biomarkørkombinationer er opfyldt. Dette inkluderer disseminering i tid (DIT) eller tegn til intratekal inflammation ved påvisning af oligoklonale bånd (OCB) eller forhøjet kappa free light chain index i cerebrospinalvæske (CSF) i kombination med CVS eller PRL. Denne case illustrerer anvendelsen af de nye diagnostiske kriterier hos en patient med en solitær periventrikulær læsion med PRL.

PATIENTPRÆSENTATION: En 22-årig tidligere rask kvinde debuterede i december 2025 med langsomt progredierende kraftnedsættelse og styringsbesvær af venstre over- og underekstremitet. Objektivt fandtes venstresidig hemiparese (grad 4-4+) samt efterslæb af venstre ben ved gang. Initial udredning med MR-neuroakse med kontrast viste en solitær kontrastopladende periventrikulær læsion i højre corona radiata (2 x 1,7 cm), suspekt for MS. Oftalmologisk undersøgelse inkl. optisk kohærenstomografi (OCT) viste ingen tegn på tidlige re opticusaffektion. CSF-analyse påviste OCB samt forhøjet neurofilament light chain (NfL) (8788 ng/L). MOG- og aquaporin-4-antistoffer var negative. Patienten blev behandlet med peroral methylprednisolon (1 g i 3 dage efterfulgt

af 500 mg i 5 dage) grundet utilstrækkelig klinisk bedring efter 3 dage.

Ved opfølgning 1,5 måned senere i MS-klinikken var symptomerne stort set remitte-rede med normal kraft og gangfunktion, men fortsat udtrætning af venstre ben ved længevarende belastning (slæb af ben efter ca 2 km løb). Patienten var fortsat sy-gemeldet og beskrev mental udtrætning. Opfølgende MR-neuroakse med tilføjelse af susceptibility-weighted imaging (SWI) sekkvenser viste regression af den periventri-kulære læsion uden kontrastopladning samt hypointensitet i randen af læsionen (PRL) involverende næsten hele cirkumferensen af læsionen. Der var ingen synlig CVS og ingen nyttilkomne læsioner. På baggrund af ét MS-suspekt attack, én periventrikulær læsion med PRL samt OCB opfyldte patienten 2024 McDonald-kriterierne for MS. Patienten vil blive drøftet på næstkommende MDT-konference i april 2026 med hen-blik på videre plan og opstart af sygdomsmodificerende behandling.

DISKUSSION: Denne case illustrerer den kliniske anvendelse af de reviderede 2024 McDonald-kriterier og viser hvordan kombinationen af PRL og OCB muliggør MS-diagnose ved en solitær læsion. Casen understreger værdien af at inkludere SWI-sekvenser i MR-protokoller ved mistanke om MS, særligt ved atypiske præsentationer eller begræn-set læsionsbyrde. Tidlig identifikation af PRL kan have betydning for diagnostik og prognose.

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Patienten har samtykket mundtligt til præsentation af casen.

FLAIR-Hyperintense Lesions in Anti-MOG Associated Encephalitis with Seizures (FLAMES) and Subsequent Hemiatrophy.

Nanna Mouritzen

CASE-PRÆSENTATION: Casen omhandler en 15-årig dreng kendt med mild autisme men ellers rask. Han blev indlagt på intensiv afdeling, sederet og intuberet, efter at være fundet ukontaktbar af sine forældre efter et førstegangskrampetilfælde.

Patienten blev COVID-vaccineret for anden gang med Pfizer ca. 4 uger forinden. 1 uge herefter udviklede han feber og hovedpine, der varede 1 uge, hvorefter han umiddelbart var rask igen. 2 dage før indlæggelsen blev han let konfus, kastede op og udviklede feber.

Han fik ved modtagelsen udført akut CTC efterfulgt af MRC, disse blev umiddelbart vurderet normale. Ved revurdering af MR-scanningen så man en lille højresidig hyperintensitet kortikalt, der initielt blev tolket som en lille subarachnoidalblødning – senere på neuroradiologisk konference vurderede man, at der faktisk var tale om leptomeningeal inflammation.

Spinalvæsken var med 37 leukocytter, heraf 29 mononukleære og 8 polynukleære, glukose på 5,1 mmol/L og protein på 0,63 g/L. Der blev iværksat empirisk antiviral og antibiotisk behandling samt højdosis steroid som meningitprofylakse. Svar på mikrobiologi- og autoimmun encefalitprøver var sidenhen negative.

EEG viste ingen anfaldsaktivitet men et svært encefalopatimønster.

Efter ekstubation på dag 2 og gradvis bedring af bevidsthedsniveauet dagene efter fandtes han med en venstresidig central facialisparese, venstresidig hemiparese og kognitive deficits, der siden nærremittede under behandling med steroid og sidenhen mycophenolat mofetil og rituximab.

