Poster Tour: MS/Inflammatory

May 6, 11:45 - 12:45

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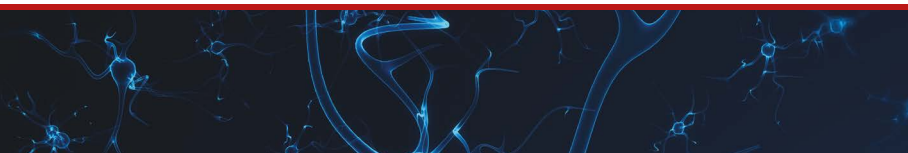

Ocrelizumab vs placebo in PPMS: efficacy and safety results of the Phase IIIb ORATORIO-HAND study

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Introduction: ORATORIO-HAND (NCT04035005) is a Phase IIIb, multicentre, randomised, double-blind, PBO-controlled trial investigating the efficacy and safety of OCR in pwPPMS, including, for the first time, more-advanced PPMS.

Methods: Adult pwPPMS (≤65 years) with an EDSS 3.0-8.0 were randomised 1:1 to OCR 600 mg or PBO every 6 months for 144 weeks (wk) or until ≥340 progression events were observed. The primary endpoint was time to onset of 12-wk composite CDP (on either 9HPT or EDSS).

Results: OCR (n=505) vs PBO (n=508) pts: median age 48 and 46, median baseline EDSS was 6.0. 12-week cCDP rates were 32.7% vs 40.4% (HR: 0.70 [30% RR]; P=0.0007). Significant RRs were also seen in 9HPT (41%; P=0.0002) and EDSS (33%; P=0.0013). In the MRI-active subset, RR on 12wk-cCDP was 55% (P<0.0001). Adverse events for OCR vs PBO (AEs,74.9% vs 71.1%; serious AEs, 12.8% vs 13.2%; infusion-related reactions, 20.8% vs. 4.3%; infections, 48.4% vs 44.7%; malignancies, 1.0% vs 0.6%).

Conclusions: In a large PPMS population, OCR significantly delayed worsening of EDSS and upper limb function (9HPT). Safety aligns with known OCR data.

Baseline Patient-Reported Outcomes Predict Clinical Progression in Progressive MS: An MS-SMART Post-Hoc Analysis

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Introduction: Patient–reported outcomes (PROs) have significant clinical and trial potential due to their regulatory appeal, cost–efficiency and potential for remote collection. However, interpreting longitudinal PRO change is complex in progressive multiple sclerosis (PMS), as perceived disability can shift as individuals adapt to their clinical status. We evaluated how baseline disability influences longitudinal PRO trajectories.

Methods: This post-hoc analysis of the phase 2 MS-SMART trial investigated the impact of baseline disability measured by the MS-Impact Scale (MSIS-29v2 PH), MS Walking Scale (MSWS-12v2), and Expanded Disability Status Scale (EDSS) on PRO change over 36 months. Patients were stratified by clinical disability (EDSS ≤ 5.0 vs ≥ 5.5) to assess PRO baseline impact across disability levels.

Results: High baseline patient-reported disability was associated with reduced longitudinal PRO change ($p < 0.001$), whereas baseline EDSS showed no significant association. Baseline PROs demonstrated a greater impact on longitudinal change in the high–EDSS group. Overall, baseline MSWS-12v2 exhibited greater predictive value across EDSS thresholds compared to MSIS-29v2 PH.

Conclusion: Longitudinal PRO change in pwPMS is primarily driven by baseline patient perception rather than clinician-reported disability. This highlights the necessity of prioritising baseline PRO scores over traditional clinical measures when assessing or predicting patient-reported functional changes in clinical trials.

Recurrent Area Postrema Syndrome in a Suspected Seronegative NMOSD: An 18-Year Follow-Up Case

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We report a case of a 28-year-old woman with no prior medical history who presented with persistent vomiting and hiccups, initially admitted under gastroenterology. During hospitalization, she developed decreased consciousness requiring ICU admission and invasive ventilation. MRI revealed high signal intensity in the posterior spinal cord and adjacent medulla with contrast enhancement. Infective and malignant causes were excluded. She was treated as inflammatory condition of uncertain aetiology with high-dose steroids and cyclophosphamide, resulting in clinical and radiological improvement. Over the subsequent four years, she experienced two further relapses with similar symptoms and imaging despite azathioprine therapy. AQP4 antibodies were negative. She was treated as a suspected NMOSD variant and rituximab was initiated, leading to sustained remission for 14 years

This case highlights a suspected seronegative NMOSD presenting with recurrent area postrema syndrome and excellent response to B-cell depletion therapy. Current NMOSD diagnostic criteria do not include recurrent area postrema syndrome as a standalone criterion. We propose consideration of recurrent area postrema syndrome in future revisions of NMOSD diagnostic criteria in seronegative cases with characteristic imaging and therapeutic response.

