ECTRIMS 2025 Clinical and AI / ML Preview

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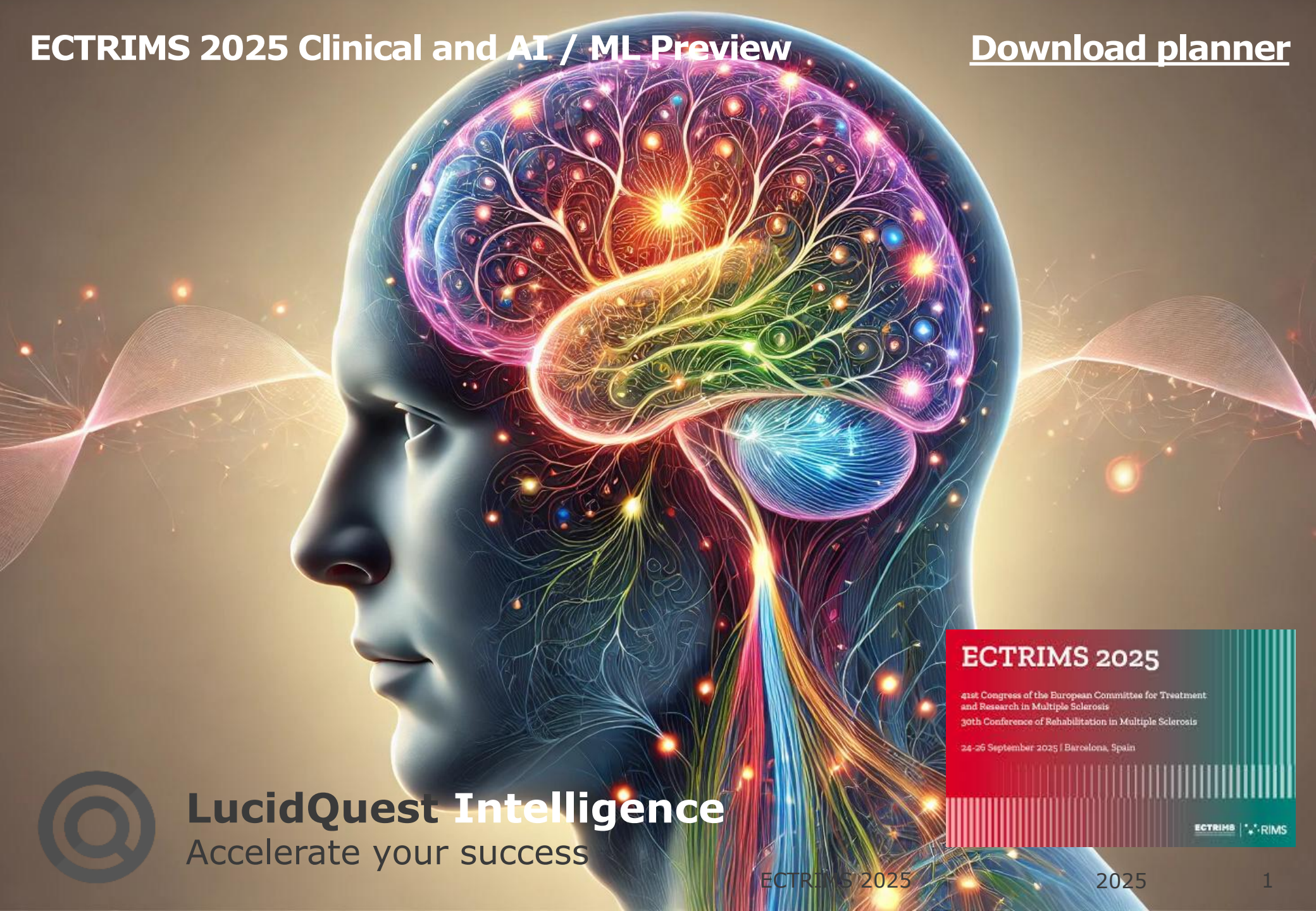

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ECTRIMS 2025 – General Overview

- **Global impact:** The largest international MS congress is set to showcase late-phase trial data, real-world evidence, and advances across MS and allied neuroinflammatory disorders
- **Multidisciplinary scope:** Sessions are expected to integrate clinical neurology, immunology, imaging, rehabilitation, and digital health, strengthening cross-disciplinary care strategies
- **Therapeutic pipeline:** Breakthroughs in BTK inhibitors, B-cell therapies, and novel modalities are prepared to dominate the treatment landscape
- **Patient engagement:** Patient-reported outcomes, quality of life measures, and shared decision-making are anticipated to gain stronger visibility in clinical presentations
- **Special populations:** Data are projected on pediatric MS, pregnancy outcomes, progressive MS, and underrepresented groups, addressing unmet needs
- **Evidence generation:** Trial emulations, registries, and long-term safety extensions are expected to reinforce real-world relevance and policy decisions

ECTRIMS 2025– Conference Themes (1/2)

- **BTK inhibitors:** Late-phase trial updates are expected to dominate, highlighting efficacy and safety in relapsing and progressive MS populations
- **Cellular therapies:** CAR-T and advanced cell platforms are projected to transform treatment options for refractory and high-burden MS cases
- **Biomarker innovation:** sNfL, GFAP, and emerging fluid and imaging markers are anticipated to drive precision monitoring and outcome prediction
- **Digital health:** AI-powered imaging, digital twins, and remote monitoring are prepared to reshape trial design and real-world patient management
- **Rehabilitation focus:** Fatigue, neurocognitive performance, and physical function interventions are expected to expand holistic MS care approaches

ECTRIMS 2025– Conference Themes (2/2)

- **Real-world evidence:** Registry-based analyses and trial emulation studies are positioned to refine long-term effectiveness and safety understanding
- **Associated disorders:** NMOSD and MOGAD data are anticipated to highlight antibody therapies and B-cell–directed treatments as future standards of care
- **Special populations:** Pediatric MS, pregnancy outcomes, and underrepresented groups are expected to receive focused data on tailored treatment strategies
- **Health equity:** Access, disparities, and patient engagement studies are projected to shape inclusive global strategies for MS and allied disorders
- **Neuroprotection & repair:** Trials targeting remyelination, neuroprotection, and mitochondrial health are anticipated to gain visibility as pathways toward long-term disease modification

Noteworthy Scientific presentations at ECTRIMS 2025

Key Topics From Notable Presentations (1/8)

- **Epidemiology, Risk & Comorbidities:** ECTRIMS 2025 is expected to spotlight how vascular risk, early-life exposures, pregnancy, and psychosocial comorbidities shape MS onset, severity, and long-term outcomes, emphasizing precision prevention and tailored interventions
  - Radiologically Isolated and Early-Life Risks: RIS management across DACH countries is expected to remain heterogeneous, with 127 neurologists reporting varied use of MRI and early DMTs. Early-life risks from maternal age, BMI, and non-Nordic origin should remain predictive for MS onset
  - Family Planning, Fatigue, and Sleep: The Ocrelizumab Pregnancy Registry (n=419) is set to show MCM rates comparable to controls. Childhood trauma-linked fatigue is expected to be mediated by emotion dysregulation, while poor sleep quality is projected to lower vitality and emotional well-being at MS onset
  - Vascular, Pain, and Minority Populations: Vascular comorbidities in MS-STAT2 (n=964) are expected to worsen cognition but show no simvastatin effect. CHIMES (n=82) should confirm that comorbidities rarely alter OCR efficacy, except for higher infusion reactions with diabetes. Chronic pain reassessments (n=183) are projected to link brainstem and sensory system involvement with neuropathic pain risk

Key Topics From Notable Presentations (2/8)

- **Diagnostics & Biomarkers:** Discussions are set to standardize multimodal diagnostics, KFLC-enhanced CSF testing, RAM-based imaging endpoints, and selective blood biomarkers—to accelerate earlier diagnosis and more sensitive disease monitoring

  - CSF immunodiagnostics (PRO-KFLC, McDonald 2024): KFLC integration is expected to raise sensitivity: among 535 samples, 10.5% OCB-negative cases will include eight with KFLC synthesis, supporting earlier MS/CIS diagnosis and guideline adoption
  - Imaging endpoints and reliability (RAM/ACES; CIS RCTs; scanner ICCs): MRI-confirmed relapses are projected to enlarge treatment effects and cut sample size by ~37%; baseline DIS will predict 5-year DIT (HR 2.40; DIT 89.9%); within-scanner ICCs ~0.72–0.76 will necessitate harmonization
  - Blood biomarkers across disorders (zonulin, NFL/GFAP, biglycan): Zonulin is expected to be higher in relapsing MS (5.8 vs 2.96 ng/mL); AQP4+ NMOSD will show ~40% higher NFL, falling after RTX/TCZ; biglycan elevations will lack EDSS correlation

Key Topics From Notable Presentations (3/8)

- **Therapeutics – Disease Modifying Therapies (DMTs):** Session will highlight consolidate disability-focused efficacy, especially BTK inhibition and durable S1P/anti-CD20 strategies, while expanding real-world safety, cognition outcomes, and next-generation options like VidoCa and CAR-T

  - BTK inhibition & disability outcomes: Tolebrutinib is expected to lower CDP and PIRA (HERCULES, GEMINI), show exposure–response, preserve HRQoL, and keep leukocytes, immunoglobulins, and platelets normal, supporting disability-focused, CNS-penetrant therapy

  - S1P modulators & cognition: Long-term S1P programs are expected to sustain low ARR and high CDA-free rates (ponesimod) and improve processing speed with ~80% CDP-6–free (ozanimod), while atrophy metrics track progression risk

  - Anti-CD20, cladribine & novel agents: Real-world and emerging strategies are expected to maintain control: tailored anti-CD20 dosing and fumarate de-escalation, cladribine ARR reduction with comparable malignancy risk, VidoCa durability, plus CAR-T, foralumab, and inebilizumab advances

Key Topics From Notable Presentations (4/8)

- **Rehabilitation, Symptom Management & QoL :** Care pathways will couple Donanemab's disease-slowing efficacy with safer dosing, while health-behavior interventions will boost prevention, together projecting earlier, broader improvements in patient outcomes and quality of life.

  - Donanemab clinical impact: TRAILBLAZER-ALZ 2 will show rapid amyloid clearance, slowed tau accumulation, biomarker shifts, and 33.6% slower clinical decline versus placebo, forecasting tangible functional gains for patients and caregivers

  - Optimized dosing and safety: TRAILBLAZER-ALZ 6 will demonstrate modified dosing reducing ARIA-E risk by 41% while maintaining amyloid and P-tau217 reductions, guiding safer rollout and monitoring in early symptomatic Alzheimer's

  - Behavioral prevention via diet: A 512-adult study will link perceived severity and cues to action with Mediterranean-diet adherence, enabling targeted cognition-informed programs that will strengthen dementia risk reduction

Key Topics From Notable Presentations (5/8)

- **Cognitive & Psychological Outcomes:** Cognition-focused strategies—validated tools, predictive markers, education, and structured rehabilitation—will define MS care, enabling earlier prognostication, therapy precision, and stronger patient-centered outcomes
  - Cognitive decline as prognostic marker: Longitudinal Australian data (n=397, mean FU 4.1y) will show early cognitive decline predicts sustained EDSS progression (aHR 1.2; Q4 vs Q1 aHR 4.72), outperforming MRI or motor measures, positioning cognition as a key prognostic tool
  - Neuropsychological tools, therapies & education: Ecuadorian BICAMS norms (n=136) expected to validate SDMT, BVMT-R, PAMCL with 52% impairment prevalence; natalizumab 48-month real-world follow-up (n=60) will enhance SDMT, fatigue, depression, and productivity; modafinil trials (n=64) will explore precision-targeted cognition therapy; UMIMS RCT (n=120) will raise MRI risk knowledge (+4.0 vs +2.7)
  - Rehabilitation trials & methodological frameworks: NEuRoMS will demonstrate SMART goal-setting reliability (ICC=0.86) improving NPR outcomes, while European clinician surveys (n=50) will expose barriers in NPR/VR RCT design—bias control, outcome selection, training—driving demand for structured guidance

Key Topics From Notable Presentations (6/8)

- **Trial Design, Methodology & Real-World Evidence :** Integrated methodological advances, head-to-head strategies, and stronger registries/digital tools are set to tighten causal inference, streamline trials, and translate real-world insights into earlier, more personalized MS decisions

  - Endpoints & causal methods: Registry-based target-trial emulation is set to reproduce RCT effects (ARR 7/8; EDSS all 6), while MRI-confirmed relapses (RAM) are projected to double the treatment effect and cut sample sizes ~37%

  - Strategy trials & comparative effectiveness: Strategy studies are poised to clarify care: TREAT-MS (~900) and DELIVER-MS (816) will compare EHT vs escalation; NEOS (129) will test PedMS noninferiority; pediatric MOGAD signals IVIG HR 0.28

  - Real-world, digital measures & transparency: Real-world infrastructure is set to mature: TRUSTED will boost recruitment (MSBase ×2; +1070 UKMSR); INTONATE-MS (n=1,915) highlights outcome gaps; AI harmonization will improve MRI quality metrics 15–43%; publications hover ~50%

Key Topics From Notable Presentations (7/8)

- **Patient Experience, Surveys & Health Literacy:** Co-designed tools, equitable recruitment, and targeted education are set to strengthen patient agency, improving acceptability, access, and outcome relevance across MS, MOGAD, and NMOSD

  - Trial participation & equity: Patient knowledge is widespread yet uneven; 42% plan enrollment, progressive MS 65%. RIGHT-MS shows longer diagnosis for underserved groups, and trial participation skews (White 42% vs Asian 20%, Black 17%)

  - Preferences, burden & digital navigation: MOGAD respondents prioritize vision and relapse prevention; placebo acceptability doubles with enhanced monitoring (33→66%). NMOSD surveys indicate nurse access 60%, satisfaction 85%, with US–Europe gaps in digital navigation and communication

  - Patient-centered outcomes & biomarkers: GFAP evidence is expanding: 14 RCTs identified, with siponimod lowering serum GFAP by 7.4 pg/mL. A tailored MCAT HRQoL item bank is expected to add work and financial dimensions soon

Key Topics From Notable Presentations (8/8)

- **Other / Mixed Mechanistic & Translational:** Translational programs will prioritize remyelination-supportive immunotherapies, metabolic conditioning, and complement inhibition, while neutral probiotic data and better AE standards will sharpen future mechanistic trials and rehabilitation design

  - Acute relapse rescue & neuroprotection: Escalation trials will suggest IA benefits optic neuritis to day 180, and a NAC pilot will lower/stabilize GFAP (−10.1 vs +39.5 pg/mL), supporting antioxidant neuroprotection signals

  - Repair biology & physiological conditioning: Post-hoc ADVANCE/ASCEND analyses will show T1w/T2w recovery with peg-IFNβ-1a (p=0.02) and natalizumab (p=0.046); intermittent hypoxia will improve 9-HPT, T25FW, SDMT, while probiotics will not reduce fatigue

  - Real-world control & rehabilitation outcomes: NMO SPOTLIGHT will report ARR dropping 0.50→0.02 on C5 inhibitors; CoreDIST will improve work disability (MSWDQ-23, p=0.02) and trunk control; an AE-methods review will standardize rehab RCT reporting

Focus of Key Industry-Sponsored Sessions at ECTRIMS 2025 (1/6)

- **Novartis:**
  - Focus Areas: Early Intervention & Anti-CD20 Therapies
  - Sessions will highlight long-term outcomes with ofatumumab in early MS, and evolving strategies for earlier, optimized use of anti-CD20s to improve disease control and disability outcomes
- **Roche:**
  - Focus Areas: NMOSD, MOGAD & Brain Health in MS
  - Presentations will explore age effects in NMOSD/MOGAD, pediatric-onset MS, individualized NfL Z-scores, protecting brain health, subcutaneous Ocrevus, and the transformative role of anti-CD20 therapies in MS management

Focus of Key Industry-Sponsored Sessions at ECTRIMS 2025 (2/6)

- **Bristol Myers Squibb:**
  - Focus Areas: Ozanimod Safety & CAR-T Therapy in MS
  - Sessions will address ozanimod's differentiated safety profile in RMS and investigate next-generation immune reprogramming strategies, including CAR-T therapy, for treatment-resistant MS populations
- **Merck (Merck Healthcare KGaA / EMD Serono):**
  - Focus Areas: Diagnostics & Disease Control
  - Discussions will cover the practicality of the 2024 McDonald criteria, MRI-informed practice, and novel treatment approaches aimed at achieving optimal long-term disease control in relapsing MS

Focus of Key Industry-Sponsored Sessions at ECTRIMS 2025 (3/6)

- **Alexion AstraZeneca:**
  - Focus Areas: NMOSD Pathogenesis & Complement Inhibition
  - Presentations will address evolving paradigms in AQP4-Ab+ NMOSD, including complement C5 inhibition therapies, clinical insights, and real-world evidence shaping next-generation treatment standards
- **UCB:**
  - Focus Areas: MOGAD Unmet Needs
  - Sessions will highlight recognition and management of MOGAD, with emphasis on unmet clinical needs and strategies to improve diagnosis and treatment outcomes in this rare disorder

Focus of Key Industry-Sponsored Sessions at ECTRIMS 2025 (4/6)

- **Sandoz:**
  - Focus Areas: Risk Stratification & Disability Measurement
  - Sessions will focus on JCV stratification to balance risk and optimize MS care, alongside innovations in disability measurement tools to improve patient monitoring and clinical trial endpoints
- **Sanofi:**
  - Focus Areas: Progressive MS & Disability Accumulation
  - Discussions will examine CNS inflammation in non-relapsing MS, therapeutic progress in progressive disease, and novel strategies to address disability accumulation as treatment goals evolve

Focus of Key Industry-Sponsored Sessions at ECTRIMS 2025 (5/6)

- **Juvisé Pharmaceuticals:**
  - Focus Areas: S1PR Modulators in RMS
  - Sessions will trace the evolution of S1PR modulators in relapsing MS, presenting long-term evidence and their role in optimizing disease management across treatment lines
- **Amgen:**
  - Focus Areas: NMOSD Biomarkers & B-cell Targeting
  - Presentations will emphasize biomarker discovery, advanced imaging, and targeting CD19+ B cells, shaping the next phase of personalized therapy in NMOSD

Focus of Key Industry-Sponsored Sessions at ECTRIMS 2025 (6/6)

- **Chugai:**
  - Focus Areas: Satralizumab & NMOSD Care
  - Sessions will explore optimization of satralizumab in NMOSD, linking mechanistic insights with global clinical experience to enhance treatment outcomes and broaden accessibility worldwide

Notable Presentations And Late-breaking Sessions At ECTRIMS 2025

Notable Presentations At ECTRIMS 2025
Epidemiology, Risk & Comorbidities (1/6)

Date	Title	Author	Summary
24 Sep 2025	Real-World Practices and Challenges of Radiologically Isolated Syndrome (RIS): Results of a Cross-Sector Survey by the DACH MS Guidelines Group	Friederike Held	• **Introduction:** Radiologically Isolated Syndrome (RIS) is diagnosed in asymptomatic individuals with incidental demyelinating CNS lesions, but there are no standardized guidelines for diagnosing, treating, or monitoring RIS in clinical practice. This study aimed to assess clinical practices for managing RIS, identify gaps, and inform the development of strategies for better care. • **Methodology:** A survey was conducted in October 2024 across neurologists in Germany, Austria, and Switzerland. Questions covered RIS diagnosis, treatment, monitoring, and challenges in clinical practice. • **Results:** 127 physicians responded, treating a median of 61 RIS patients. MRI was the primary diagnostic tool, with most physicians recommending clinical follow-ups, while 54% considered disease-modifying therapy (DMT) after a single MRI lesion. Key challenges included regulatory uncertainties and patient education. • **Conclusions:** RIS care in the DACH region is heterogeneous, highlighting the need for national guidelines, structured training, and better cross-sector collaboration to optimize care for RIS patients.
24 Sep 2025	Maternal and pregnancy-related factors and associations with multiple sclerosis in offspring: preliminary results from a population-based case-control study	Huiling Xu	• **Introduction:** This study aimed to investigate the association between maternal and pregnancy factors and the development of MS in offspring. • **Methodology:** A Swedish nationwide population-based case-control study identified MS patients from the National Patient Register, linking them with birth data from the Medical Birth Register. Factors analyzed included maternal characteristics and pregnancy-related factors. • **Results:** The study included 2,384 MS cases and 23,840 matched controls. MS mothers were more likely to be older (≥35 years), overweight, have lower education levels, and be born outside the Nordic countries. Pregnancy-related factors showed similar distributions across groups. • **Conclusions:** Maternal age, BMI, education level, and non-Nordic origin were associated with MS in offspring. Further analysis is required to better understand these factors' interactions and their predictive value for MS.

