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Cyprus Multiple
Sclerosis Association
P.O.Box 26749, 1647 Nicosia, Cyprus
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Ο Παγκύπριος Σύνδεσμος Πολλαπλής Σκλήρυνσης
σας προσκαλεί σε Διάλεξη με θέμα:

Πολλαπλή Σκλήρυνση: Επικαιροποιημένη Ενημέρωση

Κυριακή 5 Οκτωβρίου 2025 στις 12.30μ.μ,
Δημοσιογραφική Εστία, Λευκωσία

Ομιλητής: ***Δρ. Μάριος Παντζαρής,***
Νευρολόγος, Ινστιτούτο Νευρολογίας και Γενετικής Κύπρου

Μεγάλος Υποστηρικτής

ΟΠΑΠ ΚΥΠΡΟΥ

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GENESIS pharma

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Χορηγοί Εκδήλωσης

Roche

Papaloisou

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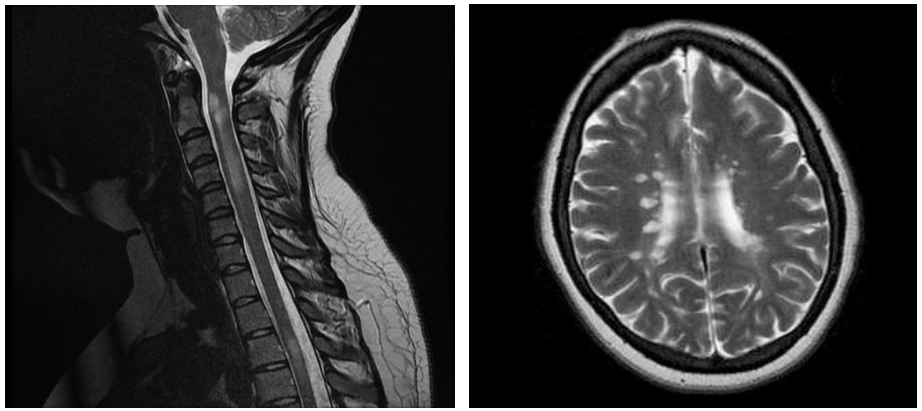
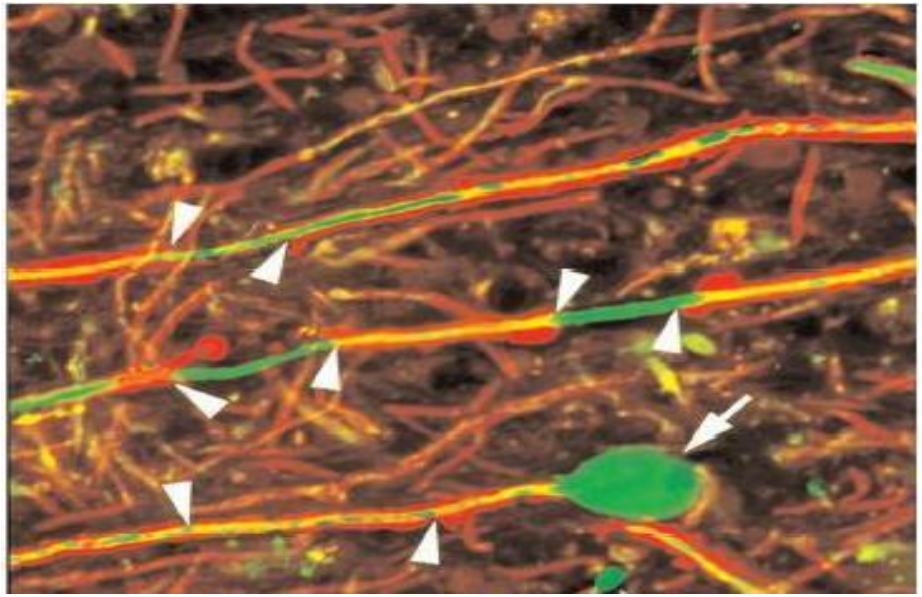
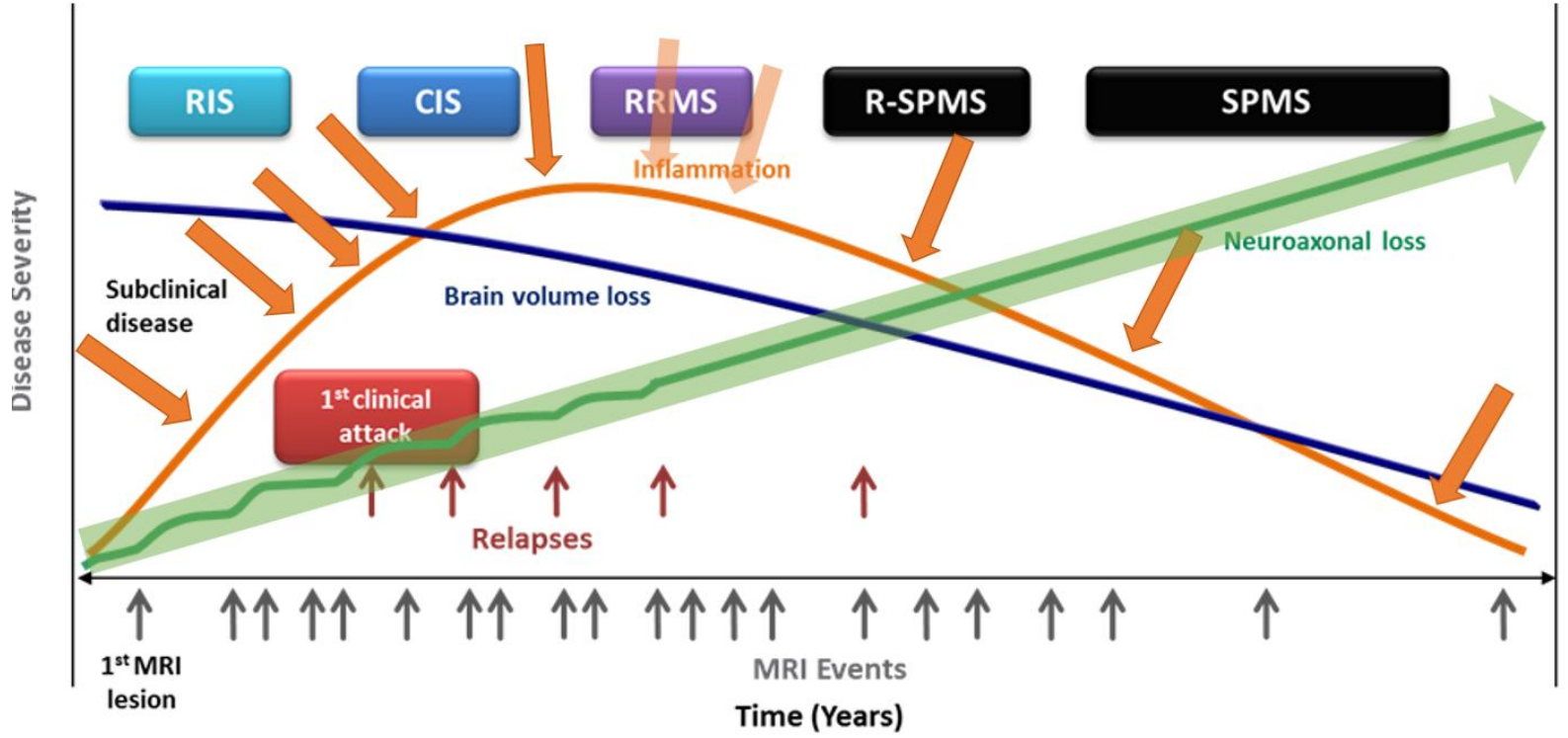
Multiple Sclerosis- Chronic Neurodegenerative Disease