MOG-antistof test blev udført på serum og var negativ på dag 2 men svagt positiv på

dag 29. Gentagne serumværdier for MOG-antistof ved live cell-based assay var stærkt positive med stigende titre.

1 måned efter symptomdebut var den leptomeningeale opladning forsvundet på kontrol MRC, men der var tilkommet bilaterale, subkortikale FLAIR-højtsignalforandringer mest udtalt på højre side. Derudover sås en overraskende progressiv højresidig cerebral hemiatrofi ledsaget af en venstresidig cerebellar hemiatrofi på de opfølgende MR-scanninger.

Den endelige diagnose på denne patient var FLAIR-hyperintense lesions in anti-MOG associated encephalitis with seizures (FLAMES), som først kunne stilles ca. 1 måned efter symptomdebut.

Casen er unik, da progressiv hemiatrofi ikke er et tidligere beskrevet scanningsfund i litteraturen efter FLAMES. Den bidrager således til at udvide den aktuelle forståelse af det i forvejen brede spektrum inden for anti-MOG associeret sygdom.

Scientific Session



Basic Research II & Cases

Severe multifocal relapse despite b-cell depletion on Rituximab – possible rebound activity post fingolimod.

Jesper Nørregaard

CASE-PRÆSENTATION: 45-årig mand. Kendt RRMS samt astma og hypertension. MS-debut i 2002. Diagnosen stillet i 2005. Initialt behandlet med mitoxantron i 8 måneder og siden interferon beta-1^a men udviklede 3 angreb 2009 til 2010. Skiftede til natalizumab men fik 2 nye angreb. Efter 3 måneders washout opstartedes i februar 2013 fingolimod som han, fraset radiologisk carry-over aktivitet, var velbehandlet på fra 2013 frem til 2025 med stabil EDSS på omkring 1.5.

Diagnosticeredes med membranøs glomerulonefrit, der planlagdes opstart af rituximab. Stoppedes fingolimod primo september 2024. Planlagt opstart af rituximab primo oktober 2024 blev udskudt pga lave b-lymfocytter (0.016) til medio oktober, hvor han behandledes med 1 gram rituximab. Genbehandledes 14 dage senere med yderligere 1 gram.

Udviklede medio marts 2025 sensorisk angreb med grænse omkring Th11 og ned på højre side. Ved klinisk vurdering primo april 2025 (EDSS 3.0) behandledes med medrolkur. Revurderedes 10 dage senere da med sensorisk grænse sv.t. Th4, tilkomst af paraparese og urininkontinens. Genbehandledes under indlæggelse med 4 dages medrol. Medio april fortsat marginal klinisk effekt af medrol. MR viste relevant ny højresidig, kontrastopladende læsion på Th3/Th4 niveau. Gennemgik derefter 5 dages plasmaferesebehandling. Havde ved behandlingsafslutning ingen selvstændig stand- eller gangfunktion og nedsat sensibilitet. Angav selv en smule bedring i forbindelse med plasmaferese. EDSS 7.5.

Ved telefonkontakt primo maj rapporteredes let subjektiv bedring, men også en "ny lille plet" i synsfeltet og at venstre hånd "drillede lidt". Akut klinisk vurdering viste abducensparese, venstresidig central facialisparese, OE parese og forværring i

UE. Blev indlagt til ny plasmaferese, MR og lumbalpunktur.

MR neuroakse viste flere nytillkomne kontrastopladende DS plaks i begge hemisfærer, i hjernestammen ses en stor læsion i højre crus cerebri mesencephali samt i højre side af pons. I medulla ses en progredierende langstrakt kontrastopladende transversiel myelit på niveau Th3-Th5. Mindre kontrastopladende læsioner ses på niveau C7, Th5, Th6 og Th10/Th11.

CSV: Celletal 43, monocytter 39. Protein 0,96, albumin 456. Albumin-ratio 11.4. CXCL-13 normal. IgG index 2.14. Biofire negativ. Borrelia PCR-negativ. B-lymfocytter i blod med begyndende repletion på 0.011.

Patienten forværredes yderligere og blev bl.a. svært kognitivt påvirket i en grad som gjorde, at han ikke kunne følge simple opfordringer og talte med imaginære folk i lokalet. Ekstensiv udredning med bl.a. hjernebiopsi udelukkede lymfom og anden potentiel udløsende årsag.

Alt udredning kom negativt tilbage uden forklaring. Biopsisvaret viste infiltration foreneligt med demyeliniserende plaque. Konklusionen på udredningen blev et voldsomt rebound efter stop af fingolimod trods opstart af rituximab.