Notable Presentations At ECTRIMS 2025
Epidemiology, Risk & Comorbidities (2/6)

Date	Title	Author	Summary
24 Sep 2025	Maternal and infant pregnancy outcomes in women with MS who received ocrelizumab versus a comparator MS population: results of the Ocrelizumab Pregnancy Registry	Kerstin Hellwig	• **Introduction:** The study assessed maternal, fetal, and infant outcomes in WwMS exposed to OCR in the Ocrelizumab Pregnancy Registry (WA4063). • **Methodology:** The study enrolled WwMS receiving OCR during pregnancy or <6 months before the last menstrual period (LMP). Outcomes included major congenital malformations (MCMs), spontaneous abortions, and birth outcomes. Subgroup analysis was conducted for OCR administration >3 months vs <3 months before LMP. • **Results:** The study included 419 pregnancies (OCR, n=19; COM, n=20). The prevalence of MCMs in the OCR group was 6.3%, compared to 4.9% in the COM group, with an adjusted prevalence ratio of 1.26. MCM prevalence was lowest when OCR was administered <3 months before LMP. • **Conclusions:** MCM prevalence in WwMS receiving OCR was similar to that in the COM group (GA or no DMT). The long-term outcomes of children born from OCR-exposed pregnancies will be evaluated in the MAGIORE study.
24 Sep 2025	The impact of childhood trauma on fatigue Preliminary results highlighting emotion dysregulation as mediator in multiple sclerosis	Kadriye Agan	• **Introduction:** This study investigates the association between adverse childhood experiences (ACEs) and fatigue in MS patients, examining whether this relationship is mediated by emotion dysregulation. • **Methodology:** The study included cognitively competent MS patients at Marmara University. ACEs were assessed using the Childhood Trauma Questionnaire (CTQ-28), emotion dysregulation via the DERS-16, and fatigue using the Fatigue Severity Scale. Mediation effects were evaluated using PROCESS Macro v4.2 in SPSS. • **Results:** Nineteen patients participated (71.4% women, mean age 37.45 years). Emotional abuse and neglect were associated with fatigue ($p<0.05$). Emotion dysregulation fully mediated the effect of emotional abuse (total effect = 0.81) and emotional neglect (total effect = 0.6) on fatigue. • **Conclusions:** The study highlights that emotional neglect and abuse are associated with fatigue in MS patients, with emotion dysregulation fully mediating these effects. Interventions targeting emotion regulation may mitigate the impact of ACEs on MS-related fatigue.

Notable Presentations At ECTRIMS 2025
Epidemiology, Risk & Comorbidities (3/6)

Date	Title	Author	Summary
24 Sep 2025	Vascular Risk in Progressive MS: Analysis from the MS-STAT2 Randomised Controlled Trial	Thomas Williams	• **Introduction:** This study investigates the relationship between vascular risk and MS severity in a large clinical trial cohort. The primary analysis focused on cognitive performance and examined whether simvastatin, a vascular risk modifier, can influence this relationship. • **Methodology:** In the MS-STAT2 trial (n=964, secondary progressive MS), participants were randomized to 80mg simvastatin or placebo for 3 years. Vascular risk was quantified using QRISK3 scores and premature vascular risk (PVR) was assessed. The relationship between PVR and cognitive performance (Californian Verbal Learning Test - CVLT-I) was analyzed using mixed-effect models. • **Results:** The mean age was 54 years, with a median EDS score of 6.0. A 10-year higher PVR was linked to a 4.2-point worse baseline CVLT-I score ($p<0.01$). There was a trend toward faster decline in CVLT-I over 3 years with higher PVR ($p=0.087$), but no significant difference between simvastatin and placebo groups ($p=0.405$). Similar results were found for other cognitive and physical outcomes. • **Conclusions:** Premature vascular risk is associated with worse current and future disease severity in MS, but simvastatin treatment did not modulate this relationship over 3 years.
24 Sep 2025	Associations between comorbidities, disease activity and response to ocrelizumab in the CHIMES trial	Anthony Reder	• **Introduction:** This study aims to assess the relationship between modifiable comorbidities and OCR treatment outcomes in Black and Hispanic people with relapsing MS (BpwRMS and HpwRMS) enrolled in the CHIMES trial. • **Methodology: T**he impact of comorbidities (obesity, hypertension, diabetes, hyperlipidemia) on efficacy (relapse rates, MRI disease activity, confirmed disability progression) and safety (adverse events, infusion reactions) was assessed. Odds ratios (ORs) were calculated for these associations. • **Results:** Among 13 BpwRMS and 69 HpwRMS, obesity was common in both groups. No significant differences in relapse rates or MRI outcomes were observed based on comorbidity status. However, participants with diabetes experienced more frequent infusion reactions (OR 4.18, 95% CI 1.01–17.32). Comorbidities did not affect MS disease activity or adverse events. • **Conclusions:** Comorbidities in BpwRMS and HpwRMS receiving OCR did not significantly influence efficacy or safety outcomes, except for an increased risk of infusion reactions in diabetic participants.

Notable Presentations At ECTRIMS 2025
Epidemiology, Risk & Comorbidities (4/6)

Date	Title	Author	Summary
24 Sep 2025	Burden-of-Illness in people with progressive MS: Insights from the MACSiMiSE-BRAIN clinical trial	Eline Van Doninck	• **Introduction:** This study aims to estimate the societal cost and resource use associated with non-active PMS and to support future cost-effectiveness evaluations, including for metformin. • **Methodology:** The MACSiMiSE-BRAIN trial enrolled patients with non-active PMS and Expanded Disability Status Scale (EDSS) scores of 2.0–6.5. Patient-reported questionnaires gathered data on healthcare use, informal care, productivity loss, and health-related quality of life (HRQoL) over 96 weeks. Costs were categorized into direct medical, non-medical, and productivity-related indirect costs, estimated using unit prices and the human capital approach. • **Results:** As of March 2025, 12 patients (56% female) had been enrolled. The median EDSS score was 5.2, and 24% were not on disease-modifying therapies (DMTs). Fatigue and cognitive difficulties were reported by 97% and 54% of patients, respectively. Of participants under 67 years, 42% were employed, with 64% reporting reduced productivity, primarily due to fatigue and mobility issues. Employment status correlated with EDSS score (OR = 0.6, p = 0.01). Ongoing analyses will examine healthcare use, resource consumption, and HRQoL. • **Conclusions:** This study provides valuable insights into the societal burden of non-active PMS, which will inform future health economic evaluations, including for metformin in the MACSiMiSE-BRAIN trial. It also highlights the need for structured economic assessments to guide healthcare policies and reimbursement strategies.
25 Sep 2025	Long-term follow-up study of chronic pain in a cohort of patients with Multiple Sclerosis: preliminary results	x	• **Introduction:** This study reassesses the original cohort to determine the frequency of chronic and neuropathic pain and identify long-term pain predictors in MS patients. • **Methodology:** During routine visits, patients completed questionnaires: DN4, BPI, NPSI, BDI, MFIS, and BAI. • **Results:** So far, 183 patients have been reassessed (131 females, 52 males; mean age: 52 years). Median disease duration was 19 years. 35% suffer from chronic pain, 21% from neuropathic pain (DN4 ≥ 4). 58% of those with neuropathic pain are on preventive medication. Predictors for both chronic and neuropathic pain include EDS >1.5 (OR: 3.2 and 3.8, respectively). Brainstem involvement (OR: 2.5) had the largest effect on both pain types, and sensory system involvement predicted neuropathic pain (OR: 2.4). • **Conclusions:** EDS, especially brainstem and sensory system involvement, predict long-term chronic and neuropathic pain in MS patients. More patients are now on preventive medication compared to 2015.

Notable Presentations At ECTRIMS 2025 Epidemiology, Risk & Comorbidities (5/6)

Date	Title	Author	Summary
25 Sep 2025	The effect of high dose simvastatin treatment in progressive MS: impact on vascular perfusion and oxidative damage. The MS-OPT Trial.	Alessia Bianchi	• **Introduction:** To explore mechanisms of high-dose simvastatin in pwPMS using brain and retinal imaging and biomarkers for oxidative and vascular damage. • **Methodology:** The MS-OPT trial enrolled 40 pwPMS (18–70 years) receiving simvastatin or placebo for 16 weeks. Imaging methods included optical coherence tomography (OCT), adaptive optics scanning laser ophthalmoscopy (AOSLO), and MRI. Serum biomarkers for oxidative stress were also measured. • **Results:** Among 40 patients (mean age 54.1), simvastatin did not significantly affect brain/retinal imaging measures, disability scores, or most serum biomarkers. However, simvastatin reduced serum oxidative stress markers (8-OHG/8-OHdG) by 24.4% compared to a 26.7% increase in the placebo group (effect size=3.6, p=0.014). Retinal blood velocity was significantly reduced in the simvastatin group (−13.4% vs. +5.4%, effect size=3.31, p=0.040). • **Conclusions:** Simvastatin did not show significant effects on MS biomarkers except for oxidative stress and retinal blood velocity. These findings suggest that simvastatin might have some benefit in reducing oxidative stress but did not impact overall disease progression or imaging biomarkers in pwPMS.
All days	Fine Motor Impairment in Early-Phase Multiple Sclerosis Without Disability: A Comparison with Matched Healthy Controls	Turhan Kahraman	• **Introduction:** This study aimed to assess upper limb function in early-phase MS patients (≤2 years from diagnosis) with no disability (EDS = 0) compared to age- and sex-matched healthy controls (HC). • **Methodology:** A cross-sectional study was conducted with 50 MS patients and 50 HC. Upper limb function was evaluated using the Nine-Hole Peg Test (9HPT) for both hands and handgrip strength using a Jamar dynamometer. Group differences were assessed using the Mann-Whitney U test with rank-biserial correlation. • **Results:** MS patients showed significantly slower performance on the dominant-hand 9HPT (8% slower than HC, p = 0.019, rank-biserial correlation = 0.2736). No significant differences were observed for the non-dominant hand 9HPT, total 9HPT time, or grip strength measurements (p > 0.05). • **Conclusions:** Even without measurable disability, early-phase MS patients exhibit subtle fine motor impairments in the dominant hand. This highlights the need for sensitive functional assessments in early MS, as upper limb dysfunction may develop before overt disability.

Notable Presentations At ECTRIMS 2025
Epidemiology, Risk & Comorbidities (6/6)

Date	Title	Author	Summary
All days	Assessment of General Health, Sleep Health and Polysomnographic Parameters in Naive MS; Preliminary results of the study	Furkan Saridas	• **Introduction:** This study aimed to examine the relationship between sleep quality, overnight polysomnography (PSG) findings, and overall quality of life in naïve MS patients. • **Methodology:** PSG was performed in 18 consecutive naïve patients with newly diagnosed MS in this prospective study. The Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ES), and Short Form (36) Health Questionnaire (SF-36) were applied to the patients. • **Results:** The mean age was 36.6 ± 10.9 years with an EDS of 1.35 (0–5) in the 18 patients (1 woman, 7 men). SF-36 scores were lower in women than in men. In MS patients, vitality and role emotional scores were significantly lower in women (p=0.015, 0.020). The mean global PSQI score was 6.1 ± 4.07, with half of the patients having a poor score (>5). No significant association was found between poor scores and sleep stages, sleep efficiency, or sleep latency. Patients with poor sleep quality had lower vitality and general health in SF-36 subparameters (p=0.013, 0.042). According to ES, 16 patients had normal daytime sleepiness, while 2 had mild sleepiness. No relationship was found between ES and PSG parameters. • **Conclusions:** In naïve MS patients, QoL is lower in women. There was no significant relationship between sleep quality and PSG parameters, possibly due to the small sample size. However, good sleep quality seems to be associated with increased energy and emotional well-being.

Notable Presentations At ECTRIMS 2025
Diagnostics & Biomarkers (1/5)

Date	Title	Author	Summary
24 Sep 2025	Kappa free light chains and oligoclonal bands in the diagnosis of Multiple Sclerosis: preliminary results of the PRO-KFLC study (a study on behalf of the German Society for Cerebrospinal Fluid Diagnostics and Clinical Neurochemistry (DGLN))	Franz Felix Konen	• **Introduction:** McDonald 2024 revision proposes κ free light chains (KFLC) alongside oligoclonal bands (OCB) for early MS diagnosis. KFLC may complement OCB by detecting intrathecal humoral inflammation in OCB-negative patients. • **Methodology:** PRO-KFLC is a prospective, multicenter study coordinated by DGLN. Paired CSF/serum from MS or CIS patients analyzed across 14 centers using nephelometry/turbidimetry for KFLC, and isoelectric focusing plus immunoblotting/electrophoresis for OCB. • **Results:** 535 samples analyzed; female-to-male ratio 2.7, median age 35. CIS n=45. KFLC index <6.1 in 8.2% (n=4). OCB absent in 10.5% (n=56); notably, 8 OCB-negative patients showed KFLC synthesis, highlighting complementary diagnostic utility. • **Conclusions:** KFLC complements OCB in detecting intrathecal inflammation, improving sensitivity of MS/CIS diagnostic work-up. Ongoing analyses will refine diagnostic performance, supporting integration of KFLC into 2024 McDonald criteria.
24 Sep 2025	Serum zonulin levels in newly diagnosed multiple sclerosis patients: associations with disease phenotype and activity. Results from the PROMISING study	Caterina Ferri	• **Introduction:** Intestinal barrier dysfunction is linked to MS. Zonulin, a biomarker of permeability, has shown inconsistent associations with MS activity. This study explored zonulin levels in newly diagnosed, treatment-naïve patients. • **Methodology:** Cross-sectional analysis of 78 MS patients (63 relapsing, 15 progressive) from University Hospital Ferrara (2020–2024). Serum zonulin, EDSS, recent relapses, and MRI activity assessed. Non-parametric tests evaluated associations. • **Results:** Zonulin higher in relapsing vs progressive MS (5.8 vs 2.96 ng/mL, p=0.031), but lost significance after age/EDSS adjustment. Trends toward higher levels with MRI activity and relapses were nonsignificant. Zonulin inversely correlated with EDSS (ρ=−0.307, p=0.06). • **Conclusions:** Zonulin may reflect disease presentation, being higher in relapsing MS and inversely linked with disability. Findings warrant longitudinal studies to clarify predictive and clinical relevance.

Notable Presentations At ECTRIMS 2025
Diagnostics & Biomarkers (2/5)

Date	Title	Author	Summary
24 Sep 2025	Longitudinal dynamics of sNFL and sGFAP in NMOSD patients: real-world results of a 3 to 10 years follow-up	Sala Arianna	• **Introduction:** NMOSD lacks reliable biomarkers. NFL reflects neuronal injury, GFAP astrocytic damage. Longitudinal biomarker monitoring could enhance disease tracking and therapeutic evaluation, especially in AQP4+ vs AQP4– subsets. • **Methodology:** Fifteen NMOSD patients (7 AQP4+, 8 AQP4–) contributed ~7 timepoints each (range 4–11). NFL and GFAP were measured using Quanterix Simoa assays. Treatments included rituximab (n=12) and tocilizumab (n=3). • **Results:** AQP4+ patients had consistently higher NFL (~40% increment), reaching significance at 36 (p=0.062) and 48 months (p=0.035). GFAP elevated 47% at baseline. NFL/GFAP levels paralleled clinical and radiological stability. Rituximab/tocilizumab lowered NFL within 6 months. • **Conclusions:** OrNFL and GFAP show clinical relevance in NMOSD longitudinal monitoring, differentiating AQP4 status and reflecting treatment efficacy. Larger cohorts are needed to validate biomarkers and define standardized cut-offs.
24 Sep 2025	Single silent lesions matter: a comprehensive assessment of the prognostic impact of clinically silent MRI lesions in RRMS, and an emulated trial of treatment escalation	Cyrus Daruwalla	• **Introduction:** To evaluate MRI-confirmed relapses (RAM) as a novel endpoint in MS trials, differentiating them from ACES to improve relapse assessment and treatment evaluation. • **Methodology:** A meta-analysis of 10 RCTs was conducted using data from the French MS registry. A logistic model was developed to predict RAM vs. ACES, with comparisons of treatment effects and statistical power. • **Results:** Using RAM as the endpoint resulted in larger treatment effects and a reduction in sample size by ~37%. ACES showed no significant difference across treatment arms. • **Conclusions:** MRI-confirmed relapses (RAM) offer a more accurate MS trial endpoint, improving treatment effect estimation and reducing sample size requirements by excluding ACES, which are not targeted by current DMTs.

Notable Presentations At ECTRIMS 2025
Diagnostics & Biomarkers (3/5)

Date	Title	Author	Summary
24 Sep 2025	Assessing dissemination in space for multiple sclerosis diagnosis: an analysis of the clinically isolated syndrome trials	Agustín Pappolla	• **Introduction:** MS diagnostic criteria continue to evolve; DIS remains central, while DIT is no longer required. Understanding how DIT occurs post-CIS may clarify prognostic markers. • **Methodology:** Harmonized data from six CIS RCTs (n=3,079). Baseline MRI assessed for DIS and lesion count/topography. DIT defined as new/enhancing T2 lesions or relapses. Kaplan-Meier and Cox models estimated DIT risk over 5 years. • **Results:** At baseline, DIS in 77%, DIT in 17%. Five-year DIT probability was 89.9%. Baseline DIS predicted higher DIT risk (HR 2.40; 95%CI 1.31–4.39). Increasing lesion topographies improved specificity (up to 97%) and PPV. • **Conclusions:** Most CIS patients fulfill DIT within 5 years. Baseline DIS robustly predicts DIT, supporting early MS diagnosis without awaiting DIT when typical features are present.
25 Sep 2025	Prodromal Phase or Diagnostic Delay? A population-based retrospective cohort study of People with Multiple Sclerosis in Italy, 2015-2021.	Giuseppina Affinito	• **Introduction:** The existence of a prodromal phase in MS is debated. While administrative datasets suggest early pre-onset changes, clinical data have not confirmed this, raising the possibility that observed prodromal patterns reflect diagnostic delays. • **Methodology:** A retrospective population-based study (Campania, Italy, 2015–2021) analyzed 3,696 incident MS cases. Administrative cohorts assessed outpatient service use pre-diagnosis. A subset (n=382) with linked clinical data defined three phases: pre-onset (POP), onset-to-clinical diagnosis (OCP), and clinical-to-administrative diagnosis (CAP). Negative binomial regression adjusted for demographics and follow-up. • **Results:** Outpatient services peaked in the year before administrative diagnosis, then declined progressively (−13.6% at year 2; −43.6% at year 6, p<0.01). In the clinical subset, service utilization rose by 21% in OCP (Coef 1.21, CI 0.96–1.47) and 47% in CAP (Coef 1.47, CI 1.16–1.80) compared to POP. • **Conclusions:** Findings suggest higher healthcare use between clinical and administrative recognition, supporting delayed identification rather than a true prodromal phase. This distinction is critical for interpreting population-based MS studies.

Notable Presentations At ECTRIMS 2025
Diagnostics & Biomarkers (4/5)

Date	Title	Author	Summary
25 Sep 2025	Update on the assessment of long-term safety and tolerability of vidofludimus calcium in patients with relapsing-remitting multiple sclerosis up to 5.5 years: the open-label extension period of the phase 2 trial (EMPhASIS) study.	Robert J. Fox	• **Introduction:** Vidofludimus calcium (VidoCa), an oral DHODH inhibitor and Nur1 agonist, showed strong efficacy and placebo-like safety in the EMPhASIS phase 2 RMS trial. The OLE extends long-term safety data. • **Methodology:** After 24 weeks double-blind (N=268), 254 (95%) entered open-label extension with 30/45 mg daily. Data cut-off: Jan 14, 2025. Descriptive safety/tolerability analyses were conducted. • **Results:** By cut-off, 182 (71.6%) remained on treatment; 134 ≥264 weeks (~5 years), totaling 952 patient-years. Discontinuation: 6.4% annually. Frequent TEAEs: COVID-19 (9.4%), nasopharyngitis (5.9%), back pain (5.1%), headache (4.7%). Renal/hepatic TEAEs: 3.5% and 3.1% yearly. Five discontinuations (DVT, Gilbert's, 2 breast cancers, melanoma). Sixteen SAEs (0.02/patient-year), none drug-related. No hematology or new safety signals. • **Conclusions:** VidoCa demonstrated durable safety/tolerability up to 5.5 years with low discontinuation and SAE rates, supporting long-term therapeutic potential in RMS.
All days	Longitudinal atrophy measures in MS differ between scanners: implications for trials and clinical implementation	David Van Nederpelt	• **Introduction:** To evaluate the reproducibility of volumetric changes between MRI scanners in people with MS (pwMS) and healthy controls (HCs). • **Methodology:** 28 pwMS and 10 HCs underwent scans and rescans on three MRI scanners (GE Discovery MR750 [3T], Siemens SOLA [1.5T], Siemens VIDA [3T]). Longitudinal FreeSurfer processing computed Δvolume for various brain regions, with repeated-measures ANOVA assessing between-scanner differences and ICC evaluating within- and between-scanner reproducibility. • **Results:** Annual brain Δvolume in MS: -0.48% (GE), -0.73% (SOLA), -0.75% (VIDA). HC: -0.28%, -0.21%, -0.57%. VIDA showed greater Δvolume vs GE ($p<0.01$) for whole brain, GM, and DGM. SOLA had higher LaV Δvolume (2.4% vs 1.7%, $p<0.001$). Within-scanner ICCs: GE=0.72, SOLA=0.75, VIDA=0.76. Between-scanner ICCs ranged from poor to excellent, with lower agreement between GE and Siemens scanners. • **Conclusions:** FreeSurfer's longitudinal volume measurements are consistent within scanners but vary between them, potentially obscuring biological changes. Standardized harmonization is essential for reliable multi-center MS studies.