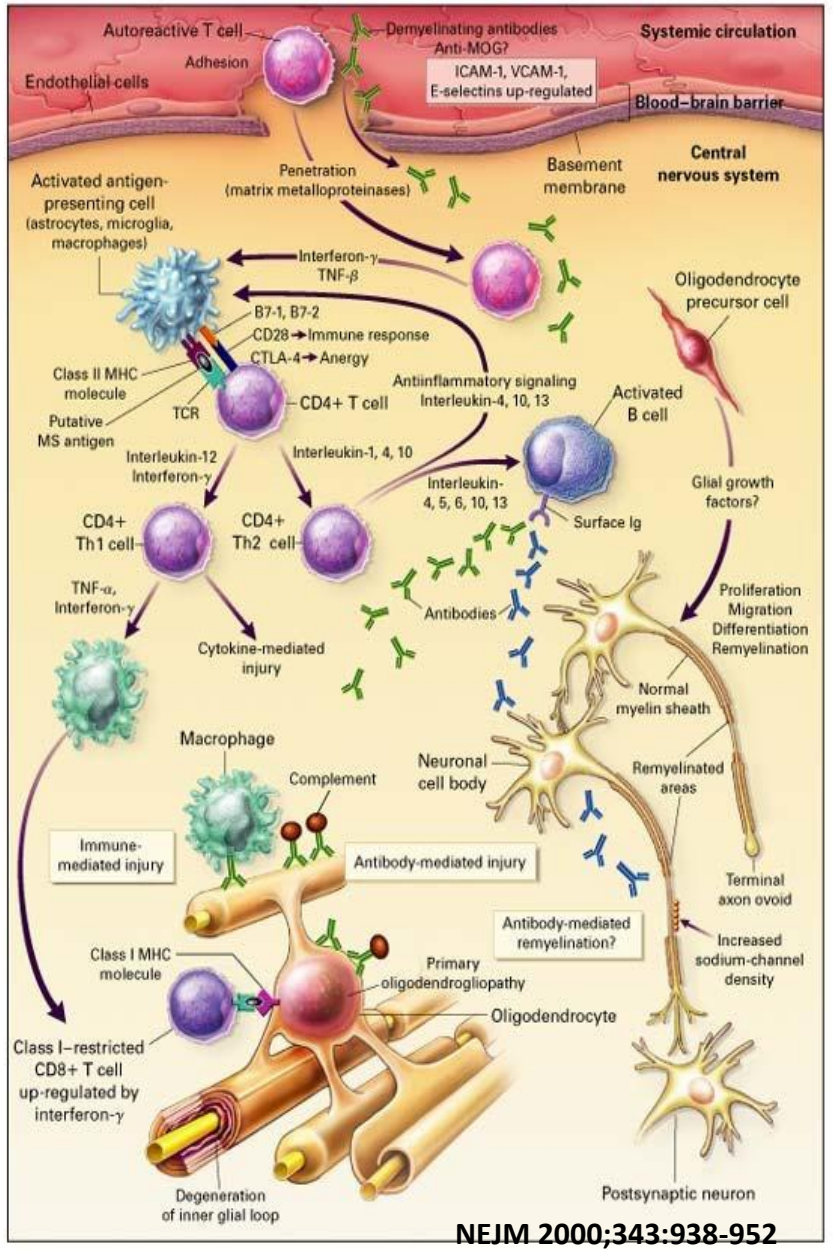
- Multiple Sclerosis (MS) is a chronic, immune-mediated, inflammatory demyelinating and degenerative disease of the Central Nervous System (CNS) affecting both the Brain and the Spinal Cord.

There are two different types of inflammation in MS patients:

The first pattern,

which is associated with: the focal bulk invasion of inflammatory cells into the brain and the formation of new focal lesions mainly in the white matter.