Denne case illustrerer, at man kan få et alvorligt angreb under fuld B-celle deplektion. Trods ekstensiv udredning fandt man ikke nogen udløsende agens eller årsag. Det voldsomme multifokale angreb med multiple kontrastopladende læsioner under B-celle depleterende behandling leder tankerne hen på rebound angreb efter fingolimod behandling. I dette tilfælde bemærkes 6 ugers wash-out før opstart af B-celle depleterende behandling samt debut af rebound angreb 6 måneder efter behandlingsstop.

Diagnostic challenge with isolated inflammatory steroid responsive rhombencephalitis.

Hacer Cetinalp

Medforfattere: Casper Emil Christensen (Speciallæge), Daniel Tolnai (Neuroradiolog), Stephan Bramow (Overlæge).

CASE-PRÆSENTATION: 25-årig kvinde, kendt med episodisk migrænoid hovedpine, med og uden aura, ca. 2-3 gange ugentligt. Beskrevet som dunkende karakter og NRS 6-8, forværring ved let fysisk aktivitet, samt med ledsagende foto- og fonofobi samt kvalme.

Debutterer slut juli 2023 med pludselig opstået højresidig hemicrania, paræstesier og dødhedsfornemmelse i hele højre side af kraniet, ansigtet og højre side af mundhulen. Symptomerne med let udviklet i løbet af morgenen, opnåede plateau kortvarigt efter, med delvis remission. Havde fortsat persisterende kronisk højresidig hemicrania, NRS 4-5, af borende og trykkende karakter, lokaliseret parietotemporalt. I samme periode oplevet forværring af kendt episodisk migrænoid hovedpine siden juli 2023. Desuden nytillkommet neuralgiforme jag omkring højre øje, som kan ledsages af let tåreflåd. I øvrigt upåfaldende neurologisk status.

Udredes med MR-NA, hvor man finder randopladende højintens læsion i pons sv.t. trigeminus højresidigt, der korrelerer med patientens symptomer.

I forløbet kontrolskannet med hhv. MR-C og MR-NA med kontrast gange flere med stationære forhold. I marts 2025 findes størrelsesprogression af pontin læsion med kontrastoplading, der korrelerer med patientens højresidig hemikranielle hovedpine.

Der er gennemført en omfattende udredning med henblik på afklaring af mulig infektiøs, inflammatorisk, autoimmun eller neoplastisk ætiologi.

Billeddiagnostisk (helkrops- og hjerne-PET/CT) findes hypermetabol aktivitet svarende til kendt læsion, men uden tegn til systemisk sygdom, herunder ingen mistanke

om neoplasi eller sarkoidose.

Gentagne cerebrospinalvæskeundersøgelser er uden patologiske fund, herunder negativ oligokloni, Anti-MOG, anti-abe-cerebellum IgG, GFAP-Ab, og normal IgG-indeks.

Supplerende serologiske og immunologiske analyser, inkl. infektiøse, inflammatoriske og systemiske autoimmune markører, er ligeledes uden patologiske fund.

Opstartes i Rituximab, men trods B-celle depletion med fortsat let kontrastoplading, uden sikker størrelsesprogression.

I den symptomatiske behandling af de tre hovedpinetyper, har patienten eklatant effekt på højdosis steroid sv.t. den højresidige hemicrania, der forværres ved nedtrapning under 37,5 mg.

Er velkontrolleret for sin episodiske migræne med forebyggende behandling med candesartan. Desuden velkontrolleret med carbamazepin mod de neuralgiforme jag.

Der er således tale om en kronisk inflammatorisk rhombencefalit med steroid respons, af uafklaret ætiologi, hvor flere differentialdiagnoser har været overvejet og ekstensivt undersøgt uden klare parakliniske holdepunkter eller fund. Dette efterlader fortsat et åbent diagnostisk felt, hvor også sjældnere, arvelige tilstande – herunder leukodystrofier – må inddrages i de videre overvejelser.

Abstracts



Videnskabelige posters

Self-reported employment status and quality of life in patients referred to the Danish MS Hospitals – a cross-sectional study.

Schmidt, Anne Mette¹; Taul-Madsen, Laurits¹; Skjerbæk, Anders G.¹; Svendsen, Mia J. B.¹; Hvid, Lars G.^{1,2} ¹The Danish MS Hospitals, Ry and Haslev, Denmark ²Exercise Biology, Department of Public Health, Aarhus University, Aarhus, Denmark.

BACKGROUND & AIM: Persons with multiple sclerosis (pwMS) experience lower employment rates and higher sickness absence, flexible employment, and disability pension than the general population. Invisible symptoms, particularly cognitive impairments and fatigue, are considered major barriers to work participation. Lower employment levels reduce individual income and increase societal costs. To inform development of a vocational rehabilitation intervention at the Danish MS Hospitals, this study compared self-reported quality of life (QoL) across employment groups, with specific focus on cognition and fatigue.