Notable Presentations At ECTRIMS 2025
Diagnostics & Biomarkers (5/5)

Date	Title	Author	Summary
All days	A blood-based biomarker measuring degradation of biglycan is upregulated in patients with multiple sclerosis compared to healthy donors: Results from the VACCINE and EXIT studies	Anna San Torcuato	• **Introduction:** This study aims to evaluate BGM levels in MS patients and determine if it correlates with disease severity, as measured by the Expanded Disability Status Scale (EDS). • **Methodology:** BGM levels were quantified in serum samples from relapsing MS patients (EXIT20, n=184; VACINE, n=58) and matched healthy donors. Statistical comparisons were made using Welch's t-test, and correlation with EDS was assessed. • **Results:** BGM levels were significantly higher in MS patients compared to healthy controls (EXIT20: $p < 0.001$; VACINE: $p < 0.001$). Mean BGM levels were 10.4 ng/mL and 7.7 ng/mL, respectively. No significant correlation with EDS was found. • **Conclusions:** BGM is elevated in MS patients and could serve as a potential biomarker for disease monitoring and treatment response. However, no correlation with disease severity (EDS) was observed.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (1/15)

Date	Title	Author	Summary
24 Sep 2025	Tolebrutinib Plasma Exposure and Efficacy Response in the Phase 3 HERCULES Trial in nrSPMS	Olivier Nicolas	• **Introduction:** This study aims to assess the association between tolebrutinib and its M2 active metabolite plasma exposure and their effect on disability accumulation in HERCULES. • **Methodology:** Blood samples from HERCULES at Months 6, 9, and 12 were analyzed for tolebrutinib and M2 plasma concentrations using liquid chromatography-mass spectrometry. A population pharmacokinetic (PK) approach assessed PK exposures and the influence of intrinsic and extrinsic factors. The relationship between AUC of tolebrutinib, M2, and combined tolebrutinib/M2 and the primary endpoint of time to 6-month confirmed disability progression was examined using a three-compartment model for tolebrutinib and one-compartment model for M2. • **Results:** Higher exposures of tolebrutinib, M2, and the combined drug were associated with greater effects on disability accumulation in participants with nrSPMS. • **Conclusions:** These findings suggest that higher drug exposures are linked to greater effects in slowing disability accumulation.
24 Sep 2025	Safety and Tolerability of BMS-986353, a CD19-Directed Chimeric Antigen Receptor T Cell Therapy in Relapsing or Progressive Forms of MS: A Phase 1, Single-Arm, Dose-Escalation Study (Breakfree-2)	Refik Pul	• **Introduction:** To evaluate the association between tolebrutinib and its M2 active metabolite plasma exposures and their effect on disability accumulation in HERCULES. • **Methodology:** Blood samples from HERCULES were analyzed for tolebrutinib and M2 plasma concentrations at Months 6, 9, and 12 using liquid chromatography-mass spectrometry. A population pharmacokinetic approach assessed PK exposures and intrinsic/extrinsic factors. The relationship between AUC for tolebrutinib, M2, and combined tolebrutinib/M2 and disability progression was examined. • **Results:** Higher exposures of tolebrutinib, M2, and their combination were linked to a greater effect in slowing disability accumulation in nrSPMS participants. • **Conclusions:** Higher exposures of tolebrutinib and M2 were associated with greater effects in reducing disability accumulation.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (2/15)

Date	Title	Author	Summary
24 Sep 2025	Long-Term Safety of Ponesimod in Relapsing Multiple Sclerosis: Final Results of over 7 Years Exposure to Ponesimod in OPTIMUM Open-Label Extension Trial	Ludwig Kappos	• **Introduction:** To report long-term safety data (up to 7.9 years) from the completed Phase 3 OLE study (data cut-off: 16 January 2024). • **Methodology:** After completing the core study and a washout period, patients received ponesimod 20 mg in the OLE study. Safety outcomes were analyzed across the core and OLE periods, and separately for the OLE period. • **Results:** In the combined analysis period (n=565 for ponesimod), 96.1% of patients reported at least one adverse event (AE). Common treatment-emergent AEs (TEAEs) included nasopharyngitis (26.5%), increased ALT (25.7%), COVID-19 (20.5%), headache (19.1%), and hypertension (13.6%). 16.6% experienced serious AEs (SAEs), with 14.9% discontinuing due to TEAEs. Three cases of opportunistic infections were reported (0.3%), but no cases of progressive multifocal leukoencephalopathy (PML). • **Conclusions:** The safety profile of ponesimod in the OLE study was consistent with the core study, showing no unexpected findings after up to 7 years of treatment. Long-term ponesimod exposure did not increase the incidence of SAEs.
24 Sep 2025	Blood Immunoglobulin Levels and Immune Cell Populations in the Phase 3 HERCULES Trial of Tolebrutinib in Non-Relapsing Secondary Progressive Multiple Sclerosis	Amit Bar-Or	• **Introduction:** To assess changes in blood immune cell populations, immunoglobulin levels, and platelet counts in the HERCULES trial. • **Methodology:** Blood samples were collected at baseline and during the treatment period (median 3 months). Immunoglobulin (IgG, IgM) levels were measured by immunoturbidimetry, and blood counts including leukocytes, lymphocytes, neutrophils, monocytes, and platelets were analyzed. • **Results:** Over 42 months, mean leukocyte, total lymphocyte, neutrophil, and monocyte counts remained stable within normal ranges in both treatment groups. IgG levels remained stable, while IgM levels stayed above the lower limit of normal (0.4 g/L) in both groups. Platelet counts remained within the normal range (140–400 x 10^9/L). • **Conclusions:** Immune cell counts, immunoglobulin levels, and platelet counts remained stable in participants treated with tolebrutinib, supporting its safety profile as an immunomodulatory agent that does not deplete circulating leukocytes, immunoglobulins, or platelets.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (3/15)

Date	Title	Author	Summary
24 Sep 2025	Ublituximab exerts a rapid B and T Cell depletion in Multiple Sclerosis Patients: preliminary results	Doriana Landi	• **Introduction:** To evaluate the changes in blood immune cell populations, immunoglobulin levels, and platelet counts in the HERCULES trial. • **Methodology:** Blood samples were collected at baseline and during the treatment period (median 3 months). Immunoglobulin (IgG, IgM) levels were measured by immunoturbidimetry, and blood counts including leukocytes, lymphocytes, neutrophils, monocytes, and platelets were analyzed. • **Results:** Over 42 months, mean leukocyte, lymphocyte, neutrophil, and monocyte counts remained stable within normal ranges in both tolebrutinib and placebo groups. IgG levels remained stable, while IgM levels stayed above the lower limit of normal (0.4 g/L) in both groups. Platelet counts remained within the normal range (140–400 x 10^9/L). • **Conclusions:** Immune cell counts, immunoglobulin levels, and platelet counts remained stable in participants treated with tolebrutinib, supporting its safety profile as an immunomodulatory agent that does not deplete circulating leukocytes, immunoglobulins, or platelets.
24 Sep 2025	Long Term Extension of Ponesimod Phase III Study in Relapsing Multiple Sclerosis: Final Efficacy Results of over 7 years Treatment with Ponesimod	Xavier Montalban	• **Introduction:** This study reports the final efficacy results of up to 7.9 years of treatment with ponesimod 20 mg from the OLE study. • **Methodology:** Patients from the core study (ponesimod 20 mg or teriflunomide 14 mg) transitioned to ponesimod 20 mg in the OLE study. Clinical outcomes were evaluated across both the core and OLE periods. • **Results:** Of 565 patients from the core study, 87 entered the OLE. The average annualized relapse rate (AR) in the OLE period was 0.16 in the ponesimod group and 0.147 in the teriflunomide group. By week 384 (7 years), 56.7% of ponesimod patients remained relapse-free. The 24-week confirmed disability accumulation (CDA) rate at week 384 was 21.3%, showing over 78% of patients were CDA-free. • **Conclusions:** These final data from the Phase 3 OLE study demonstrate the long-term efficacy of ponesimod, with sustained relapse reduction and minimal disability progression over up to 7.9 years, supporting its viability as a long-term treatment for relapsing MS.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (4/15)

Date	Title	Author	Summary
24 Sep 2025	Long-Term Brain Atrophy in Female and Male Patients with Relapsing Multiple Sclerosis in the SUNBEAM, RADIANCE, and DAYBREAK Trials of Ozanimod	Jeffrey Cohen	• **Introduction:** To evaluate the relationship between tolebrutinib and its active metabolite (M2) plasma exposure and their effect on disability accumulation in HERCULES. • **Methodology:** Blood samples collected from HERCULES participants at Months 6, 9, and 12 were analyzed to measure tolebrutinib and M2 concentrations. Population pharmacokinetic models assessed the impact of drug exposure on disability progression, using AUC for tolebrutinib and M2. • **Results:** Higher exposure to tolebrutinib and M2 was associated with a greater effect on disability accumulation in participants with nrSPMS. • **Conclusions:** These findings suggest that higher plasma exposure to tolebrutinib and M2 is associated with greater effects in slowing disability accumulation.
24 Sep 2025	Tolebrutinib treatment induces complex alterations of the peripheral immune-regulatory network in the blood of patients with non-relapsing secondary progressive MS – results from the TOLEDYNAMIC study	Luisa Klotz	• **Introduction:** This study aimed to explore the effects of Tolebrutinib on the peripheral immune system by evaluating immune cell subsets at randomization, month 3, and month 12 using spectral cytometry. • **Methodology:** Peripheral blood mononuclear cells (PBMCs) from patients in Europe were analyzed using five antibody panels on a Cytek Aurora spectral cytometer. Data from 30 patients at randomization, 1 at M3, and 31 at M12 were analyzed for treatment effects. • **Results:** Tolebrutinib influenced immune cells, notably reducing inflammatory monocyte subsets. While B and T cell populations remained stable, differentiation patterns in both B cells and CD4 T helper subsets, particularly T follicular helper cells, were altered. • **Conclusions:** BTK inhibition with Tolebrutinib induces shifts in immune cell differentiation, which may contribute to its efficacy in delaying disease progression in non-relapsing SPMS.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (5/15)

Date	Title	Author	Summary
24 Sep 2025	Eight-Point Change in Symbol Digit Modalities Test Scores: Findings From the Phase 3 SUNBEAM and DAYBREAK Ozanimod Trials Stratified by Sex	Ludwig Kappos	• **Introduction:** Evaluate the effects of 6–8 years of OZA treatment on CPS, using the 8-point SDMT score change, in RMS patients stratified by sex. • **Methodology:** In the SUNBEAM trial (NCT0294058), adults with RMS were randomized to receive oral OZA 0.46 or 0.92 mg/day or intramuscular IFN 30 µg/week for ≥12 months. Completers were eligible for the OZA 0.92 mg open-label extension (OLE) trial (DAYBREAK, NCT02576717). Post hoc analysis of SDMT score changes was conducted. • **Results:** In the OLE, 250 female and 147 male patients received OZA 0.92 mg, while 259 female and 136 male patients received IFN. At baseline, mean SDMT scores for female patients were 49.2 (OZA) vs 48.0 (IFN), and for male patients, 46.1 (OZA) vs 46.4 (IFN). A significantly larger proportion of females on OZA achieved an 8-point improvement compared to IFN (15.6% vs 8.1%, OR: 2.2 [1.2–3.9], P<0.01). A similar trend was seen in males (17.0% vs 1.0%, OR: 1.5 [0.7–3.0], P=0.26). After 6–8 years, continuous OZA-treated patients showed more improvement and less worsening compared to those initially on IFN. This pattern was observed in both sexes, though the differences were not statistically significant. • **Conclusions:** These results align with previous studies indicating that male patients with RMS have slightly worse CPS than female patients, and suggest that OZA treatment may lead to improved CPS in both sexes over long-term treatment.
24 Sep 2025	INFORM-MS: Study design of a Phase 2a double blind placebo-controlled trial of nasal foralumab in non-active secondary progressive multiple sclerosis	Tanuja Chitnis	• **Introduction:** The study's primary objectives are to assess the safety and tolerability of 50 µg/dose and 100 µg/dose nasal foralumab versus placebo, and to evaluate its effect on microglial activation as measured by [18F]PBR06-PET scans after 12 weeks. • **Methodology:** This double-blind, placebo-controlled study examines 50 µg and 100 µg doses of nasal foralumab over three months in 54 subjects with na-SPMS. The primary outcome is the change in microglial activation measured by TSPO PET, with secondary outcomes including EDSS, MSFC-4, and MFIS. Statistical analyses will use T-distribution for means and Clopper-Pearson intervals for response data. • **Results:** As of March 31, 2025, 17 subjects have been enrolled, 9 randomized, and 7 completed the core phase. Baseline characteristics will be presented by September 2025. • **Conclusions:** This phase 2a trial investigates nasal foralumab in na-SPMS, with TSPO-PET scans as the primary outcome.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (6/15)

Date	Title	Author	Summary
24 Sep 2025	48-month follow-up of Maven4: a Phase IV non-interventional, prospective, Spanish multicenter study to assess the long term effectiveness of Cladribine tablets in real-world clinical practice	Yolanda Aladro-Benito	• **Introduction:** This publication reports the Maven4 interim analysis, evaluating the effectiveness and safety of cladribine tablets after four years of follow-up. • **Methodology:** Maven4 is a non-interventional, prospective cohort study of patients with relapsing MS initiated on cladribine tablets in routine clinical practice, assessing effectiveness and safety with up to 7 years of follow-up. This report includes baseline demographic and clinical characteristics, previous disease-modifying therapies (DMTs), 48-month treatment data, and subgroup analysis based on prior DMT use. • **Results:** From June 2019 to February 2020, 450 patients were recruited. Baseline data showed 76.8% were female, with a mean age of 39.2 years and disease duration of 7.1 years. The mean number of relapses in the previous two years was 1.2, with 28.1% having active gadolinium lesions and 80.2% having ≥9 T2 lesions. Of 36 patients (83%) remaining on therapy at 48 months, 204 patients had a 68.7% reduction in the annualized relapse rate (AR), with a mean AR of 0.07. AR reduction was highest in treatment-naïve patients (87.3%). • **Conclusions:** Maven4 interim analysis supports the pivotal trials (CLARITY and CLARITY EXT) on the efficacy and safety of cladribine tablets. Early use may lead to better clinical outcomes
25 Sep 2025	Real-World Use of Inebilizumab in Neuromyelitis Optica Spectrum Disorder: Results of the German NEMOS Cohort	Katinka Fischer	• **Introduction:** Study aims to evaluate the efficacy and safety of INE in the real-world setting using the NEMOS registry. • **Methodology:** This retrospective multicenter analysis assessed INE outcomes in AQP4-IgG-positive NMOSD patients, evaluating clinical efficacy (EDSS, AR, MRI stability), laboratory parameters (immunoglobulin levels, leukocyte/lymphocyte counts), and patient-reported infections (frequency/severity) versus pre-treatment, including rituximab (RTX). • **Results:** Of 23 enrolled patients (87% female, mean age 49.3 years, median AR 0.5), 36% had received RTX prior to INE. Clinical stabilization was seen under INE, with AR reduced from 0.5 to 0 (p=0.01). 95.7% remained relapse-free. Infection risk did not increase with INE compared to pre-treatment (R=0.747, p=0.160) or RTX (R=0.89, p=0.657). Treatment-naïve patients reported more recurrent infections, though without statistical significance. Seven patients had reduced immunoglobulin levels, but no association with infection susceptibility was found (OR: 0.732; 95% CI: 0.012–1.593). • **Conclusions:** This real-world study confirms INE's high efficacy in relapse prevention for AQP4-IgG+ NMOSD, with infection risks comparable to RTX.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (7/15)

Date	Title	Author	Summary
25 Sep 2025	Rationale and design of a phase III randomised, double-blind, placebo-controlled, multicentre study evaluating the efficacy and safety of treatment with corticoSTeroids at onset, And Rituximab at relapse, of MOG-antibody-associated disease (STAR-MOG)	Isabella Cotter	• **Introduction:** This study evaluates the safety and tolerability of two doses (50 µg and 100 µg) of foralumab nasal spray compared to placebo and its impact on microglial activation using [18F]PBR06-PET scans after 12 weeks of treatment. • **Methodology:** This randomized, double-blind, placebo-controlled phase 2a trial involves 54 participants, randomly assigned to 50 µg foralumab, 100 µg foralumab, or placebo. The primary endpoint is the change in microglial activation as assessed by TSPO-PET. Secondary outcomes include safety, clinical measures (EDSS, MSFC-4, MFIS), and exploratory analysis of biomarkers. Participants will be randomized in a 1:1:1 ratio for a three-month treatment period. • **Results:** As of March 31, 2025, 17 subjects have been enrolled, with 9 randomized and 7 having completed the core phase of the study. Baseline characteristics will be presented by September 2025, with enrollment anticipated to continue for 3.5 years. • **Conclusions:** The INFORM-MS trial aims to provide critical evidence on the efficacy and safety of foralumab in na-SPMS. This study, incorporating TSPO-PET scans, may significantly contribute to therapeutic decision-making and guideline development in MOGAD treatment.
25 Sep 2025	Effects of Tolebrutinib on Progression Independent of Relapse Activity in the Phase 3 GEMINI Relapsing MS Trials	Jiwon Oh	• **Introduction:** This study aims to assess the effects of tolebrutinib versus teriflunomide on PIRA in the GEMINI relapsing MS trials. • **Methodology:** GEMINI 1 and 2 were phase 3, double-blind, event-driven trials involving relapsing MS patients with an EDSS score ≤5.5. Participants were randomized 1:1 to receive either 60 mg daily of tolebrutinib or 14 mg of teriflunomide. Primary endpoints were annualized relapse rate (AR), and secondary endpoints included time to confirmed disability worsening (CDW) and PIRA, defined as CDW without preceding relapse. • **Results:** 1873 participants (67% female, 64% treatment-naïve) were enrolled. The 6-month CDW rate was lower in the tolebrutinib group (8.3%) versus teriflunomide (13%) (hazard ratio [HR], 0.71; 95% CI, 0.53–0.95). PIRA was less frequent with tolebrutinib (6.4%) than teriflunomide (8.5%), representing a 27% reduction in risk. • **Conclusions:** Tolebrutinib reduced PIRA events compared to teriflunomide in relapsing MS patients, supporting its efficacy in targeting disability progression independent of relapse activity.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (8/15)

Date	Title	Author	Summary
25 Sep 2025	Subgroup Analyses of the Phase 3 Tolebrutinib in nrSPMS HERCULES Trial	Robert J. Fox	• **Introduction:** To evaluate the effects of tolebrutinib versus placebo on 6-month CDP in subgroups from the HERCULES trial. • **Methodology:** Pre-specified subgroups included age (>40, ≤40), sex, region, EDSS score (≤4.5, >4.5), disease duration, gadolinium-enhancing T1 lesions, and relapse status. The annualized adjudicated relapse rate, a tertiary endpoint, was also reported. • **Results:** Tolebrutinib showed consistent effects across all subgroups, with differences in effect size observed. The annualized adjudicated relapse rate was low in both groups: 0.03 for tolebrutinib and 0.032 for placebo. • **Conclusions:** Tolebrutinib demonstrated consistent efficacy in reducing disability progression across all subgroups.
25 Sep 2025	Blood Immunoglobulin Levels and Immune Cell Populations in the Phase 3 GEMINI Trials of Tolebrutinib in Relapsing Multiple Sclerosis	Heinz Wiendl	• **Introduction:** To evaluate changes in immune cell populations, immunoglobulin levels, and platelet counts in the GEMINI trials. • **Methodology:** Blood samples were collected at baseline and during the double-blind treatment period, with a median study duration of 35 months. Samples were analyzed for immunoglobulin (IgG, IgM) levels via immunoturbidimetry and complete blood counts, including leukocytes, lymphocytes, neutrophils, monocytes, and platelets. • **Results:** Over 42 months, mean leukocyte, lymphocyte, neutrophil, and monocyte counts remained stable and within normal ranges for both tolebrutinib and teriflunomide groups. IgG levels remained stable, and IgM levels were above the normal lower limit (0.4 g/L). Platelet counts remained within the normal range (140–40 x 10^9/L). • **Conclusions:** Immune cell counts, immunoglobulin levels, and platelet counts remained normal in tolebrutinib-treated participants. These findings support tolebrutinib's safety profile as an immunomodulatory agent that does not deplete circulating leukocytes, immunoglobulins, or platelets.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (9/15)