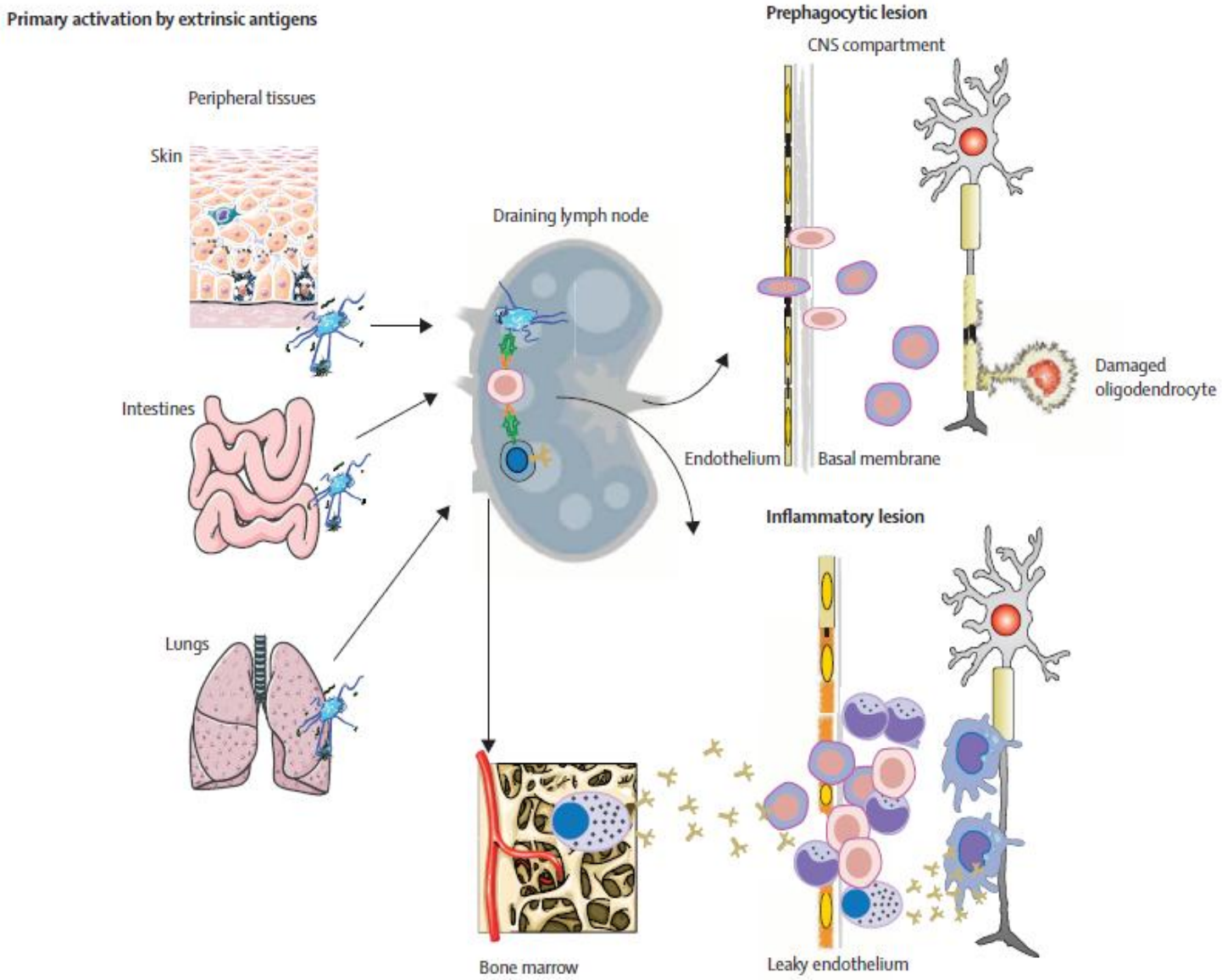
- Due to a major disturbance and ***opening of the blood-brain barrier.***
- With *lymphocytes entering* the brain in the course of immune surveillance,
- Lymphocyte *recognition of their cognate-antigen* within the central nervous system,
- *Re-activation* of these lymphocytes,
- Production of a variety of *pro-inflammatory mediators*, *activation of microglia* and
- Recruitment of additional cells and *serum components* through the *impaired blood-brain barrier*.