SHIELD: Surveillance of health and infections in MS linked to disease modifying therapies

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Background: Infection is a major cause of morbidity in multiple sclerosis (MS).

Objective: To collect detailed data on infections in people with MS (pwMS) versus household controls, to inform clinical guidance.

Methods: PwMS and their non-MS household contacts complete a weekly infection-diary and perform nasal swabs every fortnight and after flu-like illness, for 6 months. Swabs are screened for 16 respiratory pathogens.

Results: Recruitment opened in November; as of January 2026, we have recruited 36 pwMS receiving antiCD20 monoclonal antibodies (67% female, mean age 45.0, mean BMI 27.1) and 27 household controls (52% female, mean age 49.1, mean BMI 27.1). PwMS had mean disease duration 7.9years, seasonal vaccine uptake was 27(72%) for flu and 26(75%) for COVID, 3(8%) were smokers, 12(33%) had not had a recent dental check, 5(14%) reported poor gum health. As of January 2026, we have analysed 91 routine swabs and 27 from people experiencing flu-like illness (11 controls, 16 pwMS). Overall, pathogens were detected in 25% and 35% of routine swabs, and in 45% and 56% of swabs following flu-like illness from controls and pwMS respectively.

Conclusions: Data will be used to produce evidence-based guidelines for pwMS and clinicians, and to influence vaccine policy.

Changes in pre-lesional normal-appearing white matter are detectable 16 years before lesion formation in MS

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Background: The first appearance of multiple sclerosis (MS) white matter (WM) lesions is only a brief phase in their genesis and evolution. Magnetic resonance imaging (MRI) has shown changes in pre-lesional tissue nearly three years before a lesion appears, but it remains uncertain whether these changes either represent tissue vulnerability to lesion formation or a progressive pathological process.

Methods: Longitudinal MRI and clinical data from over 20 years were used from 63 people with clinically isolated syndromes (CIS), relapsing-remitting (RR) or secondary progressive (SP)MS. Normalised pre-lesional measures were evaluated at three time-points leading up to lesion first appearance, using magnetisation transfer (MTR) and T1/T2 ratio maps, assessing differences relative to the contralateral always normal-appearing (ANA)WM.

Results: A total of 2,603 lesions were sampled on MTR and 2,729 on T1/T2 ratio. Relative to the contralateral ANAWM, pre-lesional MTR and T1/T2 ratio measures were significantly abnormal at all timepoints up to 16 years before first appearance of a lesion. Longitudinal analysis showed progressive abnormalities in T1/T2 ratios over time (βchange in mean normalised intensity: -0.017, $p<0.001$).

Conclusion: WM lesions may form and evolve long before they are first overtly seen on MRI. These changes may indicate progressive WM tissue destruction.

A Scoping Review of Neurosarcoidosis: The changing treatment landscape and its clinical determinants.

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Background: Neurosarcoidosis is a disabling neuroinflammatory condition with protean clinical manifestations. There are limited real-world data to inform stratified treatment algorithms and sequencing. We aimed to review published literature to map evolving treatment strategies and their clinical determinants

Methods: A scoping review was conducted using established methodological guidance (Joanna Briggs Institute) and the PRISMA-ScR checklist. MEDLINE and Embase were searched for studies reporting Neurosarcoidosis treatment and outcomes between 2004 and 2025.

Results: 57 studies were included, predominantly case series and observational cohorts (n>2000). Mean age at onset= 44.9 years, overall sex ratios~1:1, with spinal and optic cohorts skewing younger. Ethnicity data were inconsistently reported. Diagnostic criteria varied with increased uptake of updated frameworks. Corticosteroids were the most frequently used first-line treatment (95–100% of cohorts), and methotrexate was the most commonly used second-line therapy (60–90%), followed by azathioprine, mycophenolate and cyclophosphamide. Biologic use was frequently reported in later studies (15–48%). Outcome reporting was inconsistent, most relying on subjective clinical improvement with infrequent use of structured scales or pre-defined measures.

Conclusions: The body of evidence from Neurosarcoidosis research remains fragmented and heterogeneous. A multicentre cohort study is timely to establish robust epidemiological, treatment, and outcome data and support evidence-based stratified treatment guidelines.

From Auricular Inflammation to Myelitis: The Neurological Spectrum of Relapsing Polychondritis

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Background: Relapsing polychondritis (RP) is a rare systemic autoimmune disease with occasional neurological involvement, which can mimic demyelinating disorders and complicate diagnosis. PPMS diagnosis is difficult when CSF is unavailable and immunosuppression may affect inflammatory activity

Case: A 76-year-old woman with RP, ocular inflammation (anterior scleritis, cystoid macular oedema), and primary biliary cirrhosis on mycophenolate developed a gradually progressive gait disorder over >1 year (EDSS 6.0). Brain MRI (Dec 2023) showed periventricular small vessel lesions; spinal MRI (May 2024) revealed a T1 lateral column lesion. Visual evoked potentials (Sept 2024) demonstrated marked bilateral symmetric delay consistent with optic pathway demyelination. AQP4-IgG and MOG-IgG were negative, with normal nerve conduction studies.. CSF examination was declined. Repeat contrast-enhanced MRI (Oct 2024) showed no new lesions or enhancement.