Date	Title	Author	Summary
25 Sep 2025	Effects of Tolebrutinib on MSQoL-54 in the HERCULES Phase 3 trial in nrSPMS	Patrick Vermersch	• **Introduction:** To assess the effect of tolebrutinib vs. placebo on health-related quality of life (HRQoL), measured by the Multiple Sclerosis Quality of Life-54 (MSQoL-54) questionnaire in nrSPMS. • **Methodology:** MSQoL-54 was assessed at baseline and every 6 months until the end-of-study (EOS) visit (18–43 months). The MSQoL-54 includes 12 subscale scores and 2 single-item measures, from which Physical and Mental Health Composite (HC) scores are derived. Change from baseline to EOS was analyzed using a mixed model with repeated measures. Between-group least-squares mean differences (LSMD) were estimated at EOS for composite scores and post-hoc at Months 12 and 24, averaged across visits. • **Results:** At baseline, the intent-to-treat population (N=131) had mean Physical HC of 46.4 (15.5) and Mental HC of 59.3 (18.9). The most impacted subscales at baseline were role limitation-physical, physical function, and change in health (mean scores: 26.3, 29.3, and 31.5). At Month 12, no significant differences were observed. However, at Month 24, tolebrutinib favored Physical HC (LSMD [95% CI]: 3.10 [1.27–4.94]; p=0.009), Mental HC (LSMD [95% CI]: 4.14 [1.8–6.39]; p=0.003), and 6/14 domains (physical function, role limitation-physical, role limitation-emotional, emotional well-being, social function, overall QoL). • **Conclusions:** Tolebrutinib may preserve key HRQoL domains in nrSPMS patients over time.
25 Sep 2025	Comparative Effectiveness and Safety of Ofatumumab vs Ocrelizumab in Multiple Sclerosis: A Target-Trial Emulation	Kenshiro Fuse	• **Introduction:** To compare the effectiveness and safety of ocre and ofatumumab in MS pts. • **Methodology:** Using a US claims database, MS patients (18–65) initiating either therapy (2020–2024) were 1:1 propensity-matched. Primary outcome: relapse requiring IV steroids; safety: infections, PML. Follow-up ended at event, discontinuation, or study completion. Risks were estimated with Kaplan-Meier and Cox regression. • **Results:** Of 3,489 patients, 841 per group were matched. Mean age: 42 years. Median follow-up: 258 days (ofatumumab) vs 286 (ocrelizumab). Relapses: 96 vs 126, lower with ofatumumab (HR 0.80, 95% CI 0.61–1.04). In treatment-naive patients, relapse risk favored ofatumumab (HR 0.59, 95% CI 0.39–0.84); in ages 18–40, risk was similar (HR 0.95, 95% CI 0.58–1.56). Safety HRs: serious bacterial infections 1.23, UTIs 0.98, herpes zoster 0.73. No PML reported. • **Conclusions:** Ofatumumab showed efficacy comparable to ocrelizumab, with greater benefit in treatment-naive patients. Safety was similar though estimates were imprecise.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (10/15)

Date	Title	Author	Summary
25 Sep 2025	144-Week Analysis of the Confirmed Disability Worsening Events from the Open-Label Treatment Extension of the Phase 2 EMPhASIS Study of Vidofludimus Calcium in Patients with Relapsing-Remitting Multiple Sclerosis	Andreas Muehler	• **Introduction:** To present the 14-week follow-up data on confirmed disability worsening (CDW) from the OLE phase of the Phase 2 trial in relapsing-remitting MS (RMS). • **Methodology:** Out of 268 RMS patients who started the double-blind treatment, 254 completed the 24-week phase and continued into the OLE period. Initially, patients received 30 or 45 mg VidoCa once daily, later standardized to 30 mg daily. As of January 14, 2025, approximately 953 treatment years were included in this interim analysis. 187 patients (79.5%) were evaluated up to Week 14 and included in this CDW analysis. • **Results:** At Week 14, 92.3% of patients remained free of 12-week CDW, and 92.7% remained free of 24-week CDW. Of the 29 confirmed CDW events by Week 14, 13 (4.8%) were relapse-associated, and 4 (13.8%) were progression independent of relapse activity. • **Conclusions:** In the long-term open-label phase of EMPhASIS, VidoCa-treated patients showed a low rate of confirmed disability worsening, with most events classified as relapse-associated worsening.
25 Sep 2025	Clinical progression in relapse-onset MS patients with B cell tailored dosing versus standard interval dosing ocrelizumab (BLOOMS trial): interim analysis.	Laura Hogenboom	• **Introduction:** To evaluate CDW incidence in PID versus SID of ocrelizumab. • **Methodology:** Data were derived from the ongoing BLOOMS trial. Since 2022, RMS patients treated with ocrelizumab for ≥1 year were randomized 1:1 to SID or PID. In PID, infusions were extended until CD19+ B-cell counts were below 0.01*10^9/L. Interim analysis focused on 6-month CDW by Expanded Disability Status Scale (EDSS) and 25-foot walk test (25FWT) scores. • **Results:** 111 participants (PID n=54, SID n=57) were included in this analysis. Participants had a median age of 41.7 years and 5 infusions before baseline. Nine CDW events occurred: 3 in PID and 5 in SID (one participant had 2). The difference between groups was not statistically significant (p=0.71), nor was the incidence of 6-month CDW on 25FWT (PID n=2, SID n=4, p=0.67). • **Conclusions:** CDW events were rare in both groups, with no significant difference between PID and SID. Final results will be available after all 300 participants complete the 2-year follow-up, expected in 2027.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (11/15)

Date	Title	Author	Summary
25 Sep 2025	Prospective De-Escalation from B-cell Depletion to Fumarates: Interim 1-year results	Enrique Alvarez	• **Introduction:** To evaluate the transition from B-cell depletion to fumarates in MS patients, with 1-year interim results from a 2-year trial. • **Methodology:** MS patients aged >18, transitioning from B-cell depletion to fumarates, will be followed for 2 years. Patients must be stable for 2 years and have EDSS ≤6.5. The primary endpoint is a composite of relapses, new T2/enhancing lesions, and 6-month confirmed disability progression. • **Results:** By July 2024, 10 patients enrolled. One failed screening (EDSS >6.5). Mean age: 50.8 years (SD ±10.4), 80% female, all non-Hispanic white. Half were on ocrelizumab, 40% on rituximab, and 10% on ofatumumab. Eight patients transitioned to diroximel fumarate (DRF), 2 to dimethyl fumarate (DMF). Three discontinued DRF due to tolerability; 2 completed 2 years. No relapses, new lesions, or infections. IgG levels stable at 12 months. • **Conclusions:** De-escalating from B-cell depletion to fumarates appears to maintain efficacy. The ongoing 2-year study will provide further data on efficacy and safety.
25 Sep 2025	Dimethyl fumarate treatment in multiple sclerosis is associated with a decrease in serum glial fibrillary acidic protein. Results from the RIFUND-MS trial	Fadi Shawket	• **Introduction:** To compare rituximab (RTX) and dimethyl fumarate (DMF) on sNfL and sGFAP in a randomized trial. • **Methodology:** RIFUND-MS (NCT0274674), a rater-blinded phase 3 trial, compared RTX and DMF for relapse prevention in largely treatment-naïve RMS patients. Serum was collected at months 0, 6, 12, and 24. sNfL and sGFAP concentrations were measured using SIMOA (Quanterix 2-PLEX). Analyses were performed for intention-to-treat (IT), per protocol (PP), and switch groups. • **Results:** Among 201 randomized patients, 197 were analyzed. In IT, sNfL decreased ~50% with RTX (p=3.1e-10) and 46% with DMF (p=3.6e-10), with no between-arm differences (global p=0.065). In contrast, sGFAP declined 13.5% with DMF (p=3.7e-5) but not RTX (p=0.83), with global p favoring DMF (IT=0.018; PP=0.040). • **Conclusions:** Both RTX and DMF reduced sNfL similarly, but only DMF lowered sGFAP, suggesting potential effects on progression mechanisms independent of inflammatory activity.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (12/15)

Date	Title	Author	Summary
25 Sep 2025	Incidence rate of malignancies in people with multiple sclerosis newly initiating cladribine tablets or fingolimod: Second interim results from CLARION	Anna Glaser	• **Introduction:** To characterize malignancy incidence rates (IR) and incidence rate ratios (IRR) in PwMS starting CladT or fingolimod. • **Methodology:** CLARION uses registry and primary data. Malignancy IR for first events was estimated per 100 patient-years (95% CI), excluding prior malignancies. Subgroup analyses included disease-modifying treatment (DMT) history. • **Results:** By April 2023, 402 PwMS were in the CladT cohort and 3120 in the fingolimod cohort (prior malignancies: n=49, n=17). Mean follow-up: 1.9 ±1.2 years (CladT) vs 2.8 ±1.3 (fingolimod). DMT-naïve: 42.9% vs 41.3%. Malignancies: 26 (CladT, IR 3.17; 95% CI 2.16–4.6) vs 38 (fingolimod, IR 4.41; 95% CI 3.21–6.06). IRR = 0.72 (95% CI 0.4–1.18). Among DMT-naïve: IR 2.95 (CladT, 1/26 cases) vs 4.6 (fingolimod, 15/38). With prior DMT: IR 3.35 (CladT, 15/26) vs 4.26 (fingolimod, 23/38). Follow-up time limits interpretation. • **Conclusions:** This interim analysis found no difference in malignancy IR between CladT and fingolimod. Data are limited by short follow-up and small event numbers. Long-term CLARION results will better guide treatment decisions.
25 Sep 2025	TREATMENT CONTINUATION WITH CLADRIBINE: WHAT CAN WE EXPECT FROM YEAR 5? RESULTS FROM A TERTIARY CARE HOSPITAL.	Alexandra Rincón Valencia	• **Introduction:** To evaluate factors influencing clinical management of RMS patients on cladribine beyond year 4. • **Methodology:** Retrospective analysis of 214 RMS patients, including 92 who began cladribine in 2018–2021 with 5-year follow-up. • **Results:** Among 92 patients (71% female, mean age 38, baseline EDSS 2.7, mean prior DMTs 1.45), 48.9% switched due to poor efficacy. Pre-treatment AR was 0.49. Twenty-four discontinued: 5 stopped, 1 died, 18 switched (due to relapses, neoplasm, lymphopenia, radiological activity, or disability progression). One patient required retreatment in year 4. Of the 68 who continued, 3 had radiological activity in years 1–2, 2 relapsed in years 3–4, and 12 showed disability progression without inflammation. By year 5, 18 were retreated, 15 switched DMT, and 35 remained under surveillance. • **Conclusions:** Structured monitoring during treatment-free years is effective. Retreatment benefits those with poor prognosis or radiological activity. Findings support cladribine's durable efficacy and align with expert recommendations.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (13/15)

Date	Title	Author	Summary
All days	Study Design of Two Phase 1/2 Studies to Assess Safety and Efficacy of YTB323, an Autologous CD19-Directed CAR-T Cell Therapy, in Multiple Sclerosis	Robert Hoepner	• **Introduction:** To assess the safety, efficacy, and cellular kinetics of YTB323 in MS patients. • **Methodology:** These ongoing, open-label, multicenter Phase 1/2 studies use ascending single-dose designs. The RMS study (NCT061793) enrolls ambulatory participants (EDS ≤6.5) aged 18–60 years with RMS duration <15 years and breakthrough disease after ≥6 months on HET. Breakthrough disease includes confirmed clinical relapse or persistent MRI activity. The PMS study (NCT0675864) enrolls patients aged 18–60 years with non-active secondary or primary progressive MS, EDS 3–6.5, disease duration <15 years, no relapse in the previous year, and disease progression ≥0.5 EDS points. Primary endpoint: incidence of adverse events. Secondary endpoints: efficacy (disability, MRI lesions, fatigue) and pharmacokinetics/cellular kinetics of YTB323. • **Results:** Both trials are recruiting. Safety data will be reviewed after each sentinel cohort before dosing the next. Approximately 28 participants will be treated in each trial. Following a 2-year core study, participants will be monitored for an additional 13 years. • **Conclusions:** These studies will provide evidence for the development of YTB323 in MS.
All days	Long-term Efficacy and Safety of Divozilimab in Patients with Relapsing Multiple Sclerosis: Results of BCD-132-EXT Trial	Alexey Boyko	• **Introduction:** To assess the long-term efficacy and safety of DIV in relapsing multiple sclerosis (RMS) patients. • **Methodology:** BCD-132-EXT was an open-label, single-arm trial with 4 RMS patients who completed the phase II MIRANTIBUS trial. Patients received 50 mg DIV intravenous infusions every 24 weeks over 4 years, including a 2-year trial period. Efficacy endpoints included annualized relapse rate (AR), proportion of relapse-free patients, confirmed disability progression (CDP3mo), and MRI parameters (contrast-enhancing T1 lesions and combined unique active lesions). • **Results:** Most patients had no relapses. The relapse-free proportion was 7.3% over 4 years. AR decreased from 0.091 in year 1 to 0.023 in year 4. The proportion of patients with no CDP3mo was 95.5%. At the end of the follow-up, 93.2% had no T1Gd+ lesions, with an adjusted T1Gd+ number per scan of 0.01. Adjusted CUA per scan was 0.018. Treatment-related adverse events occurred in 59.1% of patients, including lymphocyte, leukocyte, and neutrophil count reductions and infusion reactions. No serious adverse events were observed. • **Conclusions:** DIV treatment for 4 years provided sustained efficacy in RMS patients. The safety profile was favorable and consistent with previous studies.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (14/15)

Date	Title	Author	Summary
All days	Different Definitions of Confirmed Disability Progression and Their Association With Brain Atrophy in Patients With Relapsing Multiple Sclerosis Treated With Ozanimod for up to 8 Years in the Phase 3 SUNBEAM/RADIANCE and Open-label DAYBREAK Studies	Cristina Granziera	• **Introduction:** To report long-term CDP in patients with relapsing MS (RMS) treated with ozanimod, and explore the relationship between CDP and brain atrophy. • **Methodology:** Patients with RMS were treated with ozanimod 0.46 or 0.92 mg/d, or interferon β-1a 30 µg/wk for 24 months in RADIANCE or ≥12 months in SUNBEAM. Completers enrolled in DAYBREAK for up to 6.5 years. CDP-6 was defined as a ≥1-point EDSS increase confirmed after 6 months. PIRA occurred if CDP-6 onset happened without relapse for ≥90 days. RAW was defined for relapses with incomplete recovery. SEDSS-6 was a score of 6 sustained for 6 months. Event and atrophy rates were analyzed for progressors vs non-progressors. • **Results:** After 6–8 years of ozanimod treatment (n=2256), 80.1% were free of CDP-6, 9.9% had PIRA, 10.5% had RAW, and 3.9% reached SEDSS-6. In 762 patients on ozanimod 0.92 mg/d for ~8 years, 80.1% were free of CDP-6, 10.5% had PIRA, 9.7% had RAW, and 3.7% reached SEDSS-6. At month 84, whole brain atrophy rates were 2.4% vs 1.9%, 2.2% vs 2.0%, 2.6% vs 2.0%, and 2.8% vs 2.0% in progressors vs non-progressors. Thalamic atrophy rates were 5.1% vs 4.1%, 4.1% vs 4.3%, 6.6% vs 4.1%, and 5.7% vs 4.3%. The largest differences were seen in RAW and thalamic volume. • **Conclusions:** After ~8 years of ozanimod treatment, <4% of patients reached SEDSS-6. All CDP definitions, RAW, and PIRA were linked to brain and thalamic atrophy.
All days	Long-term effects of treatment with cladribine tablets on cognition and treatment satisfaction in people with relapsing multiple sclerosis: 4-year results from the non-interventional CLADQoL study	Iris-Katharina Penner	• **Introduction:** To evaluate changes in cognitive functioning (CF) and treatment satisfaction (TS) over 4 years of CladT treatment. • **Methodology:** CF was measured by the Symbol Digit Modalities Test (SDMT) at baseline (BL), month 24 (M24), and month 48 (M48), using ≥4- or ≥8-point changes and age/education-adjusted Z-scores. TS was measured with the Treatment Satisfaction Questionnaire for Medication (TSQM v1.4) at BL, M6, M18, and M48. • **Results:** Analysis included 305 patients (70.8% female, mean age 38.1 years, disease duration 8.3 years); 85.6% had prior MS therapy. At M24, 7.6% improved in SDMT (≥4 points), rising to 72.9% at M48. Cognitive impairment decreased: no impairment increased from 45.6% at BL to 58.7% at M24, 53.5% at M48. TS improved, with mean +9.5 (±26.5) from BL to M18. Annualized relapse rates were low (0.03 at M24, 0.04 at M48). No new safety signals emerged. • **Conclusions:** CLADQoL showed sustained cognitive and treatment satisfaction improvements over 4 years of CladT.

Notable Presentations At ECTRIMS 2025
Therapeutics – Disease Modifying Therapies (DMTs) (15/15)

Date	Title	Author	Summary
All days	Real world clinical experience from ENABLE, the first Phase 4 observational study for patients with relapsing multiple sclerosis initiating ublituximab	Angel Chinea	• **Introduction:** To evaluate the real-world clinical experience of patients with RMS treated with UBL. • **Methodology:** This analysis included 17 participants enrolled in ENABLE from July 2024 to February 2025, summarizing demographics, disease history, prior disease-modifying therapy (DMT) use, and clinical outcomes on UBL. Enrollment is ongoing, with a target of at least 50 participants. • **Results:** The cohort had a slightly older mean age (42.8 years) than in ULTIMATE I (35.4 years), with a higher proportion of females (72.9% vs. 62.9%). 19.8% were Black/African American, and 16.9% Hispanic/Latino. Disease duration was 10.7 years, with 4.1% relapse-free and 28.8% having one relapse in the previous 2 years. 57.1% had no gadolinium-enhancing lesions, and 45.2% had no new/enlarging T2 lesions. 31.1% were treatment-naïve, while 65.5% switched from prior DMTs, including anti-CD20 therapy (42.2%) and natalizumab (20%). Over 67% switched due to inadequate efficacy. Additional efficacy and safety data will be presented. • **Conclusions:** The real-world cohort from ENABLE represents a slightly older, more diverse MS population with longer disease duration than ULTIMATE. These findings may inform clinical decisions for patients initiating UBL or transitioning from prior therapies.

Notable Presentations At ECTRIMS 2025
Rehabilitation, Symptom Management & QoL (1/5)

Date	Title	Author	Summary
24 Sep 2025	Effects of Resistance vs Aerobic training on serum light chain neurofilament and glial fibrillary acidic protein levels in Multiple Sclerosis: A Randomized Clinical Trial	Alba Chavarria-Miranda	• **Introduction:** This study aimed to assess the impact of physical exercise on GFAP and NfL in MS patients. • **Methodology:** A randomized trial included an intervention group (8 weeks of resistance training 3 days/week) and a control group (aerobic training). Participants with stable MS (EDS ≤ 4) and low physical activity were enrolled. Serum NfL and GFAP levels were measured before and after the program. Only participants with ≥75% adherence were analyzed. • **Results:** 40 participants (19 resistance, 21 aerobic) were analyzed. 85% were women, with an average age of 30±10 years. No significant differences in serum NfL and GFAP were observed between groups. The resistance training group showed significant improvements in muscle thickness (p=0.08), timed up-go test (p=0.07), and sit-to-stand test (p<0.01), while no significant changes were observed in the aerobic group. • **Conclusions:** Resistance and aerobic training had no effect on NfL or GFAP in MS patients, but resistance training improved functional measures. Further investigation is needed on the impact of exercise on neuronal biomarkers.
24 Sep 2025	MitoQ for Fatigue in Multiple Sclerosis: A Randomized, Placebo-Controlled Trial	Vijayshree Yadav	• **Introduction:** This Phase I/I clinical trial evaluates the safety, tolerability, dose-finding, and efficacy of oral MitoQ in pwMS experiencing fatigue. • **Methodology:** A double-blind, placebo-controlled, 12-week trial compared 20 mg and 40 mg doses of MitoQ to a placebo. The primary outcome was fatigue reduction (measured by the modified fatigue impact scale [MFIS]), and secondary outcomes included disability, depression, cognition, blood cytokines, and oxidative stress biomarkers. • **Results:** Of 45 pwMS enrolled, 43 completed the trial. 13 received 40 mg MitoQ, 15 received 20 mg, and 15 received placebo. No significant difference in MFIS change was observed between the placebo and MitoQ groups (p=0.52). The MitoQ group showed a 7.0-point improvement, while the placebo group improved by 9.1 points (p=0.71). No differences based on MitoQ dosage were found. • **Conclusions:** MitoQ was not associated with improved fatigue in pwMS in this pilot trial. Further studies are needed to assess the role of mitochondrial modification in symptom management for pwMS.