NEJM 2000;343:938-952

Role of the innate and adaptive immune responses in the course of multiple sclerosis

Review Bernhard Hemmer, Martin Kerschensteiner, Thomas Korn *Lancet Neurol* 2015; 14: 406–19



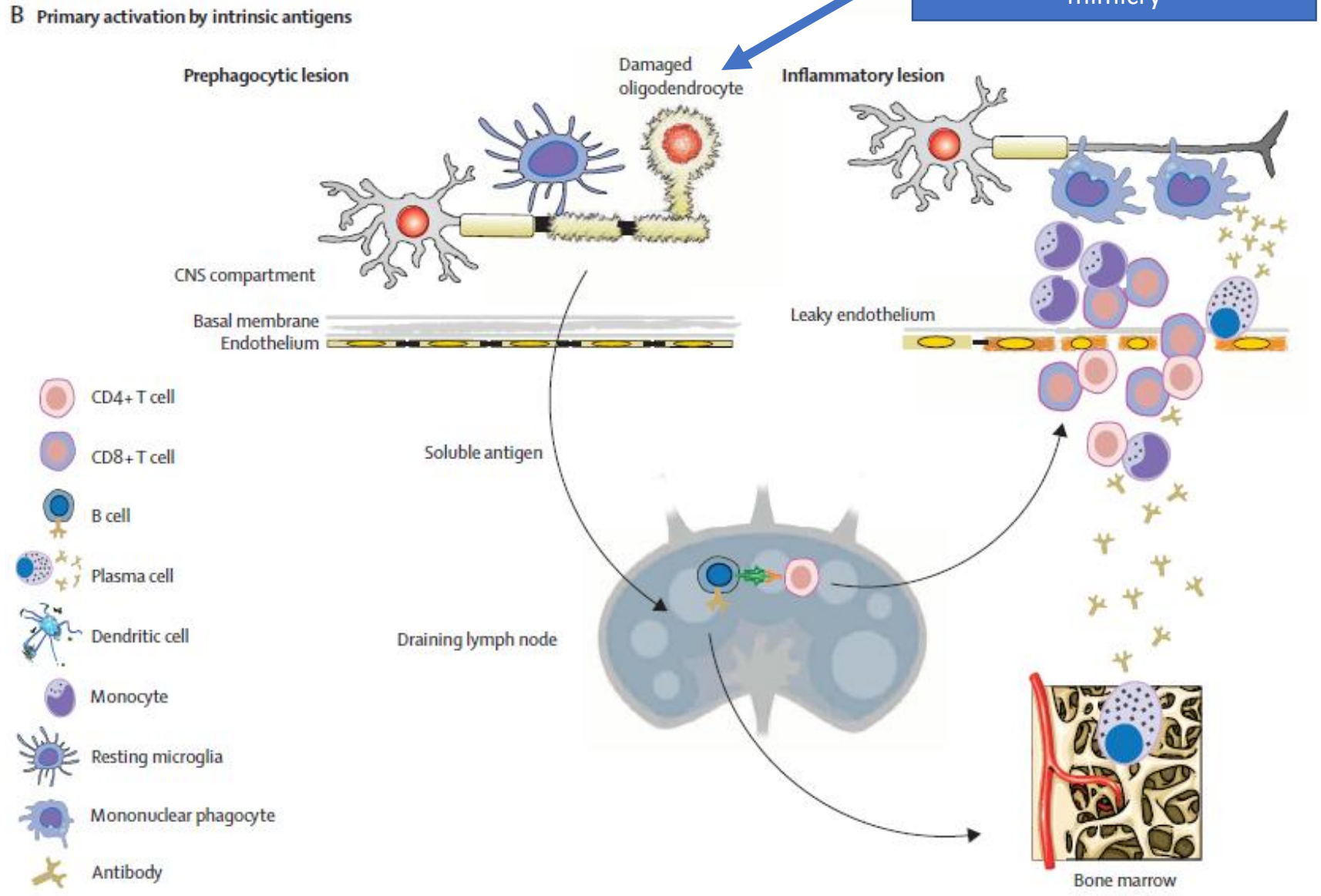
Outside-in Model

A **major hypothesis** in multiple sclerosis pathology is that a CNS antigen-specific immune activation occurs first in **the periphery** and is then transferred to the previously unaffected CNS.
After migration to the lymph nodes, a few of these antigen-specific T cells and B cells will invade the CNS compartment during the pre-phagocytic phase of lesion development.