METHODS: A cross-sectional study included pwMS aged 18–66 years (working age) referred to the Danish MS Hospitals during 2024–2025. Employment status was categorised into three groups: employment (full- or part-time), flexible employment (reduced work capacity employment), or pension (disability or early retirement pension). Disease-specific QoL was measured by the Functional Assessment of Multiple Sclerosis (FAMS; range 0–176, higher score indicates better QoL), including the subscales for mobility, symptoms, emotional well-being, general contentment, thinking and fatigue, and family/social well-being. FAMS total and subscale scores were compared across employment groups. Analyses were adjusted for age, sex, disease duration, MS type, and disability status measured by Patient Determined Disease Steps (PDDS; 0–8, higher score indicates higher level of disability).

RESULTS: A total of 3,093 pwMS were included (age 50±10 years; 69% female; disease duration 12±9 years; MS type 61%

relapsing-remitting, 25% progressive, 14% unknown; PDDS 2.9±2.0). Of these, 1,228 were employed, 691 in flexible employment, and 1,174 on pension. FAMS total was highest among employed pwMS (109±28) and lower in flexible employment (-3.4 [-5.9;-1.0], p=0.006) and pension (-13.3 [-15.4;-11.1], p<0.001). Similar patterns were observed across all subscales, including thinking and fatigue, where the score was also highest for employed (17.9±8.6), yet reduced in flexible employed (-1.3 [-2.1;-0.6], p=0.001), and pension (-1.6 [-2.3;-1.0], p<0.001). Findings remained consistent after adjustments (data not shown).

DISCUSSION: Both the total QoL score, and subscale scores differed across employment groups in this large sample of pwMS, with the lowest QoL observed among those receiving pension. These findings support the development of a future vocational rehabilitation intervention at the Danish MS Hospitals.

Patient-reported polysymptomatology in persons with multiple sclerosis at the Danish MS Hospitals.

Taul-Madsen, Laurits¹; Schmidt, Anne Mette¹; Svendsen, Mia JB¹; Skjerbæk, Anders G¹; Hvid, Lars G^{1,2} ¹The Danish MS Hospitals, Ry and Haslev, Denmark ²Exercise Biology, Department of Public Health, Aarhus University, Aarhus, Denmark.

BACKGROUND & AIM: Numerous symptoms are well-documented in persons with multiple sclerosis (pwMS). However, limited research has addressed polysymptomatology – the intricate interplay of multiple and concurrent symptoms. Understanding hereof could potentially have great implications for clinical referral pathways and help optimise rehabilitation strategies. We aimed to investigate this in a large cohort of pwMS referred to MS specialized rehabilitation at the Danish MS Hospitals..

METHODS: A total of n=3833 pwMS (68% females, 54±13 yrs, Patient Determined Disease Steps (PDDS) 3.1±2.1, disease duration 13±11 yrs, 54/30/16% relapsing–remitting/progressive/unknown) were enrolled. Six common and debilitating patient-reported symptoms registered prior to hospitalization were selected for analysis; mobility, pain, bladder, fatigue, cognition, and depression. Each symptom was scored across three prevalence and severity categories; not affected, affected, or highly affected. Polysymptoms were defined as two or more symptoms rated 'affected or highly affected', whereas severe polysymptoms were defined as two or more symptoms rated 'highly affected'.

RESULTS: High prevalences were reported across all symptoms, including mobility (43% affected/35% highly affected), pain (50%/25%), bladder (36%/10%), fatigue (47%/49%), cognition (60%/18%), and depression (50%/10%). A total of 94.7% reported polysymptoms, with 6.5% reporting two symptoms, 15.6%, 25.5%, 31.8%, and 18.3% reporting 3, 4, 5, and 6 symptoms, respectively. For severe polysymptoms, a total of 42.1% reported this, with 22.6%

reporting two symptoms, 12.3%, 5.7%, 1.4%, and 0.1% reporting, 3, 4, 5, and 6 symptoms, respectively.

DISCUSSION: In addition to high prevalence rates across the six symptoms, a large proportion had polysymptoms (94.7%) and a substantial proportion also had severe polysymptoms (42.1%).

Patient satisfaction after switching to subcutaneous ocrelizumab: preliminary data from the DREAMS study.

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BACKGROUND & AIM: Given twice a year as a 10-minute injection, subcutaneous ocrelizumab (SC-OCR) appears to deliver the same clinical benefit as the 2–4 hour-long infusions, but in a more convenient setup. The majority (92.3%) of patients were satisfied or very satisfied with SC-OCR in the OCARINA trials. Most patients also felt the formulation convenient or very convenient to use (90.1%) and that the time taken to get the injection was just right (90.5%). Here, we examined satisfaction and convenience with SC-OCR in a real-world study.