Notable Presentations At ECTRIMS 2025
Rehabilitation, Symptom Management & QoL (2/5)

Date	Title	Author	Summary
25 Sep 2025	Fatigue Alleviation through Neuromodulation Therapy in Multiple Sclerosis (FANTiMS study) – preliminary feasibility of a randomised double blind controlled trial	Mads Alexander Just Madsen	• **Introduction:** This trial aims to investigate rTMS as a treatment for MS-related fatigue by targeting the dorsal premotor cortex. • **Methodology:** In a double-blind, placebo-controlled trial, 60 pwMS will receive rTMS (20-40mg doses) targeting the dorsal premotor cortex. Outcomes include fatigue (measured by MFIS), disability, depression, cognition, and biomarkers of oxidative stress. • **Results:** Of 35 screened participants, 16 were included, and 13 completed the protocol. AEs were mild (e.g., sleepiness and tiredness), with only 1 TMS session paused for discomfort. Adherence was high, with 12 participants willing to continue if the therapy proved effective. • **Conclusions:** This study supports the feasibility and tolerability of rTMS in pwMS and provides valuable insights into cortical excitability and fatigue. Further research is needed to confirm the efficacy of rTMS in MS-related fatigue treatment.
25 Sep 2025	Endocannabinoid modulation using monoacylglycerol lipase inhibition in multiple sclerosis spasticity: A phase 1b, randomised, placebo-controlled study	Robert Naismith	• **Introduction:** This study evaluates the effect of 5 weeks of Lu AG0646 (30 mg/day) on spasticity in MS using the Numerical Rating Scale-Spasticity (NRS-S). • **Methodology:** This double-blind, placebo-controlled phase 1b study (NCT0490219) involved 20 patients with clinically stable MS and moderate-to-severe spasticity. The primary outcomes at week 5 included spasticity response (≥30% improvement in NRS-S) and change from baseline in NRS-S. • **Results:** No significant differences were found between Lu AG0646 and placebo in NRS-S scores. The NRS-S responder rates were 0.2 for Lu AG0646 and 0.25 for placebo (treatment difference: -0.028 favoring placebo). The mean change in NRS-S at week 5 was -0.387 for Lu AG0646 vs -1.490 for placebo (treatment difference: 1.10, p=0.23). The study was terminated early due to lack of efficacy signal. Treatment-emergent AEs were reported in 39% of the Lu AG0646 group and 57% of the placebo group, with no serious AEs. • **Conclusions:** The study was terminated early due to slow recruitment and no favorable trend in efficacy. The safety profile of Lu AG0646 was similar to placebo.

Notable Presentations At ECTRIMS 2025
Rehabilitation, Symptom Management & QoL (3/5)

Date	Title	Author	Summary
25 Sep 2025	AEROBIC AND COGNITIVE TRAINING EFFECTS ON INSULAR RESTING-STATE FUNCTIONAL CONNECTIVITY IN PROGRESSIVE MULTIPLE SCLEROSIS: COGEX TRIAL	Matteo Albergoni	• **Introduction:** This phase I/II trial evaluated the safety, tolerability, and efficacy of oral MitoQ (30 mg/day) in MS patients with fatigue. • **Methodology:** In this double-blind, placebo-controlled trial, participants were randomized to receive either MitoQ or placebo for 12 weeks. The primary outcome was fatigue improvement (Modified Fatigue Impact Scale [MFIS]), and secondary outcomes included disability, depression, cognition, blood cytokines, and oxidative stress biomarkers. • **Results:** Of the 45 enrolled patients, 43 completed the 12-week treatment. No significant differences were found in MFIS between MitoQ and placebo. The MitoQ group showed a 7.0-point improvement in MFIS, while placebo showed 9.1 points. There was no significant difference based on MitoQ dosage (p=0.71). • **Conclusions:** MitoQ did not significantly reduce fatigue in MS patients in this pilot trial. Further studies are needed to explore the role of mitochondrial modification in managing MS-related symptoms.
All days	The Effect of Sexual Counselling with the PLISSIT Model on Sexual Function and Sexual Quality of Life in Women with Multiple Sclerosis: A Randomized Controlled Trial	Cansu Polat Dünya	• **Introduction:** This study aimed to evaluate the 12-month effects of PLISIT-based sexual counseling on sexual function and quality of life in women with MS. • **Methodology:** A single-blind, randomized controlled trial was conducted with women aged 18–45 years with an EDSS ≤5.5. Participants were assigned to either the sexual counseling group (n=31) or the control group (n=32). The intervention included four structured sessions based on the PLISIT model delivered over four weeks. Assessments were conducted at baseline, 3, 6, and 12 months using the MSISQ-15 and SQOL-F scales. • **Results:** The intervention group showed significant within-group improvements in sexual function ($F = 3.198$, $P = 0.027$), and SQOL-F scores significantly increased at 6 months ($P = 0.02$) and 12 months ($P = 0.032$). A significant increase in weekly sexual intercourse frequency was observed at 6 months ($P < 0.01$), sustained at 12 months ($P = 0.06$). No significant between-group differences were observed. • **Conclusions:** PLISIT-based sexual counseling may lead to long-term improvements in sexual quality of life and activity frequency among women with MS. While no significant between-group differences were found, within-group improvements suggest that structured sexual counseling can be beneficial. Larger, multi-centered studies are needed to confirm these findings.

Notable Presentations At ECTRIMS 2025
Rehabilitation, Symptom Management & QoL (4/5)

Date	Title	Author	Summary
All days	Perceptual Sensitivity to Changes in Self-Paced Maximal Walking Speed During the Six-Minute Walk Test in Individuals With Multiple Sclerosis and Healthy Controls: Preliminary Results	Gianluca Florio	• **Introduction:** The aim of the study was to examine perceptive sensitivity to performance variations in PwMS and healthy controls (HC), focusing on the perception of gait speed during the 6MWT. • **Methodology:** Eight mildly-disabled PwMS (median age: 39, median EDSS: 3) and 8 HC (median age: 31) were included. Participants performed an instrumented 6MWT with 6 wearable inertial measurement units, carrying a handheld sensor to report perceived gait speed variations. Detection rates were calculated as the ratio between report quantity and speed variability (CV), compared with subjective confidence ratings (Visual Analog Scale). • **Results:** PwMS had lower walking speed compared to HC (median: 1.529 m/s vs 1.891 m/s). Detection rates were higher in HC (median: 4.67) compared to PwMS (median: 1.19), despite similar walking speed variability. PwMS reported higher subjective confidence ratings (median: 80%) compared to HC (median: 62.5%). • **Conclusions:** PwMS may have reduced sensitivity to perceive variations in their walking performance, potentially due to overconfidence or perceptual impairments.
All days	Effects of Oral Magnesium Supplementation on Cognition, Mood, and Fatigue in Patients with Relapsing-Remitting Multiple Sclerosis: A Triple-Blind Randomized Controlled Trial	Ali Rezaei	• **Introduction:** This study aimed to evaluate the effects of oral magnesium supplementation on cognitive performance, mood, fatigue, and related serum biomarkers in RMS. • **Methodology:** In this triple-blind randomized controlled trial, 60 RMS patients were randomized into two groups: one received magnesium oxide 250 mg three times daily (n = 30) and the other a placebo (n = 30) for 90 days. Cognitive function (MACFIMS), mood (Beck Anxiety and Depression Inventories), and fatigue (Fatigue Severity Scale) were assessed at baseline and after 3 months. Serum magnesium, superoxide dismutase (SOD), brain-derived neurotrophic factor (BDNF), and interleukin-6 (IL-6) were also measured. • **Results:** Forty-five completed the trial (23 magnesium, 22 placebo). At 90 days, depression improved in the magnesium group (BDI p=0.09 vs placebo p=0.718). Anxiety improved (BAI p=0.05), while placebo worsened (p=0.387); between-group difference was significant (p=0.049). Fatigue did not change. Cognition improved in verbal learning (CVLT-I p=0.03), long-delay recall (CVLT-LD p=0.029), and processing speed (SDMT p=0.08) with magnesium. No significant biomarker changes were seen. • **Conclusions:** Magnesium supplementation improved depression, anxiety, and select cognitive domains in RMS, supporting its potential as an adjunctive therapy for mood and cognition.

Notable Presentations At ECTRIMS 2025
Rehabilitation, Symptom Management & QoL (5/5)

Date	Title	Author	Summary
All days	The impact of combination of flax (Linum usitatissimum) and black seed (Nigella sativa) hydroalcoholic extracts on fatigue in RRMS patients; a parallel randomized double-blind placebo-controlled clinical trial	Reza Mosaddeghi-Heris	• **Introduction:** This study aimed to assess the effects of hydroalcoholic extracts of flax (Linum usitatisimum) combined with black seed (Nigella sativa) on fatigue in MS patients. • **Methodology:** In this randomized controlled trial (RCT), patients with relapsing-remitting MS (RMS) and fatigue were given a combination of hydroalcoholic extracts of Nigella sativa and flaxseed for three months. The Comprehensive Fatigue Assessment Battery for Multiple Sclerosis (CFAB-MS) was used to assess fatigue and related factors at baseline and after 3 months. Statistical analysis was performed using SPS software, version 23. • **Results:** Out of 50 randomized participants, 35 completed the trial. The average age was 34.1 years (SD = 9.10), with 85.7% female. The hydroalcoholic extracts did not significantly improve fatigue or related factors such as pain, sleep issues, stress, mood, anxiety, nutrition, or mobility ($p > 0.05$). The only significant change was in nutritional status, measured by VAS, in the treatment group. • **Conclusions:** The study found no significant improvement in fatigue or related factors with hydroalcoholic extracts of Nigella sativa and flaxseed in RMS patients compared to a placebo.
All days	The effectiveness of combining a home-based Digital motor Telerehabilitation program with conventional therapy in Progressive Multiple Sclerosis: a multicentre, randomized controlled trial	Sofia Straudi	• **Introduction:** To assess the impact of combining home-based telerehabilitation with in-hospital rehabilitation on mobility in SPMS/PMS. Secondary aims: motor, cognitive, psychological outcomes, fatigue, pain, QoL, and cost-effectiveness. • **Methodology:** In this multicenter, randomized, single-blind trial (NCT0648515), 78 patients were planned. The experimental group (EG) received a 12-week telerehabilitation program plus 10 in-hospital sessions; controls (CG) received in-hospital rehab only. Assessments occurred at baseline (T0), post-rehab (T1), week 12 (T2), and week 24 (T3). • **Results:** To date, 26 participants were enrolled (EG=15, CG=11; mean age 57.4 ±10.6; median EDSS 5). No significant group differences were observed in the primary outcome (TUG) at T1 ($p=0.601$) or T2 ($p=0.730$). Secondary outcomes were also comparable, except B-IPQ, favoring EG ($p=0.043$). User satisfaction was high (TSQ-WT 3.28 ±1.46). • **Conclusions:** Early results show digital telerehabilitation is feasible, well-tolerated, and may complement MS rehabilitation. Full-sample analysis will clarify its clinical and economic impact.

Notable Presentations At ECTRIMS 2025
Cognitive & Psychological Outcomes (1/4)

Date	Title	Author	Summary
25 Sep 2025	Cognitive change-based component scores significantly predict subsequent EDSS progression in a prospective cohort of RRMS: results from the ImproveMS cohort study	Tomas Kalincik	• **Introduction:** Prognostication in RMS remains challenging; this study assessed cognition, performance, and MRI-based scores as predictors of disability progression. • **Methodology:** 397 RMS patients (mean follow-up 4.1 years, six Australian clinics) underwent biannual MSPT/MSReactor assessments and annual MRI. PCA derived seven components explaining 56.8% variance; Cox regression tested associations with EDSS progression, relapse, and disability outcomes. • **Results:** Cognitive decline (C5 component) predicted sustained EDSS progression (aHR=1.2; top vs bottom quartile aHR=4.72, 95%CI=1.52–14.6, ptrend=0.02). Neither MRI nor motor components predicted disability progression; no predictors for EDSS decrease or relapse. • **Conclusions:** Early cognitive decline robustly predicted disability worsening, independent of demographics and DMT use. Cognition-based metrics may enable medium-term prognostication and guide precision treatment strategies.
All days	Preliminary results of validation of the brief international cognitive assessment for multiple sclerosis (BICAMS) tool and potential predictors of BICAMS test in an Ecuadorian population with multiple sclerosis	Pedro Abreu	• **Introduction:** To validate BICAMS in Ecuador, establish regression-based norms, test reliability, estimate prevalence of impairment, and assess demographic predictors of performance. • **Methodology:** BICAMS was administered to 50 MS patients and 86 matched controls. Tests included SDMT, BVMT-R, and PAMCL. Regression-based Z-scores identified impairment (<5th percentile). Reliability was assessed via 15-day test–retest. Regression analyses examined predictors. • **Results:** Patients scored significantly lower on SDMT (d=0.35), PAMCL (d=0.54), and BVMT-R (r=0.46). Test–retest correlations were strong (SDMT r=0.95; PAMCL r=0.74; BVMT-R r=0.69). Age and lower education predicted poorer SDMT and PAMCL performance; female gender favored CVLT, while older age/lower education related to BVMT-R outcomes. Cognitive impairment was identified in 52% of patients. • **Conclusions:** Ecuadorian BICAMS showed strong validity and reliability, with impairment rates consistent with regional data. Age, education, and gender influenced test performance, supporting the need for culturally adapted norms in MS cognitive monitoring.

Notable Presentations At ECTRIMS 2025
Cognitive & Psychological Outcomes (2/4)

Date	Title	Author	Summary
All days	Impact of natalizumab on cognitive, functional, social, and psychological outcomes in people with MS: results from the prospective multicentre real-world TYPIFI study.	Pedro Abreu	• **Introduction:** Patient-reported outcomes provide holistic insights into MS impact. This study examined natalizumab's effects beyond disease activity, focusing on cognition, fatigue, psychological well-being, and social/functional outcomes. • **Methodology:** Prospective 48-month observational study in nine Portuguese centers included 60 RMS patients (80% female, mean age 31.9). Assessments: SDMT, fatigue, depression (BDI-I), MS impact scale, work productivity/activity. • **Results:** At 12 months, 97.8% achieved NEDA3, maintained through follow-up. SDMT improved (57.5 vs 45.0, p=0.01). Fatigue and depression decreased significantly (BDI-I: 4.5 vs 8.5, p=0.01). Work productivity improved (time worked 96.1% vs 86.1%, p=0.02). • **Conclusions:** Natalizumab sustained disease control and enhanced cognitive, psychological, and functional outcomes, reinforcing its value in real-world, patient-centered MS management.
All days	Beyond SMART: evaluating goal setting in a neuropsychological rehabilitation trial in multiple sclerosis	Gogem Topcu	• **Introduction:** Goal setting in neuropsychological rehabilitation (NPR) enhances motivation, tailoring, and measurement. Applying SMART criteria offers structure for evaluating attainment in MS rehabilitation trials. • **Methodology:** Fifty participants' goals (n=134) from the NEuRoMS trial were rated twice by independent raters, with adjudication for discrepancies. Intra-class correlations (ICC) assessed reliability. Goals were scored using traffic-light SMART criteria (red, amber, green). • **Results:** Of 134 goals, blinded ratings classified 12% green, 83% amber, 5% red. Unblinded ratings: 98% green. ICC showed strong agreement blinded (0.86, p<0.01), moderate unblinded (0.76, p<0.01), but poor at second timepoint unblinded (−0.06). • **Conclusions:** Refined goal-setting criteria improved accuracy and consistency. Updated training materials emphasized SMART applicability to neuropsychological goals, supporting robust outcome measurement in NPR trials.

Notable Presentations At ECTRIMS 2025
Cognitive & Psychological Outcomes (3/4)

Date	Title	Author	Summary
All days	Understanding the training needs in Europe for designing high-quality neuropsychology and vocational rehabilitation trials in multiple sclerosis	Blanca De Dios Perez	• **Introduction:** Designing robust RCTs for neuropsychological (NPR) and vocational rehabilitation (VR) in MS faces methodological and resource barriers, limiting evidence generation for these complex interventions. • **Methodology:** An online survey of 50 MS clinicians/researchers across nine European countries assessed barriers, resource constraints, and training needs in rehabilitation RCT design. Descriptive analysis identified gaps and support requirements. • **Results:** Key barriers: outcome selection, eligibility criteria, bias minimization, limited funding, and insufficient trial methodology expertise. Only ~50% used reporting guidelines, often deemed inadequate. Respondents highlighted reliance on peer literature, informal support, and a strong demand for structured training/workshops • **Conclusions:** Addressing methodological gaps with structured education, collaborative platforms, and tailored guidance could improve RCT quality, strengthen rehabilitation evidence, and enhance outcomes for people with MS.
All days	MODAFIMS: study protocol of an open-label, single-center clinical trial to evaluate predictors of response to MODAFinil in the treatment of cognitive deficits in patients with Multiple Sclerosis	Alessandro Franceschini	• **Introduction:** Cognitive impairment affects QoL in pwMS, with no approved therapies. Modafinil, used for narcolepsy, is hypothesized to improve cognition, particularly processing speed deficits. • **Methodology:** Prospective trial enrolling 64 pwMS; modafinil 20 mg daily for 12 weeks. Assessments: SDMT, rs-fMRI, Go/No-Go fMRI, PROs, MFIS, safety, neuropsychological battery. Responders vs non-responders identified via SDMT improvements. • **Results:** By Feb 2025, 35 screened, 27 enrolled, 18 completed. Median age 50, EDSS 3.5 (range 1–6.5), SDMT median 31 (range 4–54). Recruitment ongoing; completion expected June 2025. • **Conclusions:** If effective, modafinil could offer a novel therapy for MS-related cognitive deficits. Baseline fMRI predictors may enable precision targeting of responders.

Notable Presentations At ECTRIMS 2025
Cognitive & Psychological Outcomes (4/4)

Date	Title	Author	Summary
All days	Effectiveness of an Evidence-Based Online MRI Education Tool for People with Multiple Sclerosis: A Randomised Controlled Trial	Christoph Heesen	• **Introduction:** MRI is central in MS management, but complexity limits patient understanding. UMIMS, an interactive EBPI tool, was developed to improve MRI-related knowledge and support shared decision-making (SDM). • **Methodology:** Double-blind RCT enrolled 120 RRMS/CIS patients. Participants randomized to UMIMS vs control website. Primary endpoint: change in MRI-specific risk knowledge (MRI-RIKNO 2.0). Secondary endpoints: MRI-related emotions, autonomy, SDM, QoL. • **Results:**UMIMS group showed greater risk-knowledge gain (+4.0 vs +2.7; p=0.019). Feelings of competence improved in both arms, more in controls. MRI-related anxiety, autonomy, and SDM remained unchanged; baseline levels were high across groups. • **Conclusions:** UMIMS significantly enhanced MRI risk-knowledge, though without added impact on emotions or SDM. The tool supports informed appraisal of MRI findings and may strengthen patient engagement in MS care.

Notable Presentations At ECTRIMS 2025
Trial Design, Methodology & Real-World Evidence (1/6)

Date	Title	Author	Summary
24 Sep 2025	Target trial emulation to assess the comparative effectiveness of treatments for first relapse prevention in MOGAD	Akash Virupakshaiah	• **Introduction:** Effective relapse prevention in pediatric MOGAD is uncertain. • **Methodology:** Using real-world US Pediatric MS Network data, a target trial emulation with propensity score–matched cohorts compared treated (≥90 days) vs untreated patients. Cox models adjusted for immortal time bias. • **Results:** Among 312 patients, IVIG reduced relapse risk by 71% (HR 0.28), while anti-CD20 and other agents showed modest non-significant benefit. Oral steroids increased relapse risk (HR 2.18). None reached statistical significance. • **Conclusions:** IVIG showed the strongest protective trend, underscoring the urgent need for larger, randomized pediatric MOGAD trials.
24 Sep 2025	Investigating the effect of trial participation on clinical outcomes in multiple sclerosis: a United Kingdom Multiple Sclerosis Register study	Ger Mullan	• **Introduction:** Clinical trial participation may enhance patient experience, but its effect on MS outcomes is unclear. • **Methodology:** Using UK MS Register data, trial participants (active/control) were 1:1 propensity-matched to non-participants by age, baseline EDSS, and DMT. Regression models adjusted for key covariates with pseudo-trial windows for controls. • **Results:** Among 4341 patients, 527 had trial exposure. No significant EDSS differences were found: Active vs Never (0.474 vs 0.076; p=0.061) and Control vs Never (-0.487 vs -0.340; p=0.186). • **Conclusions:** Trial participation did not significantly affect disability progression. Further evaluation of patient-reported outcomes is warranted.