The release of inflammatory mediators will open the blood–brain barrier and attract the influx of monocytes and additional lymphocytes and other ***serum components***, leading to the formation of the phagocytic lesion.

Role of the innate and adaptive immune responses in the course of multiple sclerosis

Review Bernhard Hemmer, Martin Kerschensteiner, Thomas Korn *Lancet Neurol* 2015; 14: 406–19

Role of EBV in immune-intolerance and epitope mimicry



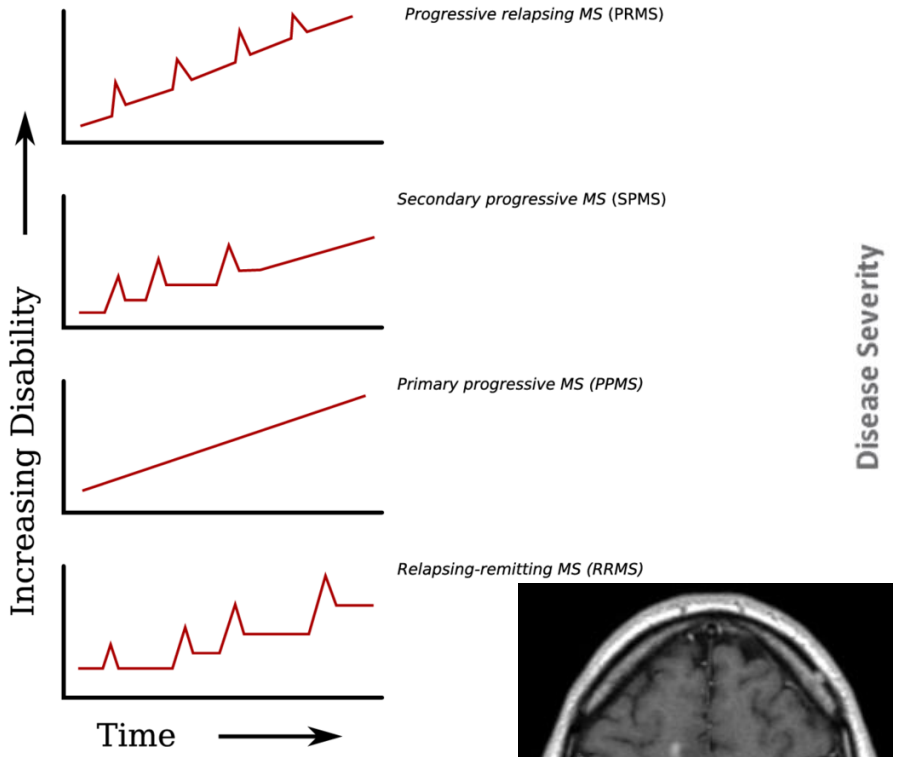
Inside-out Model

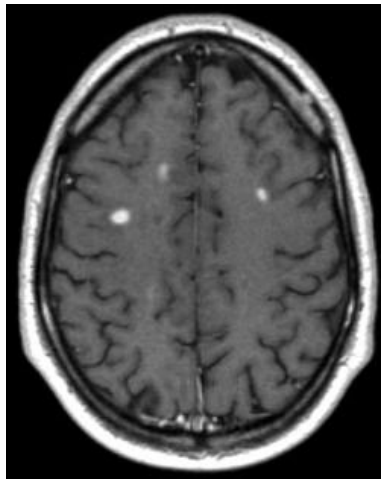
In an **alternative hypothesis,** an initiating event within the CNS causes the subsequent activation of resident microglia and an amplification of the immune reaction, with a secondary recruitment of adaptive and innate immune cells.