METHODS: So far 63 patients have been enrolled into the DREAMS study at two Danish sites. Treatment satisfaction was assessed by TSQM-II questionnaire completed by patients on the day of injection at baseline (before switching from i.v. ocrelizumab) and after 6 months across four TSQM domains: Effectiveness, Side Effects, Convenience, and Global Satisfaction. Data from patients who have been already followed up to 6 months have been analyzed (n=40), Normality of the TSQM II data was assessed using the Shapiro–Wilk test. Changes over time were examined using the Wilcoxon signed-rank test. All tests were conducted as two-tailed.

RESULTS: Across all four TSQM II domains, mean satisfaction scores increased from baseline to 6-month follow-up after switching from intravenous to subcutaneous treatment administration, although changes did not reach significance. The magnitude of change varied by domain, with the largest mean increases (improvement) observed for Side Effects (+7.30, p=0.14) and Convenience (+7.28, p=0.10). Global Satisfaction remained stable from baseline to 6 months (+6.08, p=0.18). There was no significant change in Effectiveness scores from baseline

to 6 months (+2.43, p=0.67). In terms of individual-level changes, the proportion of patients who improved was highest for Convenience and Global Satisfaction.

DISCUSSION: Across all TSQM domains, no statistically significant changes were observed from baseline to 6 months, although mean scores increased with best improvement in convenience and side effects. Collectively, the findings indicate that participants' treatment satisfaction remained stable over the 6-month period, with varying degrees of consistency across domains.

Supported by Roche

Oceans of Hope: Sailing as rehabilitation

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BACKGROUND & AIM: Oceans of Hope is an initiative enabling people diagnosed with multiple sclerosis (MS) to participate in ocean sailing to promote health and quality of life. Ocean sailing may be viewed as a low-intensity high-volume intervention with continuous demands for postural corrections and functional adjustments in motor output as a reaction to changes in afferent input, which could lead to sensorimotor adaptations. However, no studies have investigated the effects and feasibility of long-term ocean sailing in people with MS. Thus, the aim of this study was to evaluate the feasibility of ocean sailing and the effects on mechanical muscle function, physical capacity, and fine motor control in people with MS.

METHODS: In this exploratory study, 15 people with MS participated in 10 days of ocean sailing (Age: 48.1±10.2, years since diagnosis: 11.4±7.6, EDSS score: 3.0±0.8). Participants were actively engaged in onboard sailing activities such as helming, boat work, standby/lookout, and leisure activities. Lower-limb mechanical muscle function (maximal isometric leg extensor muscle strength, rate of force development, contractile muscle power, force steadiness), gait speed (Timed 25-foot Walk Test), static bilateral postural balance (sway analysis), and manual dexterity (9-Hole Peg Test) were

tested before and after the intervention. No control group was included. Feasibility was evaluated using adverse events, serious adverse events, drop-outs, and adherence.

RESULTS: No serious adverse events were reported, and one adverse event was reported (mild/moderate seasickness). Adherence was excellent. Manual dexterity improved, and body weight was reduced after the intervention ($P < 0.05$). No other statistically significant pre- to postintervention changes were found.

DISCUSSION: Ocean sailing for 10 days is feasible in people with MS, as none of the participants reported serious adverse events, and seasickness was the only adverse event. Ten days of ocean sailing did not seem to have any measurable effects on lower-limb mechanical muscle function or functional capacity in people with MS. Notably, however, no deteriorations were observed following the 10-day sailing protocol. Thus, initial evidence suggests ocean sailing may represent a feasible and safe form of physical activity for people with MS who experience mild to moderate impairments.

Epstein–Barr Virus Antibody Titers in Blood and Cerebrospinal Fluid Before and After Treatment with Dimethyl Fumarate in Multiple Sclerosis.

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BACKGROUND & AIM: Epstein–Barr virus (EBV) is strongly associated with multiple sclerosis (MS), potentially mediated by immunological mimicry. Dimethyl fumarate (DMF), a commonly used MS therapy, may exert antiviral effects. This study evaluates EBV antibody levels longitudinal in blood and cerebrospinal fluid (CSF) before and after DMF treatment and levels are correlated with disease activity.

METHODS: In a phase IV trial, we treated newly diagnosed MS (n=53). Participants fulfilled McDonald 2010, 2017 and 2024 criteria. Serum was collected at baseline, month 1,3,6,12 and 24 (n=266). CSF sampling was collected optional at baseline and month 12. EBV antibodies were quantified using the LIAISON® immunoassay. Disease activity was determined by relapses or MRI activity <24 months from treatment initiation.