Notable Presentations At ECTRIMS 2025
Trial Design, Methodology & Real-World Evidence (2/6)

Date	Title	Author	Summary
25 Sep 2025	The TRaditional versus Early Aggressive Therapy for MS (TREAT-MS) trial: design and baseline participant characteristics	Ellen M. Mowry	• **Introduction:** The benefit of early high-efficacy DMTs in MS remains untested in prospective randomized trials. • **Methodology:** TREAT-MS is a pragmatic, randomized, rater-blinded trial in treatment-naïve relapsing MS (age 18–60). Patients (n≈900) were randomized 1:1 to higher- vs moderate-efficacy DMT, with clinician/patient choice within strategy. Stratification included site and baseline disability risk. Primary endpoint: sustained EDSS-plus worsening. • **Results:** Baseline cohort: 900 patients, mean age 36, 70% women, 72% White, 19% Black, 12% Hispanic; 73% high risk for disability. Follow-up spans 18–69 months; completion August 2026. • **Conclusions:** TREAT-MS will define whether early high-efficacy DMT prevents disability progression.
25 Sep 2025	Rates of publication and publication bias in MS and NMOSD clinical trials - a databank analysis	Maximilian Pistor	• **Introduction:** Timely trial publication is critical to reduce bias and fulfill ethical obligations, yet reporting remains discretionary and poorly monitored. • **Methodology:** MS and NMOSD trials registered on ClinicalTrials.gov since 2014 were analyzed. Associated publications were identified via PubMed/Google Scholar and categorized by journal impact quartile. • **Results:** 293 MS trials: 49.5% published, mostly in Q1 (61%). Median publication lag was 26 months. 47 NMOSD trials: 51.1% published, 83% in Q1, with shorter lag (18 months). • **Conclusions:** Only ~50% of Phase 1–4 MS/NMOSD trials are published, underscoring major transparency gaps. Funding source, outcome, and adverse event reporting may influence dissemination.

Notable Presentations At ECTRIMS 2025
Trial Design, Methodology & Real-World Evidence (3/6)

Date	Title	Author	Summary
25 Sep 2025	Predicting individualized efficacies of multiple sclerosis disease modifying treatmentson disability progression and their morbidity/mortality risks by modeling clinical trialsdata and population studies	Bibiana Bielekova	• **Introduction:** MS DMT risk/benefit varies by disease stage and comorbidities; no objective estimator exists. • **Methodology:** Data from 61 randomized Phase 2b/3 trials (46,601 patients; 91,787 patient-years) informed regression models of disability-progression efficacy. Eighty extracted and 30 computed features were integrated, validated in real-world cohorts, with mortality risk modeled using age-adjusted hazard ratios. • **Results:** Efficacy rose with relapses/CELs and declined with age, duration, and trial time. Risks increased with age, disability, and comorbidities. A web-based estimator was developed. • **Conclusions:** Models support early high-efficacy therapy with de-escalation. In non–trial-like patients, DMTs may cause net harm; the tool enables personalized decisions.
25 Sep 2025	Target Trial Emulation to Replicate Randomized Clinical Trials using Registry Data in Multiple Sclerosis	Antoine Gavoille	• **Introduction:** Target trial emulation (TE) can infer causality from observational MS data; validation against RCTs is essential. • **Methodology:** OFSEP registry (Dec-2023) replicated eight RCTs by applying trial eligibility to initiators of corresponding DMTs. Targeted maximum likelihood estimation adjusted for confounding, censoring, and missingness. Outcomes: ARR (primary), EDSS progression, MRI activity. • **Results:** n=14,111. TE matched RCT effects in 7/8 ARR replications and all 6 EDSS analyses. MRI replication was weaker: 3/5 for new T2 lesions and 1/4 for Gd-enhancing T1 lesions. • **Conclusions:** Registry-based TE credibly reproduces clinical RCT outcomes (relapse, disability), but MRI endpoints are less robust; TE is a strong complement to RCTs.

Notable Presentations At ECTRIMS 2025
Trial Design, Methodology & Real-World Evidence (4/6)

Date	Title	Author	Summary
All days	Baseline Characteristics of Paediatric Patients with Multiple Sclerosis in the Phase 3 NEOS Study of Ofatumumab and Siponimod Versus Fingolimod	Kumaran Deiva	• **Introduction:** Paediatric MS (PedMS) shows higher inflammation and early brain atrophy. Fingolimod is the only globally approved DMT, highlighting unmet therapeutic needs. • **Methodology:** NEOS (NCT04926818) is a randomized, 3-arm, double-blind phase 3 study comparing ofatumumab and siponimod with fingolimod. It uses a Bayesian noninferiority design, with a 2-year core and 2–5-year extension. Primary endpoint: ARR ≤2 years. • **Results:** 129 PedMS patients enrolled; mean age 15, BMI 23.8. Female 60%, treatment-naïve 74%, pubertal 87%. Mean EDSS 1.6, diagnosis 0.7 years, first symptoms 1.3 years, mean relapses in prior year 1.3. • **Conclusions:** NEOS participants are representative of typical PedMS and comparable to PARADIGMS.
All days	Integrating multicentre data to explore rwPIRA: Results from the INTONATE-MS consortium	Jiwon Oh	• **Introduction:** Under HET, ongoing deterioration likely reflects chronic inflammation/degeneration; rwPIRA quantification is challenging • **Methodology:** INTONATE-MS federated, retrospective cohorts (2015–2023) on alemtuzumab, natalizumab, ocrelizumab, ofatumumab with ≥2 visits. Harmonized data assessed relapses, MRI activity, and outcomes (EDSS, T25FW, SDMT, clinician-rated CGI) to define "lack of disease stability" (LDS). • **Results:** Four sites; n=1,915. Annual relapse rate 7.6%; MRI activity 4.7%. Outcome capture was uneven: EDSS ≥2 measures in 69.5%, CGI 16.6%, T25FW 8.8%. • **Conclusions:** Heterogeneous real-world measurement constrains rwPIRA definition. Standardized longitudinal outcome collection is needed to detect progression, guide treatment optimization, and interrogate mechanisms.

Notable Presentations At ECTRIMS 2025
Trial Design, Methodology & Real-World Evidence (5/6)

Date	Title	Author	Summary
All days	Baseline characteristics of the Determining the Effectiveness of earLy Intensive Versus Escalation approaches for the treatment of Relapsing-remitting MS (DELIVER-MS) trial cohort	Emma Tallantyre	• **Introduction:** Early high-efficacy DMT (EHT) may improve long-term RMS outcomes, but escalation (ESC) remains widely used. Comparative randomized evidence is lacking. • **Methodology:** DELIVER-MS (NCT03535298) is a pragmatic RCT with a parallel observational arm, comparing ESC vs EHT. Primary endpoint: brain volume loss at 36 months. Baseline demographics, MRI features, and reasons for declining randomization were analyzed using logistic regression. • **Results:** 816 enrolled: 393 RCT, 374 OBS. Groups were balanced. Declining randomization: 85% due to treatment preference. OBS cohort: 67% chose EHT, 33% ESC; EHT preference higher in US vs UK (63% vs 37%, p<0.01). ESC linked to safety concerns; EHT to efficacy and higher education. • **Conclusions:** Both ESC and EHT remain viable strategies; equipoise persists. DELIVER-MS will provide critical evidence to guide first-line DMT strategy in RMS.
All days	Evaluating MRI-Confirmed Relapses as a Novel Endpoint in Multiple Sclerosis Trials	Antoine Gavoille	• **Introduction:** Clinical relapses in MS are typically symptom-defined, but many events (ACES) lack MRI activity. This risks diluting treatment effect estimates. • **Methodology:** A meta-analysis of 10 RCTs was combined with French registry (OFSEP) data. A logistic model predicted MRI-active relapses (RAM) vs ACES by patient and therapy characteristics. Treatment effects on relapses, RAM, and ACES were compared. Statistical power was modeled under different scenarios. • **Results:** RAM-based endpoints yielded larger effect sizes (up to 2×, e.g., OPERA trial) versus symptom-defined relapses, while ACES rates remained stable across arms. Using RAM reduced required sample size/duration by ~37% (AR 0.15 vs 0.30). • **Conclusions:** MRI-confirmed relapses improve trial sensitivity, exclude ACES unaffected by DMTs, and can substantially reduce study burden, offering a more precise endpoint for future MS trials.

Notable Presentations At ECTRIMS 2025
Trial Design, Methodology & Real-World Evidence (6/6)

Date	Title	Author	Summary
All days	TRUSTED: Trials and Registries Unified Sign-up Tool for Equitable Discoveries	Will Brown	• **Introduction:** MS registries remain underused in the UK (<1% in MSBase; <5% in UK MS Register), limiting trial recruitment and representativeness. • **Methodology:** TRUSTED, a national ethical sign-up tool, allows pwMS to consent once to multiple registries, observational studies, a trial eligibility checker, and the RIGHT-MS inequalities study. Piloted at 4 NHS hospitals. • **Results:** Of 3244 invited, 1372 (42%) participated. MSBase doubled (n=136); UK MS Register grew by 1070. TRUSTED boosted recruitment to a remyelination study by 71% and enrolled 61/65 NIHR underserved groups • **Conclusions:** TRUSTED empowered >3000 pwMS from 9 sites, tripling UK MSBase participation. It enhances inclusivity, accelerates trial enrolment, and reduces inequalities.

Notable Presentations At ECTRIMS 2025
Patient Experience, Surveys & Health Literacy (1/5)

Date	Title	Author	Summary
24 Sep 2025	The EMPEC Study: Perception of Clinical Trials in People with Multiple Sclerosis	Mafalda Delgado Soares	• **Introduction:** Despite advances in MS therapies via RCTs, many patients hesitate to enroll. Understanding patient perspectives is essential to improve trial communication and recruitment. • **Methodology:** PwMS attending a tertiary center (Aug–Oct 2024) completed a structured 10-minute questionnaire (knowledge, perceptions, motivations). Clinical and demographic data were extracted from records. • **Results:** Among 282 patients (mean age 43; 72% women), 90% knew of trials, though half misunderstood key concepts. Higher education improved awareness (96% vs 84%, p=0.02). Willingness to join was 42%, higher in progressive MS (65% vs 38%, p=0.04). Reluctance (17%) stemmed from safety concerns. • **Conclusions:** While knowledge exists, technical gaps and safety fears remain. Education tailored to patient needs may enhance RCT participation.
24 Sep 2025	Concerning pilot data from Reducing Inequality Gaps in Healthcare, Trials and observational research in MS (RIGHT-MS) study.	Daniela Soares Régua	• **Introduction:** UK RIGHT-MS targets quantifying healthcare inequalities across 56 underserved MS subgroups. • **Methodology:** Prospective, UK-wide integration of EHRs (Epic/PatientCare), self-identified inequality status via TRUSTED, and regional statistics; pilot reports diagnosis latency and research participation by subgroup. • **Results:** 3,025 participants from 9 sites (35–50% consent); 51/56 underserved groups represented. Median diagnosis time: 36 days; longer in 38/51 underserved groups—migrants 69 days, no internet 639 days, learning disabilities ≈4× longer (~3 years). Trial participation varied: White 42% vs Asian 20% vs Black 17%. • **Conclusions:** Marked diagnostic and research-access disparities persist. RIGHT-MS will co-design solutions with affected communities to reduce inequities.

Notable Presentations At ECTRIMS 2025
Patient Experience, Surveys & Health Literacy (2/5)

Date	Title	Author	Summary
24 Sep 2025	Evaluating public and patient involvement in interventional research – a newly developed checklist (EPPIIC) with application to the COB-MS feasibility trial in multiple sclerosis	Sinéad Hynes	• **Introduction:** Public involvement (PI) in MS trials improves research quality, accessibility, and impact, yet existing evaluation frameworks are fragmented and researcher-biased. • **Methodology:** Current PI guidelines and outcome measures were systematically reviewed. Thematically derived domains informed development of a new evaluation checklist—EPIC—co-designed with PI input. Initial testing was conducted by a researcher and PI member within the COB-MS feasibility trial. • **Results:** EPIC produced dual researcher and PI versions, with three subscales: Policy & Practice, Participatory Culture, and Influence & Impact. Findings support EPIC as a comprehensive, theory-grounded assessment tool. • **Conclusions:** EPIC addresses limitations of prior tools, offering a robust framework to evaluate and report PI in interventional MS research.
25 Sep 2025	The risk of Progression Independent of Relapse and MRI activity in Pediatric- and Adult-onset MS treated with Natalizumab in later disease phase.	Margherita Passamonti	• **Introduction:** Natalizumab (NTZ) ablates relapses/MRI activity in pediatric-onset MS (POMS), but its effect on progression independent of relapse/MRI activity (PIRMA) is unclear. • **Methodology:** Retrospective–prospective cohort with 4:1 propensity matching (AOMS:POMS) on key covariates; EDSS/MRI every 6 months; re-baseline at month 6; survival/Cox models for PIRMA. • **Results:** 35 POMS vs 140 AOMS. After 6 months of NTZ, no relapses/MRI activity, yet PIRMA occurred in 25.7% POMS and 30% AOMS (log-rank p=0.812). Baseline EDSS predicted PIRMA (POMS HR 1.618, p=0.024; AOMS HR 1.581, p<0.01); AOMS disease duration also (HR 1.04, p=0.014). PIRMA trended earlier in POMS (p=0.056). • **Conclusions:** NTZ curtails RAW but not PIRMA; baseline disability drives risk, underscoring unmet neurodegeneration targets.

Notable Presentations At ECTRIMS 2025
Patient Experience, Surveys & Health Literacy (3/5)

Date	Title	Author	Summary
All days	Patient and carer perspectives related to research priorities and clinical trials in MOG antibody-associated disease: a survey and focus group study	Isabella Cotter	• **Introduction:** MOGAD patient/caregiver perspectives are under-studied; no Class I therapeutic evidence exists. • **Methodology:** Co-designed online survey via three international support groups plus three clinician-moderated focus groups of adults and parents assessed priorities and trial acceptability. • **Results:** Respondents=105 (81 adults, 24 parents). Top priorities: cure, optimal treatments, etiology, symptom relief, relapse prevention. Placebo-trial willingness rose with enhanced monitoring (overall 33%→66%; adults 37%→69%; parents 35%→59%). Outcomes prioritized: vision (91%), relapse prevention (89%), walking (81%), pain (75%), biomarkers (68%), work/school (64%). Trial burden acceptable to 95%. • **Conclusions**: Stakeholder co-design, functional endpoints, and explicit relapse-management pathways improve MOGAD trial acceptability; insights informed STAR-MOG.
All days	The Patient Experience of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease Post-Diagnosis: Results from an International Survey	Jonathan D. Santoro	• **Introduction:** Post-diagnosis experiences in MOGAD are poorly defined; unmet needs likely affect patients and caregivers. • **Methodology:** A 57-item online survey (Oct–Dec 2024) via The MOG Project/SRNA captured access, satisfaction, and burden from adults (≥16y) and caregivers of adults/children. • **Results:** n=261 (219 adults; 42 child cases). Treatment discontinuation: adults 43%, children 42%. Access difficulties: adults 73%, children 64%. Dissatisfaction: financial support (adults 36%, children 38%), adult chronic-symptom care 35%, child psychological support 31%. Caregivers reported far higher mental-health impact than patients (92% vs 26%, $p<0.01$). • **Conclusions:** Significant access, tolerability, and support gaps persist; caregiver mental health needs targeted services.

Notable Presentations At ECTRIMS 2025
Patient Experience, Surveys & Health Literacy (4/5)

Date	Title	Author	Summary
All days	Health Literacy in Neuromyelitis Optica Spectrum Disorder: Results from a Global Online Survey	Francesco Pastore	• **Introduction:** NMOSD causes severe disability; specialized nursing and digital literacy are pivotal for navigation and communication. • **Methodology:** Cross-sectional online survey (Sep-2024–Jan-2025) via patient associations; validated HL-DIGI domains (HI, D, INT), HL-NAV, HL-COM; HLS-EU 0–10 scoring; USA–Europe comparisons. • **Results:** n=149; 85.9% female; mean EDSS 3.0. Subtypes: AQP4 51.7%, MOG 30.9%, seronegative 17.4%. Rituximab 45.6%. Nurse access 60.4%; care satisfaction 85.2%. USA outperformed Europe in HL-DIGI-D (p=0.03), HL-NAV (p=0.049), HL-COM (p=0.050). Digital navigation correlated with communication (r=0.435, p<0.01). • **Conclusions:** Substantial digital/navigation needs persist, with US–EU disparities. Strengthened nurse education, digital training, and access pathways may improve global NMOSD support.
All days	The current use of Glial fibrillary acidic protein (GFAP) as an outcome in randomized clinical trials: a systematic review	Louise Chaboud	• **Introduction:** GFAP, a marker of astrocytic injury, is linked to MS progression and may reflect treatment response, but its clinical role is unclear. • **Methodology:** Systematic review of ClinicalTrials.gov, WHO ICTRP, PubMed, and Embase identified RCTs in pwMS reporting GFAP. Study designs, interventions, populations, and GFAP effects were extracted; absolute mean differences (AMD) calculated. Authors contacted for missing data; meta-analyses planned. • **Results:** 14 RCTs included (8 completed, 6 ongoing). GFAP measured mainly in serum. Median planned n=61. GFAP primary endpoint in 3 RCTs. Available data (n=5 RCTs) showed AMD range −39 to −1.5 pg/mL; siponimod reduced GFAP by 7.4 pg/mL (p<0.001). • **Conclusions:** GFAP use in RCTs is increasing. Early data suggest treatment-related reductions, supporting GFAP as a potential biomarker of therapeutic efficacy, pending confirmatory analyses.

Notable Presentations At ECTRIMS 2025
Patient Experience, Surveys & Health Literacy (5/5)

Date	Title	Author	Summary
All days	Identifying health-related quality of life domains to develop an item bank for multidimensional computerized adaptive testing in Multiple Sclerosis: results from a literature review and a qualitative study	Andrea Giordano	• **Introduction:** HRQoL is a central outcome in MS, but existing tools lack personalization. MCAT offers improved efficiency by tailoring assessments. • **Methodology:** A literature review informed four focus groups of PwMS and healthcare professionals in Italy, exploring HRQoL domains. Transcripts were analyzed via content analysis by independent researchers. • **Results:** Two themes emerged: HRQoL Domains (physical, psychological, social, work, financial) and Mediators (personal, health-related, life-related, relational, contextual). Work and financial domains were newly identified beyond literature. • **Conclusions:** Findings validate core HRQoL dimensions and highlight underexplored mediators, informing a tailored item bank for PwMS.