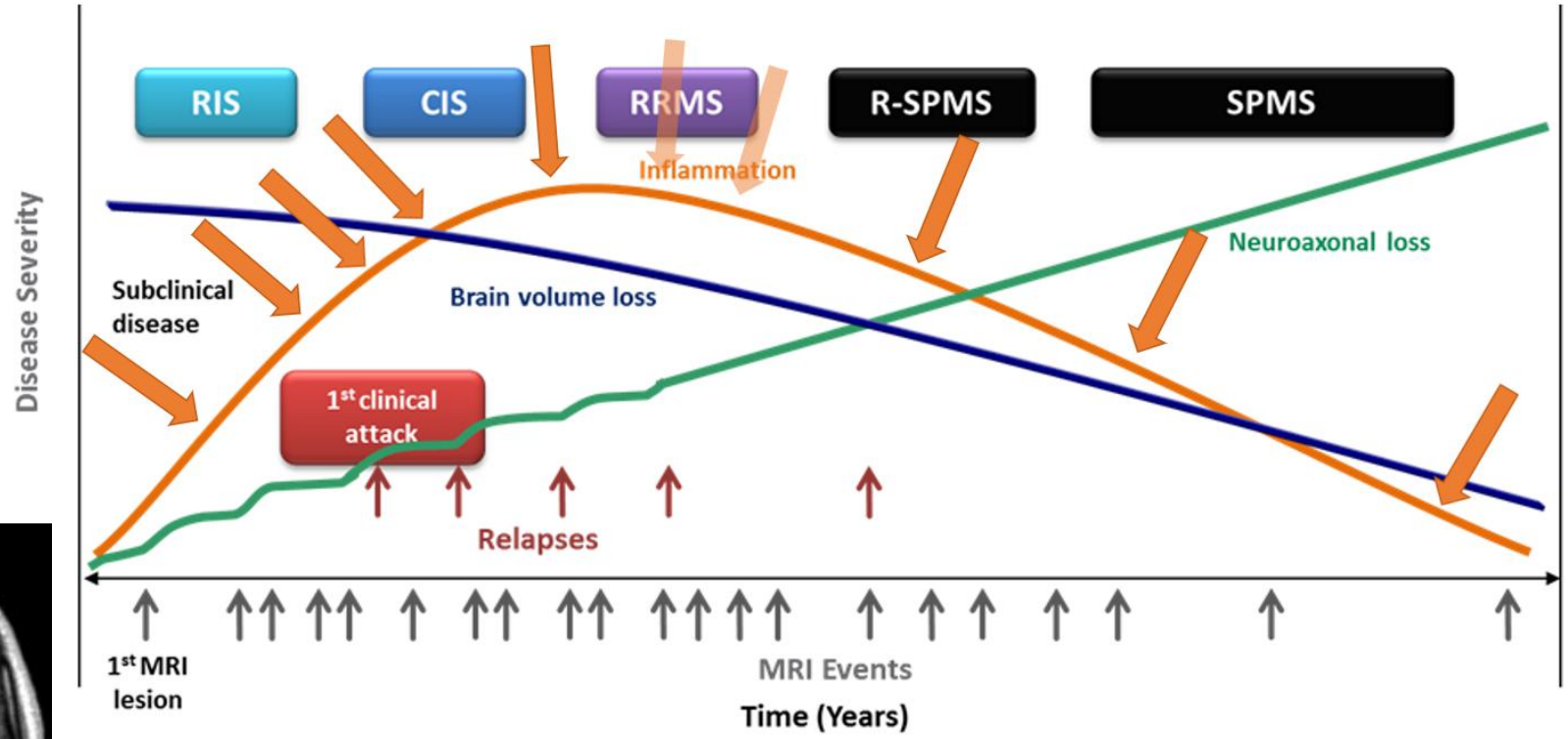
In this hypothesis, a primary defect of oligodendrocytes (eg, a genetic mutation/ viral/ toxic agent) leads to spontaneous oligodendrocyte death and consecutive activation of microglial cells, which would account for the changes noted in pre-phagocytic lesions