RESULTS: EBNA-1 IgG median levels in serum were 978.0 U/ml (range:68.2–4340) at baseline, 750.0 U/ml (range:68.5–5020) at month 1, 600.0 U/ml (range:63.0–4380) at month 3, 615.0 U/ml (range:65.2–5000) at month 6, 940.0 U/ml (range:60.4–5700) at month 12 and 552.0 U/ml (range:67.2–3583) at month 24 (all p-values:ns). EBV viral capsid antigen (VCA) IgG and IgM remained unchanged in throughout the study period. The median EBNA-1 IgG serum levels amongst those with disease activity (n=26) were 1200 (range: 244.0–4220) U/ml at

baseline, 1090 (range: 79.2–3960) U/ml at month 1, 950.0 (range: 98.2–3100) U/ml at month 3, 825.0 (range: 69.0–3800) U/ml at month 6, 988.0 (range: 85.5–3520) U/ml at month 12 and 365.0 (range: 106.0–2620) U/ml at month 24. Amongst those without disease activity (n=26), the median EBNA-1 levels in serum were 582.5 (range:68.2–4340) U/ml at baseline, 538.0 (range: 68.5–5020) U/ml at month 1, 552.0 (range:63.0–4380) U/ml at month 3, 570.0 (range: 65.2–5000) U/ml at month 6, 762.0 (range: 60.4–5700) U/ml at month 12 and 576.0 (range: 67.2–3580) U/ml at month 24 (all p-values:ns). Antibody levels in CSF were below the lower limit of detection in all samples.

DISCUSSION: Treatment with DMF did not affect EBV antibody levels in serum or demonstrate differences in participants with or without disease activity. Antibodies in CSF were not detected, which could be assay related. However, the study might be underpowered, and results should be interpreted with caution.

Virus responses in the conversion from optic neuritis to multiple sclerosis.

Trier, Nicole Hartwig, Gåsland, Helena, Kylliesbech Cecilie, Frederiksen, Jette Lautrup, Houen, Gunnar.

INSTITUTION: Department of Neurology, Rigshospitalet Glostrup

BACKGROUND & AIM: Multiple sclerosis (MS) is a chronic demyelinating disease in the central nervous system. Evidence indicate that virus infections and especially Epstein-Barr virus (EBV) are involved in the development of the disease. Here we evaluated the virus antibody profile of patients with optic neuritis (ON) and analyzed whether virus antibodies may function as a biomarker to forecast the development of MS.

METHODS: Specific IgG concentrations to common viruses such as EBV, Mumps, Measles, and Rubella were examined in serum of patients, who had ON as onset symptom (n=59) ((F:M 40:19, 41 years (age range 20-60)). Virus IgG levels were determined in serum and cerebrospinal fluid (CSF) by enzyme-linked immunosorbent assays. A total of 23 patients presented with MS following the initial ON diagnosis.

RESULTS: No notable differences in virus antibody levels to Mumps, Measles and Rubella (MMR) were determined between patients with isolated ON and MS converters. However, EBV EBNA1 IgG levels were significantly elevated ($p = 0.0180$) in CSF of MS converters compared to patients with ON. Furthermore, ON patients who developed MS were significantly younger than ON non-converters ($p = 0.0451$). Finally, the presence of oligoclonal bands was significantly different between the MS converters and the non-converters group ($p = 0.0001$).

DISCUSSION: Collectively, these findings indicate that MMR virus infections have no indicative biomarker value in terms of MS conversion, whereas the preliminary findings indicate that the presence of EBV

IgG in the CSF may function as a biomarker to forecast the development of MS. These findings confirm the crucial role of EBV in the development of MS.

Epstein–Barr virus specific T cell responses in multiple sclerosis patients treated with Ocrevus.

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INSTITUTION: Department of Neurology, Rigshospitalet Glostrup.

BACKGROUND & AIM: Multiple sclerosis (MS) is a chronic inflammatory disease associated in the central nervous system. Patients with MS are effectively treated with second line treatment strategies such as Ocrevus (OCR), which significantly reduces the number of relapses. Although the etiology of disease onset still remains inconclusive, several evidence point to Epstein–Barr virus (EBV) infections plaing a crucial role in disease onset.

METHODS: Here we evaluated the T cell response upon EBV stimulation in patients with MS following OCR treatment and in healthy controls (HCs). Blood samples were collected from MS patients before (n=13) and during OCR treatment (n=29) and from HCs (n=15), whereafter cells were stimulated with Epstein–Barr nuclear antigen (EBNA)1.