Notable Presentations At ECTRIMS 2025
Other / Mixed Mechanistic & Translational (1/5)

Date	Title	Author	Summary
24 Sep 2025	Fecal microbiota transplantation in patients with multiple sclerosis, a phase I study	Bob Van Oosten	• **Introduction:** The gut microbiome is implicated in MS pathogenesis; FMT offers a novel therapeutic approach. • **Methodology:** Ten MS patients (RRMS=3, PPMS=3, SPMS=4) received two FMTs from one screened donor via nasoduodenal tube after vancomycin and bowel prep. Clinical (EDSS, MRI), microbiota (16S sequencing), and biomarker (NfL, cytokines, lipid mediators) assessments were performed up to 6 months. • **Results:** FMT was safe; only one relapse occurred. Adverse events were mild. Microbiota shifted transiently but remained distinct from donor; richness/diversity unchanged. EDSS improved/stable in 8/10. NfL levels stable; MCP-1 rose significantly (p=0.03). Lipid mediator alterations observed. • **Conclusions:** FMT was safe with subtle immune effects but no sustained microbiota change. Larger, longer studies are needed to clarify clinical benefit.
25 Sep 2025	Escalation Treatment of the MS Relapse by Double-Dose Repeat Methylprednisolone versus Immunoadsorption: Results of the EMMA Trial	Florian Then Bergh	• **Introduction:** Escalation after inadequate IVMP for MS relapse commonly uses double-dose IVMP (d-IVMP) or immunoadsorption (IA) without RCT evidence. • **Methodology:** Publicly funded, randomized, evaluator-blinded trial (1:1 IA×5 sessions vs cumulative 10 g IVMP) in acute relapse ≤28 days with persistent ADL impairment ≥7 days post-IVMP. Primary: EDSS at day 45 (ANCOVA). Optic neuritis (ON) visual acuity prespecified. Underpowered (29/140 FAS) due to pandemic and funding constraints. • **Results:** Overall EDSS change at day 45: no significant IA–d-IVMP difference. ON subgroup: greater visual acuity gains with IA to day 180. SAEs: IA 4 vs d-IVMP 1; all resolved. • **Conclusions:** IA and d-IVMP are feasible; IA may benefit ON. Underpowered results warrant larger trials

Notable Presentations At ECTRIMS 2025
Other / Mixed Mechanistic & Translational (2/5)

Date	Title	Author	Summary
25 Sep 2025	High-Dose N-Acetyl Cysteine Stabilizes GFAP Levels: Results from a Pilot Double-blind, Placebo-Controlled Randomized Trial	Vinicius Schoeps	• **Introduction:** Oxidative stress contributes to progression in non-active progressive MS. N-acetyl cysteine (NAC) is a potent antioxidant that replenishes neuronal glutathione and may mitigate injury. • **Methodology:** In a double-blind phase 2 pilot, PMS patients (n=15) were randomized 2:1 to NAC 1250 mg TID or placebo for 4 weeks. Serum biomarkers (GFAP, NfL, cytokines, lipid mediators) were measured via Olink® multiplex assay; Wilcoxon tests compared groups. • **Results:** In a double-blind phase 2 pilot, PMS patients (n=15) were randomized 2:1 to NAC 1250 mg TID or placebo for 4 weeks. Serum biomarkers (GFAP, NfL, cytokines, lipid mediators) were measured via Olink® multiplex assay; Wilcoxon tests compared groups. • **Conclusions:** Short-course NAC reduced astrocytic injury marker GFAP and modulated immune pathways. Larger, longer trials are warranted to validate neuroprotective potential in PMS.
All days	Effect of Immunomodulatory Therapies on Imaging Measures of Remyelination in the ADVANCE and ASCEND Trials	Bastien Caba	• **Introduction:** Remyelination is an unmet need in MS. Current immunotherapies may influence repair beyond immune modulation. • **Methodology:** MRI data from ADVANCE (RMS, n=1512) and ASCEND (SPMS, n=889) were analyzed. Chronic T2 lesions >3 mm from enhancing areas were assessed. T1w/T2w ratio change from week 24 to study end was modeled, adjusting for age, sex, baseline MRI, and ventricular distance. • **Results:** Peginterferon β-1a (p=0.02) and natalizumab (p=0.046) promoted T1w/T2w recovery. Effects were strongest in deep white matter, early lesions (<1 year), and younger patients with less baseline damage. • **Conclusions:** Immunomodulators may promote remyelination, particularly in young, less damaged chronic lesions.

Notable Presentations At ECTRIMS 2025
Other / Mixed Mechanistic & Translational (3/5)

Date	Title	Author	Summary
All days	Twelve-week intermittent hypoxia intervention in multiple sclerosis – a phase II pilot trial	Sina Cathérine Rosenkranz	• **Introduction:** Intermittent hypoxia may enhance neuronal energy metabolism and resilience in MS, inspired by adaptive responses to high-altitude hypoxia. • **Methodology:** Phase Ia pilot, single-arm trial in progressive MS (n=12; EDSS ≤6.5). Intervention: 12 weeks, 2–3 weekly 2-hour sessions simulating altitudes up to 4500 m (FiO_2 11%). Primary endpoint: high-altitude sickness (Lake Louise Score). Secondary: disability, cognition, PROs, MRI, immune markers, serum NfL/metabolites. • **Results:** Ten completed. No moderate/severe altitude sickness or systemic safety issues. Improvements observed: 9-HPT dominant hand (p=0.01), T25FW (p<0.01), SDMT (p=0.028). Other markers stable. • **Conclusions:** Intermittent hypoxia was safe, well-tolerated, and associated with functional gains, supporting larger trials.
All days	Real-world clinical outcomes with eculizumab and ravulizumab in anti-aquaporin-4 antibody-positive (AQP4-Ab+) neuromyelitis optica spectrum disorder (NMOSD): results from the global NMO SPOTLIGHT Registry	Elias Sotirchos	• **Introduction:** Eculizumab and ravulizumab are approved for AQP4-Ab+ NMOSD; real-world registry data strengthen trial evidence. • **Methodology:** The global NMO SPOTLIGHT Registry (since Aug 2023) includes adults on ALXN-C5ITs, assessing relapse rates, vaccination, and infections. • **Results:** Among 56 patients (89% female, median diagnosis age 46.5y), relapse rates fell from ARR 0.50 pre-treatment to 0.02 on therapy; none had >1 relapse. RTX-switchers relapsed pre-switch but none post-switch. Ninety-three percent were vaccinated; no meningococcal infections occurred. • **Conclusions:** Registry data confirm robust relapse prevention and favorable safety of C5 inhibitors in real-world NMOSD.

Notable Presentations At ECTRIMS 2025
Other / Mixed Mechanistic & Translational (4/5)

Date	Title	Author	Summary
All days	The effects of probiotics supplementation on fatigue in relapsing-remitting multiple sclerosis; a randomized double-blinded placebo-controlled trial	Amirreza Naseri	• **Introduction:** Gut microbiome alterations may modulate inflammation and oxidative stress in MS. Probiotics are hypothesized to reduce fatigue, a key RMS symptom • **Methodology:** In a double-blind RCT, RMS patients (EDSS<4) received either probiotics (Lactocare®, twice daily) or placebo for four months. Fatigue and related domains were assessed using the MS-CFAB scale at baseline and follow-up. • **Results:** Of 90 randomized, 60 completed. Probiotics did not significantly affect fatigue or overall health (all p>0.05). Placebo improved stress (p=0.01) and anxiety (p=0.01). Probiotics improved the nutrition index (p=0.02). Intragroup changes were minor and not clinically significant. • **Conclusions:** Four-month probiotic supplementation failed to improve fatigue in RMS, though nutritional indices improved modestly. Larger trials are needed.
All days	Tailored follow-up for persons with multiple sclerosis to optimize physical functions, health and employment: a prospective single-blinded randomized controlled trial	Ellen Christin Arntzen	• **Introduction:** PwMS often experience motor, activity, and employment challenges despite mild–moderate disability, with limited evidence for integrated interventions. • **Methodology:** CoreDIST, a multicenter RCT (n=115, EDSS 0–4), compared CoreDIST vs standard care. Intervention included education, physiotherapy, employment support, supervised group training, and digital home training. Outcomes: MSWDQ-23, ActiGraph, balance, walking, fatigue, HRQoL. • **Results:** At 16 weeks, CoreDIST improved MSWDQ-23 (p=0.02), MSIS-29 (trend, p=0.06), and TIS-modNV (p=0.047). Physical activity/force platform data are pending. • **Conclusions:** Preliminary findings show CoreDIST enhances work and functional outcomes in PwMS; 52-week results due 2025.

Notable Presentations At ECTRIMS 2025
Other / Mixed Mechanistic & Translational (5/5)

Date	Title	Author	Summary
All days	Investigating Adverse Event Reporting in Rehabilitation Randomised Controlled Trials for People with Multiple Sclerosis	Laura Carey	• **Introduction:** MS rehabilitation aims to improve function and quality of life, but adverse event (AE) reporting in RCTs remains inconsistent, with limited methodological guidance. • **Methodology:** A systematic review searched 15 databases (Jan 2010–Jan 2025) for RCTs of MS rehabilitation. Independent dual screening and thematic analysis were applied to extract and synthesize AE collection, classification, and reporting methods. • **Results:** From 1073 records, 92 RCTs are undergoing full-text screening and data extraction. Early findings highlight widespread variability in AE reporting practices, with final results expected by summer 2025. • **Conclusions:** This review will clarify AE methodology in MS rehabilitation RCTs, strengthening transparency and trial reliability. Findings will inform complementary qualitative and Delphi studies within a PhD program.

Key Industry Sponsored Sessions Information

ECTRMIS 2025 Key Industry Sponsored Sessions Information (1/4)

Date	Sponsor	Title
24 Sep 2025	Novartis	Early Intervention, Long-Term Impact: A Kesimpta▼ (ofatumumab) Case Study
24 Sep 2025	Roche	NMOSD and MOGAD – What's age got to do with it?
24 Sep 2025	Bristol Myers Squibb	Ozanimod, Separating from the Crowd, Insights on Safety
24 Sep 2025	Roche	Paediatric-onset MS: Advancements and unmet needs in early-onset disease
24 Sep 2025	Roche	Beyond the Raw Number: Unlocking Individualized Insights with NfL Z-Scores in MS
24 Sep 2025	Roche	Protecting Brain Health in MS: Modern Strategies for Medical Practice
24 Sep 2025	Sanofi	Stripped Back: CNS Inflammation & The Potential For Meaningful Therapeutic Progress in Non-Relapsing Forms of Multiple Sclerosis

ECTRMIS 2025 Key Industry Sponsored Sessions Information (2/4)

Date	Sponsor	Title
24 Sep 2025	Roche	How anti-CD20 therapies have shaped our understanding of MS and sparked future innovations
24 Sep 2025	Merck	Breaking the MS barrier: moving toward optimal disease control
24 Sep 2025	Juvisé Pharmaceuticals	The Evolution of S1PR Modulators in RMS: a journey through time and evidence
25 Sep 2025	Amgen	Unmasking NMOSD: Biomarkers, Imaging, and Targeting CD19+ B cells
25 Sep 2025	Alexion, AstraZeneca	Complement Component 5 Inhibitor Therapies (C5ITs) in Neuromyelitis Optica Spectrum Disorder (NMOSD): Clinical Insights and Real-World Evidence
25 Sep 2025	Chugai	Optimizing Satralizumab Use in NMOSD: Insights from Pathogenesis to Global Clinical Experience
25 Sep 2025	Bristol Myers Squibb	Resetting Immunity: CAR T Cell Therapy in MS

ECTRMIS 2025 Key Industry Sponsored Sessions Information (3/4)

Date	Sponsor	Title
25 Sep 2025	Alexion AstraZeneca	Evolving paradigms in the diagnosis and management of patients with AQP4-Ab+ NMOSD
25 Sep 2025	Roche	Is MS one disease?
25 Sep 2025	Roche	From Data to Practice: Exploring Subcutaneous OCREVUS
25 Sep 2025	UCB	Can you RECOGNISE IT? Highlighting Unmet Needs in MOGAD
25 Sep 2025	Novartis	Keeping up with the evolution of MS: Are we using anti-CD20s early enough?
25 Sep 2025	Sanofi	Navigating the New Era of Therapeutic Strategies for MS Disability Accumulation
25 Sep 2025	Merck Healthcare KGaA	Practicality of the 2024 McDonald diagnostic criteria

ECTRMIS 2025 Key Industry Sponsored Sessions Information (4/4)

Date	Sponsor	Title
26 Sep 2025	Sandoz	Balancing Risk and Care: JCV Stratification in the Pursuit of Optimal MS Management
26 Sep 2025	Sanofi	Innovating Disability Measurement in Multiple Sclerosis

Noteworthy AI / ML presentations at ECTRIMS 2025

Themes from key AI / ML presentations at ECTRIMS 2025 (1/4)

- **ECTRIMS 2025 is set to fuse harmonized imaging, causal inference, and biomarker analytics to design smaller, faster, more inclusive MS trials with progression-focused, AI-readable endpoints**
- Check out the key AI / ML themes at ECTRIMS 2025 below:
- **AI MRI harmonization (U-Net3+, NO.MS trials)**
  - This CNN approach is expected to boost multicenter T1 quality: intensity non-uniformity +19.4%, CJV +21.6%, CNR +14.7% vs N4 across 147 scans, enabling cleaner downstream analytics
- **Auto T2-lesion segmentation (U-net)**
  - The tool is expected to deliver ICC 92–94%, voxel F1 0.73, and 10-second processing, outperforming prior methods by ~6% across heterogeneous trial MRIs
- **Synthetic-data generalization (ISBI, in-house)**
  - Domain-randomized training is set to reach Dice 0.74/0.52 (longitudinal/cross-sectional) on ISBI FLAIR and 0.83/0.41 in-house, reducing re-training across modalities

Themes from key AI / ML presentations at ECTRIMS 2025 (2/4)

- **Transformer lesion models (ISBI2015, MSEG16)**
  - SwinUNETR/SegMamba are projected to deliver Dice ≈0.66 on FLAIR and ≈0.57 on T1; combined T1/FLAIR should surpass LST-AI and Samseg
- **Choroid plexus segmentation (UNETR)**
  - UNETR is poised to robustly address MS lesion segmentation across modalities; Dice 0.84 with MPRAGE+FLAIR and 0.81 with MP2RAGE+FLAIR, standardizing CP volumetry for inflammation studies
- **Spatial lesion "MoCos" risk modeling**
  - Seven co-occurrence patterns are expected to outperform total lesion volume, with six predicting progression via Cox models in a 200-patient cohort
- **Progression prediction (multicenter n=1,176)**
  - A random-forest model should predict 2-year progression at 83% accuracy (AUC 0.85) and 5-year at 74% (AUC 0.74), supporting precision monitoring
- **RMS→SPMS transition forecasting (MSBase, Swedish registries)**
  - Conformal-prediction random forests are set to reach F1 0.83, enabling earlier, transparent SPMS identification for harmonized diagnostic triggers

Themes from key AI / ML presentations at ECTRIMS 2025 (3/4)

- **DMD failure prediction (n=865)**
  - XGBoost/Random Forest models are projected to achieve AUC 0.70–0.78, with 1-year on-therapy data expected to sharpen relapse, new T2, and CSDW predictions
- **Cladribine response DL (CLARIFY-MS, MAGNIFY-MS)**
  - Deep models should predict 4-year EDSS/SDMT improvement with an accuracy of 0.76 and an AUC of 0.68, outperforming logistic regression
- **Remote EDSS estimation via PROMs**
  - A Random Forest is expected to yield MSE 0.42 and R^2 0.89, keeping 90% predictions within ±1 EDSS for telemedicine
- **Serum omics DL diagnosis (n=1,892)**
  - DenseNet121 classifiers should post AUC 0.73, F1 0.67, and specificity 0.74, delivering interpretable, early diagnostic support
- **EBV antibody classifiers (n=1,300)**
  - Random forests are set to reach AUC 0.75; LASSO will prioritize 21 antibodies, advancing pre-clinical risk stratification

Themes from key AI / ML presentations at ECTRIMS 2025 (4/4)

- **Neurocognitive decline prediction (ResNet+clinical)**
  - A hybrid network is projected to achieve F1 0.81, accuracy 0.89, and AUC 0.87 at one year, guiding targeted cognitive interventions
- **AssistMS pragmatic AI trial (icobrain-ms, UK)**
  - A 136-patient RCT is expected to quantify AI impact on DMT decisions, resource use, and QoL using microsimulation-anchored health economics
- **Smartphone longitudinal endpoints (APS-MS, 5.3y)**
  - sSDMT and KD-CSC trajectories should reveal cognitive change with stable motor metrics, motivating linkage to MRI and clinical progression

Noteworthy AI / ML presentations at ECTRIMS 2025

Notable Presentations At ECTRIMS 2025
AI / ML (1/15)

Date	Title	Author	Summary
24 Sep 2025	Pregnancy and Future Disability in MS: Can Machine Learning Help Predict the Trajectory?	Murat Emec	• **Introduction**: This study integrates machine learning (ML) models to predict disability in women with MS (wMS) post-pregnancy, using pregnancy-related variables to enhance EDSS prediction. • **Methodology:** A retrospective analysis of wMS with one pregnancy, using clinical, demographic, and pregnancy-related data. ML models (CatBoost, XGBoost, Random Forest, Decision Tree) were trained to classify EDSS categories. • **Results:** CatBoost with hyperparameter tuning achieved the highest accuracy and F1 score. Key predictors: disease course, age, breastfeeding status, pre/post-pregnancy EDSS. • **Conclusions:** ML models, particularly CatBoost, effectively predict post-pregnancy disability, highlighting the importance of pregnancy-related factors.
24 Sep 2025	An Automated Deep Learning Segmentation Tool for Accurate and Generalizable MS Lesion Quantification	Yang Sun	• **Introduction**: This study develops a deep learning tool for automated segmentation of T2 lesions in MS patients, addressing the limitations of manual and semi-automated methods. • **Methodology:** A U-shaped network model was trained on diverse MRI scans. The tool was validated using central MRI reader results from clinical trials. • **Results:** The model achieved 92-94% T2 lesion volume ICC and a voxel-level F1 score of 0.73, outperforming existing tools by 6%. It segments images in 10 seconds. • **Conclusions:** The deep learning tool efficiently segments T2 lesions, aligning with semi-automated methods and demonstrating robust performance across various MRI protocols.

Notable Presentations At ECTRIMS 2025
AI / ML (2/15)

Date	Title	Author	Summary
24 Sep 2025	Unifying longitudinal and cross-sectional MS lesion segmentation within the same modality-agnostic deep learning model	Vicent Caselles-Ballester	• **Introduction**: This study addresses challenges in MS lesion segmentation on MRI, focusing on variability caused by scan modality and segmentation settings. Current methods struggle with generalization across different contexts. • **Methodology:** The study introduces a synthetic data generation approach, using lesion masks and domain randomization for MRI scans with varied contrasts. A UNet model was trained on synthetic data to segment lesions in both longitudinal and cross-sectional settings. • **Results:** The model achieved the best performance on FLAIR scans: Dice scores of 0.74 (long.) and 0.52 (CS) on ISBI dataset, and 0.83 (long.) and 0.41 (CS) on in-house data. • **Conclusions:** This method successfully segments lesions across multiple settings and modalities without re-training, breaking conceptual barriers in MS imaging.
24 Sep 2025	PREDICTING DEVELOPMENT OF NEUROCOGNITIVE DISORDERS IN MULTIPLE SCLEROSIS USING ARTIFICIAL INTELLIGENCE: COMBINING MRI AND CLINICAL DATA	Loredana Storelli	• **Introduction**: This study develops an AI neural network to predict neurocognitive disorders (NDs) in MS patients after one year of follow-up, using baseline clinical, demographic, and MRI data. • **Methodology:** A deep learning model combined ResNet-extracted MRI features with clinical data to classify cognitive stability. The model's performance was evaluated using 5-fold cross-validation. • **Results:** The model achieved an F1 score of 0.81, accuracy of 0.89, and AUC of 0.87, with no bias toward stable patients. • **Conclusions:** AI can effectively predict ND development in MS, enabling timely intervention.

Notable Presentations At ECTRIMS 2025
AI / ML (3/5)

Date	Title	Author	Summary
24 Sep 2025	Interpretable Machine Learning Models for Longitudinal Monitoring of Multiple Sclerosis Disability Progression	Federica Di Antonio	• **Introduction**: Predicting disability progression in multiple sclerosis (MS) is challenging due to its variability. Machine learning (ML) offers a promising approach to support clinical decision-making, complementing traditional prognostic markers. • **Methodology:** A random forest model was developed using a multicenter dataset of 1,176 MS patients. The model predicted disability progression based on baseline data, including patient-reported outcomes, clinician-assessed outcomes, and demographics. Performance was evaluated using accuracy, AUC, and Kaplan-Meier survival analysis. • **Results:** The model accurately predicted disability progression at 2 years (83%, AUC 0.85) and 5 years (74%, AUC 0.74), with Kaplan-Meier curves showing strong agreement. • **Conclusions:** The ML model provides a useful, explainable tool for long-term MS monitoring, improving clinical adoption and supporting personalized care.
24 Sep 2025	Machine Learning models for treatment response prediction in MS with clinical and MRI data	Ariadna Masot Llima	• **Introduction**: Predicting individual responses to disease-modifying drugs (DMDs) in multiple sclerosis (MS) is challenging due to heterogeneity in disease progression. Early prediction of unfavorable outcomes remains an unmet need. • **Methodology:** The study developed ML models using real-world data from 865 MS patients on DMDs. Three models (Logistic Regression, Random Forest, XGB) were trained with baseline and 1-year on-DMD data to predict new T2 lesions, relapses, and confirmed disability worsening (CSDW). • **Results:** XGB and RF models achieved AUCs of 0.70 and 0.78 for moderate and high efficacy DMDs, respectively. Adding 1-year data improved predictions. • **Conclusions:** ML models effectively predict DMD treatment failure, with improved accuracy using 1-year data, especially for high efficacy DMDs.