Discussion: Although RP can produce inflammatory or vasculitic CNS mimics, combination of periventricular and spinal lesions, objective demyelinating physiology, and progressive clinical course supports PPMS per 2024 McDonald criteria. Immunosuppression and comorbidities complicate interpretation of radiological activity and treatment eligibility, emphasizing structured diagnostic reasoning and avoiding anchoring bias.

Conclusion: PPMS can be diagnosed confidently without CSF when clinical progression is supported by characteristic MRI patterns and paraclinical evidence, even in patients with systemic autoimmune disease.

First presentation with Optic neuritis does not result in delayed DMT initiation in MS

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Introduction: Early diagnosis and disease-modifying therapy (DMT) reduce disability in multiple sclerosis (MS). First presentation with optic neuritis (ON) has historically been perceived as a more benign phenotype, with concerns that this perception may delay initiation of DMT. We assessed whether ON onset was associated with delayed DMT initiation compared with onset in other topographies.

Methods: We conducted a case review of 539 patients with MS who commenced any DMT at our centre between 1990 and 2023. Site of onset was classified using predefined criteria as ON, non-ON. Time from diagnosis to DMT initiation was analysed using a Cox proportional hazards model, adjusting for confounders.

Results: After excluding ambiguous presentations, 110 (110/416, 26.4%) had ON onset and 306 (306/416, 73.6%) had a non-ON onset. Patients with ON had a younger median age at diagnosis (32 vs 34 years; p=0.005). Median time-to-DMT initiation was 282 days (IQR 119–1024) in the ON group and 334 days (IQR 140–689) in the non-ocular group. There was no evidence that ON onset was associated with delayed DMT initiation (HR 1.00, 95% CI 0.80–1.29).

Conclusion: In this cohort, ON as the first presentation of MS was not associated with delayed initiation of DMT.

Acute Cerebellitis Following Semaglutide Use

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Glucagon-like peptide-1 receptor agonists (GLP-1 RA) are widely prescribed for the management of type 2 diabetes mellitus and increasingly used for weight loss due to their incretin-mediated glycaemic effects and appetite-suppressing properties. Whilst gastrointestinal adverse effects are well recognised, neurological complications remain rare. We report the case of a 56-year-old woman who presented with a two-week history of vomiting, diarrhoea, and progressive lethargy, followed by muscle spasms, unsteadiness and confusion. Neurological examination was unremarkable. Initial investigation revealed marked electrolyte derangement, metabolic alkalosis and acute kidney injury. Computed tomography of the brain revealed bilateral cerebellar hypodensities, with corresponding parenchymal hyperintensity on T2-weighted magnetic resonance imaging (MRI) consistent with acute cerebellitis. A comprehensive workup, encompassing cerebrospinal fluid analysis alongside infectious, autoimmune and paraneoplastic screening, was inconclusive. On further questioning, the patient disclosed recent self-administration of semaglutide for weight loss. Supportive management with intravenous fluids, electrolyte replacement, and vitamin supplementation led to marked clinical improvement, with partial resolution of cerebellar signal abnormalities on interval MRI. The temporal association between semaglutide initiation and symptom onset supports a possible drug-induced aetiology. This case highlights the need for vigilance in patients receiving GLP-1 RA therapy and contributes to the evolving understanding of their neurological safety profile.

Switching to biosimilars in multiple sclerosis: patient experiences on natalizumab

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Imperial College Healthcare NHS Trust

Background: Tyruko (natalizumab) is the first biosimilar monoclonal antibody approved for use in multiple sclerosis (MS). In May 2024, Tyruko was introduced at the Imperial College Healthcare NHS Trust replacing the originator Tysabri. This study aimed to capture patients' real-world experiences of switching to Tyruko, including implementation, perceived effects and outcomes following continuation or switch-back.

Methods: A cross-sectional survey assessing patient experiences and symptom changes before, during and after switching to Tyruko was administered in person using a paper-based format between 13-October and 21-November 2025.

Results: Of 236 patients approached, 207 completed the survey. 81.2% switched back to Tysabri, while 18.8% continued Tyruko. Median self-reported symptom severity (0-10) increased from 3 prior to Tyruko initiation to 7, falling to 4 following discontinuation. While receiving Tyruko, most reported worsening of key MS symptoms, a pattern that reversed after discontinuation. 48.7% reported no confidence in the switch decision and 60.9% felt insufficiently informed prior. The principle reasons for stopping Tyruko were worsening symptom (n=121) and side effects (n=90).

Discussion: Switching to Tyruko was associated with high discontinuation, increased patient-reported symptom burden and low confidence, highlighting the importance of careful implementation, transparent patient engagement and ongoing monitoring following biosimilar introduction.