RESULTS: Independent of OCR treatment, the percentage of activated T and NKT cells was significantly increased in RRMS patients when compared to HCs ($p = 0.0023$ – 0.0437). Similarly, a trend indicated elevated percentage of activated T cells in RRMS patients upon EBV stimulation in patients receiving OCR treatment. The opposite effect was observed for NKT cells, as the percentage of activated NKT cells were reduced upon EBNA1 in patients treated with OCR.

DISCUSSION: Collectively, these findings indicate that the NKT cells of RRMS patients treated with OCR are less responsive to EBNA1 stimulation, suggesting cellular exhaustion.

Pain severity is associated with physical activity, exercise participation, and health-related quality of life in multiple sclerosis.

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BACKGROUND & AIM: Pain is a common symptom in people with Multiple Sclerosis (pwMS), but its relationship with physical activity and exercise, key components of disease management, remains poorly understood. This study aimed to determine the prevalence and severity of pain in pwMS, and to examine its associations with physical activity, exercise participation, and health-related quality of life (HRQoL). We hypothesized that higher pain severity would be associated with lower levels of physical activity, reduced exercise participation, and decreased HRQoL.

METHODS: In our cross-sectional survey of 936 Danish pwMS, average and worst pain severity were assessed using a Numerical Rating Scale (NRS⁰⁻¹⁰); physical activity and exercise participation were assessed using the Baecke Habitual Physical Activity Questionnaire; and HRQoL using a Visual Analog Scale. Participants were stratified into three groups based on average pain: no pain (NRS=0), mild pain (NRS=1-2), and moderate-severe pain (NRS≥3). Descriptive data are presented as mean±SD or median (IQR). Linear mixed-effects models were used for statistical analysis.

RESULTS: Descriptive characteristics: 73% females, age 58±12 years, disease duration 17±11 years, patient-determined disease steps 2.8±2.2 points. Pain was reported by 76% of participants, with 24% experiencing mild pain, and 52% experiencing moderate-severe pain, based on average pain data. Median average and worst pain intensities

corresponded to 3 (1;5) and 4 (1;7), respectively. Pain was associated with lower levels of physical activity (no pain 8.64±2.48 points; mild pain -0.64 [-1.18;-0.11] (p=0.018), moderate-severe pain -0.66 [-1.12;-0.20] (p=0.005)). In addition, pain was associated with reduced exercise participation (no pain 3.16±1.76 points; mild pain -0.47 [-0.94;-0.09] (p=0.015), moderate-severe pain -0.49 [-0.82;-0.17] (p=0.003)). Lastly, pain was associated with reduced HRQoL (no pain 74.3±18.9, mild pain -5.6 [-9.3;-1.9] (p=0.003), moderate-severe pain -19.7 [-22.9;-16.5] (p<0.001)).

DISCUSSION: Pain is highly prevalent in pwMS and is furthermore significantly associated with lower levels of physical activity, reduced exercise participation, and decreased health-related quality of life. This relationship is complex, as pain can likely present as a barrier to physical activity and exercise, but preliminary evidence also suggests that exercise may have a modifiable effect on pain severity in pwMS. However, future studies are needed to elucidate this intricate relationship.

Treating lower urinary tract dysfunction in people with Multiple Sclerosis using TENS+ neurostimulation – preliminary PRO findings.