Notable Presentations At ECTRIMS 2025
AI / ML (4/15)

Date	Title	Author	Summary
24 Sep 2025	Telerehabilitation for Multiple Sclerosis: Artificial Intelligence vs Conventional Approaches in Strength Training. A Single-Blinded Randomized Clinical Trial.	Lucia Ortega-Carrion	• **Introduction**: Multiple sclerosis (MS) is a neurodegenerative, immune-mediated disease with symptoms like muscle weakness, fatigue, and balance issues. Exercise, particularly strength training, improves motor symptoms, and AI-powered tele-exercise is emerging as a potential treatment. • **Methodology:** A randomized, longitudinal trial with 58 participants compared an AI-based tele-exercise group (RehBody app) with a traditional exercise control group. Maximal strength, endurance, walking endurance, and fatigue impact were measured at baseline, 10 weeks, and 20 weeks. • **Results:** Both groups showed significant improvements in squat strength. The experimental group showed non-significant improvement in walking endurance and fatigue impact. • **Conclusions:** AI-powered tele-exercise showed similar outcomes to traditional methods, suggesting it could be a valid alternative. Further research is needed to optimize its implementation for MS patients.
25 Sep 2025	From Data to Diagnosis: Harmonizing RRMS and SPMS Classification via AI Models on Global and National Scales	Akshai Parakkal Sreenivasan	• **Introduction**: Timely identification of the transition from relapsing-remitting MS (RMS) to secondary-progressive MS (SPMS) is critical for early intervention. However, this transition is often diagnosed with a significant delay. • **Methodology:** The study developed AI models using data from the MSBase and Swedish MS registries. Random forest classifiers were trained to predict disease progression using patient data, incorporating conformal prediction and explainable AI for transparent predictions. • **Results:** The global model achieved an F1 score of 0.83, outperforming country-specific models in several regions. Clustered models showed improved local accuracy. • **Conclusions:** AI models can predict RMS to SPMS transition with high accuracy and transparency, supporting harmonized diagnostic standards and enhancing clinical trials.

Notable Presentations At ECTRIMS 2025
AI / ML (5/15)

Date	Title	Author	Summary
25 Sep 2025	Using Deep Learning on baseline MRI data for highly accurate prediction of cladribine tablets-treated MS patients who improve physical and cognitive disability in 4 years	Marco Battaglini	• **Introduction**: Cladribine tablets (CladT) improve disability in relapsing-remitting MS (pwMS). This study tests deep learning (DL) models to predict clinical improvements at 4 years. • **Methodology:** MRI data from the CLARIFY-MS and MAGNIFY-MS studies were used. Clinical improvements in EDS and SDMT were predicted using DL and compared with logistic regression. • **Results:** DL models outperformed logistic regression, achieving better accuracy (0.76 vs. 0.5) and AUC (0.68 vs. 0.56) for EDS and SDMT. • **Conclusions:** DL models predict physical and cognitive improvements more accurately, aiding personalized MS treatment strategies.
25 Sep 2025	Predicting Disability Progression in Multiple Sclerosis based on Modes of Lesion Co-Occurrence using Probabilistic Machine Learning	George Hutchings	• **Introduction**: MRI lesions are key markers of MS severity, but traditional metrics like total lesion volume ignore lesion location and spatial patterns, limiting their correlation with clinical outcomes. • **Methodology:** A novel probabilistic dimensionality reduction method was developed to identify lesion co-occurrence patterns (MoCos). Data from 200 MS patients were used to derive MoCos, which were linked to disability progression using Cox proportional hazards models. • **Results:** 7 MoCos were identified, with 6 significantly predicting disability progression. Traditional lesion volume failed to predict progression, while MoCos in specific brain regions showed strong associations with clinical outcomes. • **Conclusions:** MoCos outperformed lesion volume in predicting disability progression, highlighting the importance of spatial lesion patterns for understanding MS.

Notable Presentations At ECTRIMS 2025
AI / ML (6/15)

Date	Title	Author	Summary
25 Sep 2025	A transformer-based deep learning approach for accurate MS lesion segmentation from individual and multimodal MRI	SpaiFrancesc Vivò Pascual	• **Introduction**: Lesion segmentation in MS neuroimaging is critical, but current methods typically require both T1-weighted and FLAIR images, limiting single-modality use. • **Methodology:** A deep learning framework was developed using Vision Transformer (ViT)-based models, SwinUNETR and SegMamba, for accurate MS lesion segmentation from T1w, FLAIR, or combined T1w/FLAIR images. The framework included preprocessing steps and model validation on ISBI2015 and MSEG16 datasets. • **Results:** SwinUNETR and SegMamba showed strong performance with FLAIR (Dice: 0.658, 0.63) and T1 (Dice: 0.57, 0.531). Combined T1w/FLAIR models outperformed LST-AI and Samseg (Dice: 0.6595, 0.654). • **Conclusions:** Our models robustly address MS lesion segmentation across modalities, outperforming established methods and confirming accuracy on open challenge datasets.
25 Sep 2025	Towards Personalized MS Diagnostics and Prognostics: A Deep Learning Framework Using Serum Metabolomics and Lipidomics	Sweden	• **Introduction**: Early MS diagnosis and progression prediction remain challenges. Deep learning (DL) applied to metabolomics and lipidomics offers potential for improvement. • **Methodology:** Serum samples from 934 MS patients and 958 controls were analyzed. A DenseNet121-based model was trained to distinguish MS from controls using metabolomics and lipidomics data, with conformal prediction and explainable AI for transparency. • **Results:** The model achieved an AUC of 0.73, F1 score of 0.67, precision of 0.70, recall of 0.63, and specificity of 0.74. • **Conclusions:** DL with omics data provides a promising, interpretable method for early MS diagnosis and progression prediction.

Notable Presentations At ECTRIMS 2025
AI / ML (7/15)

Date	Title	Author	Summary
25 Sep 2025	Predicting silent progression in multiple sclerosis using brain, retinal, and serum biomarkers through supervised machine learning	Alberto Calvi	• **Introduction**: Multiple sclerosis (MS) disability progression, independent of relapse activity (PIRA), is clinically silent and heterogeneous, necessitating multi-modal biomarker integration for improved prediction. • **Methodology:** A longitudinal study of 131 MS patients analyzed brain MRI, retinal OCT, and serum biomarkers. Logistic regression with ridge regularization was used to classify PIRA status, and models were compared using AUC metrics. • **Results:** The MRI-OCT model achieved an AUC of 0.73 ± 0.12, outperforming MRI alone (AUC: 0.65). The MRI-OCT-serum model further improved prediction (AUC: 0.79 ± 0.10). • **Conclusions:** Multi-modal ML models incorporating MRI, OCT, and serum biomarkers offer superior prediction of PIRA, enhancing early detection and intervention strategies in MS.
All days	Analytical artificial intelligence in the study of cognitive impairment in multiple sclerosis: a scoping review of existing gaps and future directions	Beyza Ciftci	• **Introduction**: Cognitive impairment in MS is heterogeneous and disabling. AI techniques offer potential for improving assessment and understanding cognitive profiles. • **Methodology:** A scoping review followed PRISMA guidelines, searching PubMed and Web of Science for AI applications in MS cognitive impairment, excluding reviews and non-English papers. • **Results:** 31 studies with 6,780 participants were included. Most studies used MRI features, with some incorporating clinical and demographic data. Cognitive impairment prediction was the primary outcome. • **Conclusions:** AI is effective for predicting cognitive impairment but limited by small sample sizes and inconsistencies. Larger, standardized studies are needed.

Notable Presentations At ECTRIMS 2025
AI / ML (8/15)

Date	Title	Author	Summary
All days	Defining composite markers to predict EDSS progression in SPMS by artificial intelligence	Ásta Theódórsdóttir	• **Introduction**: Composite markers are hypothesized to predict progression better than single features, with their definition varying based on disability levels. • **Methodology:** A study of 61 SPMS patients classified as stable or with EDS worsening over 24 months. AI models, including Random Forest and logistic regression, evaluated 29 features such as clinical measures, cognition, biomarkers, MRI metrics, and PROs. • **Results:** For moderate disability (EDS 3.5-4.5), AI achieved 67% accuracy with ≤3 features. For advanced disability (EDS ≥5.0), accuracy was 80% with 2-5 features. Key predictors included cognition, PROs, and MRI features. • **Conclusions:** AI-defined composites outperformed single features in predicting SPMS progression, with differences based on disability level.
All days	Predicting EDSS scores using patient-reported outcomes and baseline clinical data in multiple sclerosis: a machine learning approach	Carolina Díaz-Pérez	• **Introduction**: EDS is the gold standard for MS disability assessment, but its in-person requirement limits telemedicine. Combining PROMs with clinical data could enable remote EDS prediction. • **Methodology:** Data from 240 MS patients were analyzed, combining PROMs (MSIS-29, FS, HAQ, Neuro-QoL) and clinical data. Various regression models were trained, and performance was evaluated using MSE and R^2. • **Results:** The Random Forest model achieved an MSE of 0.42 and R^2 of 0.89, with 90% of predictions having an error ≤1 EDS point. • **Conclusions:** PROMs and clinical data can reliably estimate EDS, supporting their use in telemedicine.

Notable Presentations At ECTRIMS 2025
AI / ML (9/15)

Date	Title	Author	Summary
All days	Predicting multiple sclerosis onset using EBV-related antibodies and machine learning methods in Swedish population	Ingrid Kockum	• **Introduction**: EBV infection is implicated in MS pathogenesis, with molecular mimicry potentially triggering cross-reactive antibodies that target CNS proteins and myelin, contributing to MS development. • **Methodology:** Serum samples from 650 MS patients and 650 healthy controls were analyzed for IgG reactivity against three candidate proteins. Predictive models were built using antibody levels and machine learning techniques, including logistic regression, LASO, and random forest. • **Results:** Initial models achieved an accuracy of 0.65, with random forest models improving AUC to 0.75. LASO regression identified 21 antibodies with similar performance. • **Conclusions:** EBV-related antibodies show promise for early MS prediction, and further refinement using advanced machine learning techniques is needed to improve diagnostic accuracy.
All days	Using fMRI machine learning and structural brain connectomics to identify neurobehavioral mechanisms of fear and anxiety in multiple sclerosis	Lil Meyer-Arndt	• **Introduction**: Anxiety is common in MS, but its neurobehavioral mechanisms remain unclear. This study examines fear generalization in MS-related anxiety. • **Methodology:** The study involved 18 PwMS with anxiety, 36 PwMS without anxiety, and 23 healthy controls. fMRI and diffusion-weighted MRI were used to assess fear generalization and brain connectivity. • **Results:** PwMS with anxiety showed fear overgeneralization. Machine learning models predicted fear responses accurately, revealing altered brain activity in regions like the hippocampus and amygdala. • **Conclusions:** Fear overgeneralization is a key mechanism in MS-related anxiety, driven by generic fear mechanisms rather than MS-specific factors.

Notable Presentations At ECTRIMS 2025
AI / ML (10/15)

Date	Title	Author	Summary
All days	Automated MS Lesion Detection with NeuroQuant: Comparing the Hybrid Machine and Deep Learning Version to Its Predecessor	Wibeke Nordhøy	• **Introduction**: NeuroQuant MS (NQ-MS) software detects and analyzes MS lesions. Version 4.0 integrates machine and deep learning (ML/DL) algorithms to enhance lesion detection compared to its predecessor. • **Methodology:** Fifty-one MS subjects underwent scans with NQ-MS-compatible data. Lesion detection volume was set to 3 m^3, and sensitivity thresholds were applied. Results were reviewed by an MS-specialized neuroradiologist. Statistical analysis compared both NQ-MS versions. • **Results:** Version 4.0 showed higher lesion counts and volumes, except for periventricular lesions. Visual inspections showed more precise lesion segmentation, with no significant visual differences after adjusting sensitivity. • **Conclusions:** Version 4.0, with ML/DL integration, demonstrated higher sensitivity and improved lesion detection, highlighting advancements in MS lesion analysis.
All days	Deep learning-based Segmentation of the Choroid Plexus in Multiple Sclerosis Using MPRAGE, FLAIR, and MP2RAGE	Po-Jui Lu	• **Introduction**: The choroid plexus (CP) appears enlarged in MS, but in vivo CP segmentation is time-consuming. Deep learning (DL) tools could enhance automatic CP segmentation on T1-weighted images. • **Methodology:** A DL model, UNETR, was developed for CP segmentation on T1w, MPRAGE+FLAIR, and MP2RAGE+FLAIR images. The model was trained on data from 17 PwMS and validated using 5-fold cross-validation and testing on two datasets. • **Results:** UNETR outperformed existing methods with Dice scores of 0.76 (MPRAGE), 0.84 (MPRAGE+FLAIR), and 0.81 (MP2RAGE+FLAIR). • **Conclusions:** UNETR achieved superior CP segmentation, especially with FLAIR, demonstrating strong applicability for MS analysis.

Notable Presentations At ECTRIMS 2025
AI / ML (11/15)

Date	Title	Author	Summary
All days	Comparing Deep Learning Models for MS Lesion Segmentation in Brain MRI: AClinically-Oriented Evaluation of UNet, CDCG-UNet, and Swin-UNet	Mert Fidan	• **Introduction**: Automated segmentation of MS lesions using deep learning is crucial for diagnosis and treatment but remains underexplored. • **Methodology:** This study compares UNet, CDCG-UNet, and Swin-UNet for MS lesion segmentation using MSEG 2016 and Shifts 2.0 datasets. Metrics like Dice score, IoU, Precision, Recall, and F1 score were used. • **Results:** Swin-UNet outperformed other models in all views, with the highest IoU and F1 scores across coronal, axial, and sagittal planes • **Conclusions:** Swin-UNet showed superior accuracy, making it a promising tool for MS lesion segmentation in clinical practice.
All days	AssistMS – Artificial intelligence-assisted magnetic resonance imaging for quality, efficiency and equity in the NHS care of multiple sclerosis	Klaus Schmierer	• **Introduction**: With over 130,000 people with MS in the UK, effective monitoring of disease activity is crucial for treatment optimization. Current MRI assessment methods are time-consuming and prone to error. Icobrain-ms, an AI technology, aims to improve this process. • **Methodology:** A randomized UK trial compares MRI assessments with and without icobrain-ms assistance. Health-economic analysis uses a microsimulation model. The study will measure impact on DMT prescribing, healthcare resource use, and quality of life. • **Results:** 136 participants will be recruited, with challenges in software installation at NHS sites overcome. • **Conclusions:** AssistMS will be the first UK trial of AI in MS MRI assessment, with broad support from the MS community.

Notable Presentations At ECTRIMS 2025
AI / ML (12/15)

Date	Title	Author	Summary
All days	Machine learning-based prediction of disability progression in multiple sclerosis using clinical, performance-based, and patient-reported outcomes	Zuhal Abasiyanik	• **Introduction**: Clinical predictors of disability progression in MS are well-established, but the role of patient-reported outcome measures (PROMs) remains underexplored. • **Methodology:** Data from 182 pwMS, including clinical, performance-based, and PROMs data, were used to develop a machine learning model for predicting disability progression over 3 years. • **Results:** Linear Regression performed best (MAE: 0.321, R^2: 0.951), followed by Random Forest (MAE: 0.347, R^2: 0.935). Decision Tree and SVR underperformed. • **Conclusions:** Linear Regression and Random Forest showed high accuracy, suggesting a strong linear relationship and robustness in predicting MS progression. Future work should explore hybrid models for improved accuracy.
All days	Artificial Intelligence Driven Prediction of Cognition Using Estimated Structural and Functional Connectivity in Multiple Sclerosis	Ceren Tozlu	• **Introduction**: MS causes cognitive and ambulatory impairment, with 40-65% of patients affected. Neuroimaging biomarkers, including structural and functional connectivity (eSC and eFC), offer potential for predicting cognitive decline and enabling personalized treatment. • **Methodology:** 171 MS patients were assessed using cognitive tests (SDMT, CVLT, BVMT). eSC and eFC were estimated using lesion masks and AI models. Ridge regression predicted cognition at baseline and 4-year follow-up, incorporating MRI metrics and demographics. • **Results:** The highest prediction accuracy for SDMT was achieved with regional eSC and eFC (r=0.58 and r=0.56). eFC in the default mode network was linked to lower SDMT scores. • **Conclusions:** eSC and eFC can effectively predict cognition, supporting personalized treatment strategies to preserve cognitive function in MS.

Notable Presentations At ECTRIMS 2025
AI / ML (13/15)

Date	Title	Author	Summary
All days	Machine learning-based prediction of new neurological lesions in multiple sclerosis using routinely collected clinical and patient-reported data	Carolina Díaz-Pérez	• **Introduction**: MRI is essential for detecting new lesions in MS, but its high cost and logistical demands necessitate optimizing its use. • **Methodology:** A cohort of 240 MS patients was followed for 18 months. Clinical data, PROMs, and baseline variables were used to train ML models (Random Forest, SVM, XGBoost) to predict new lesions, prioritizing sensitivity. • **Results:** The PROMs-based Random Forest model achieved 64% accuracy with 10% sensitivity and no false negatives. The AI-data model improved accuracy to 72%, maintaining perfect sensitivity. • **Conclusions:** ML models, particularly PROMs-based, can predict lesion risk, optimizing MRI use and reducing healthcare costs.
All days	The AIMS project - How Artificial Intelligence can help people understand systematic reviews on complementary therapies for Multiple Sclerosis	Birgit Bauer	• **Introduction**: The AIMS-Project explores how AI, particularly Large Language Models (LMs), can help people with MS (PwMS) understand systematic reviews on complementary therapies. • **Methodology:** The project uses participatory research, including co-creative workshops with PwMS, healthcare professionals, and AI experts to assess AI's usability and trustworthiness in translating scientific content into accessible language. • **Results:** Preliminary findings show that PwMS are open to using AI tools but face a knowledge gap in effective use and critical evaluation. • **Conclusions:** AI can support PwMS in making informed health decisions. The project fosters co-creation and digital literacy for empowered patient education.

Notable Presentations At ECTRIMS 2025
AI / ML (14/15)

Date	Title	Author	Summary
All days	Preliminary results of AI-based harmonization of brain MRIs from several MS clinical trials	Laura Gaetano	• **Introduction:** Multicenter brain MRI heterogeneity (scanner/protocol/reconstruction) limits pooling and generalizability in MS studies. • **Methodology:** From 7 NO.MS trials, 147 baseline T1 scans were used. Ten reference scans generated 12,000 synthetic 2D images via 20 k-space contrast perturbations. A U-Net3+ CNN with an added first–last skip was trained (MSE+L2). Quality on the remaining 137 scans was assessed by MRIQC vs originals and N4 bias-corrected images. • **Results:** AI harmonization improved intensity non-uniformity (+19.4% vs N4; +5.2% vs original), coefficient of joint variation (+21.6%; +43.4%), and contrast-to-noise ratio (+14.7%; +29.1%). SNR/Dietrich SNR were unchanged (N4 +2%). • **Conclusions:** AI harmonization reduces contrast artifacts and rivals established methods, enabling more reliable multicenter MRI analytics.
All days	Preliminary Results of Long-Term Home-Based Smartphone Monitoring in Multiple Sclerosis	Daan De Jong	• **Introduction:** Smartphone apps provide ecologically valid monitoring in MS, but long-term reference data are scarce. • **Methodology:** In the APS-MS cohort, participants were reassessed 5.3y after baseline. Tools included MS Sherpa (s2MWT, sSDMT) and Neurokeys (KD-MSC, KD-CSC). Clinical outcomes (EDSS, T25FW, 9-HPT, oral SDMT) were measured at baseline and follow-up. Paired t-tests/Wilcoxon tests compared change. • **Results:** 83/102 completed follow-up. Cohort: 60% RRMS, 28% SPMS, 12% PPMS; median EDSS 3.5. Over time, sSDMT ($p<0.01$) and KD-CSC ($p=0.035$) increased; SDMT showed trend ($p=0.09$). Motor function (EDSS, T25FW, HPT, s2MWT, KD-MSC) remained stable. • **Conclusions:** Smartphone outcomes captured long-term cognitive signals, while motor metrics were stable. Anchoring digital measures to clinical/MRI progression is warranted.

Notable Presentations At ECTRIMS 2025
AI / ML (15/15)

Date	Title	Author	Summary
All days	Deep Learning-Driven Prognosis of Multiple Sclerosis Using Multimodal MRI and Clinical Features Deep Learning driven prediction of Multiple Sclerosis using structural MRI data	Adil Maarouf Mirela Cerghet	• **Introduction**: MS progression varies, and accurately predicting it is crucial for personalized treatment. AI offers potential for enhancing predictive capabilities. • **Methodology:** A deep learning framework combines multimodal MRI and clinical data to predict MS disability progression. The model uses 3D ResNet for spatial features and bidirectional GRU for temporal patterns, with CAM-based saliency mapping for interpretability. • **Results:** Preliminary analysis showed 90% training accuracy and 8% validation accuracy, indicating potential for early prediction. • **Conclusions:** AI models can predict MS progression from MRI and clinical data, supporting early intervention and personalized treatment strategies.

Strategic Insights and Strategy Development is our focus