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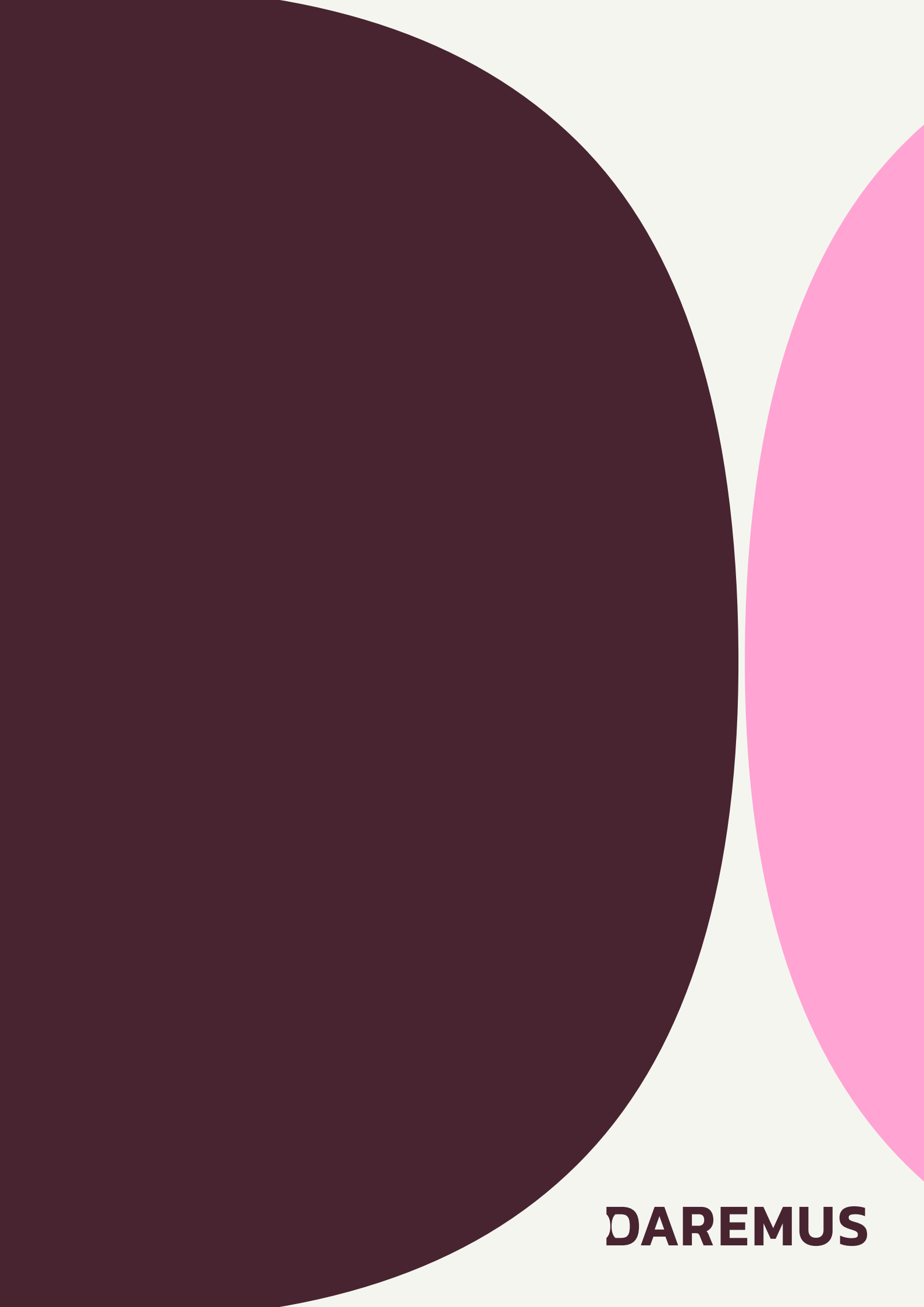
BACKGROUND & AIM: Lower urinary tract dysfunction (LUTD), encompassing both voiding and storage symptoms, is highly prevalent in people with Multiple Sclerosis (pwMS) and has profound implications for quality of life (QoL). Neuromodulation via neurostimulation – specifically of the posterior tibial nerve – is a guideline-endorsed treatment for idiopathic LUTD, yet evidence in pwMS remains limited. While most existing research has focused on percutaneous neurostimulation, only a few studies have evaluated the effectiveness of the simple, user-friendly transcutaneous device TENS+. To address this gap, we conducted a 12-week, single-arm intervention study in a cohort of pwMS.

METHODS: A total of 18 pwMS (61% females, age 52±14 years, Patient-Determined Disease Steps 3.9±2.3, time since diagnosis 11±10 years) were enrolled in this single-arm, open-label study. During a 2-week inpatient stay at the Danish MS Hospitals, clinical consultations and patient-defined goals were used to identify eligible pwMS for whom LUTD was a primary symptom with a substantial impact on daily life. All participants were trained in the use of the TENS+ device prior to discharge. The intervention protocol required 20-min daily at-home use over a 12-week period. Standardized and validated questionnaires from the International Consultation on Incontinence Questionnaire (ICIQ) were used to assess patient-reported outcomes. Specifically, the ICIQ-OAB (scoring 0–16 points) measured frequency, nocturia, urgency, and urge urinary incontinence, while the ICIQ-OABqol (scoring 25–160

points) evaluated the impact on QoL. Lower scores indicate a reduced symptom burden and improved QoL, respectively.

RESULTS: Following the 12 week-intervention, ICIQ-OAB was reduced by -2.1 points [95% CI: -3.3;-0.8], mainly reductions in frequency (-1.0 [-1.6;-0.4] points) and nocturia (-0.6 [-1.1;-0.1] points). Furthermore, ICIQ-OABqol was reduced by -22 [-29;-14] points. Based on clinical evaluation and a threshold of ICIQ-OAB change ≥ -1, n=13 (72%) pwMS were classified as treatment responders.

DISCUSSION: In pwMS with substantial LUTD, the use of the TENS+ neurostimulator led to significant reductions in symptom severity and a concomitant improvement in bladder-related QoL in almost three-quarters of participants. A next step includes evaluation of 12-month follow-up in treatment responders to determine whether the positive effect is sustained over time.



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