In this proposed hypothesis, antigens drain out of the CNS into deep cervical lymph nodes to induce a secondary adaptive immune response in the periphery.

Multiple Sclerosis- First Pattern of Inflammation



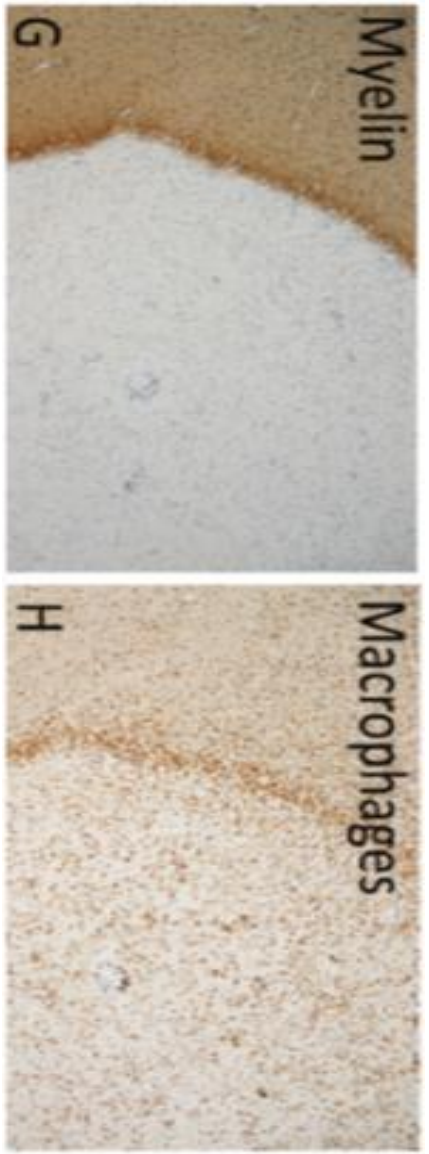




There are two different types of inflammation in MS patients:

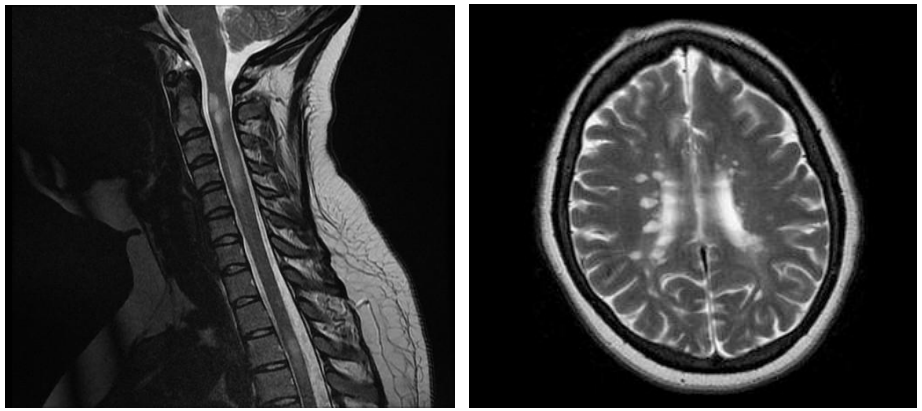
The Second Pattern,

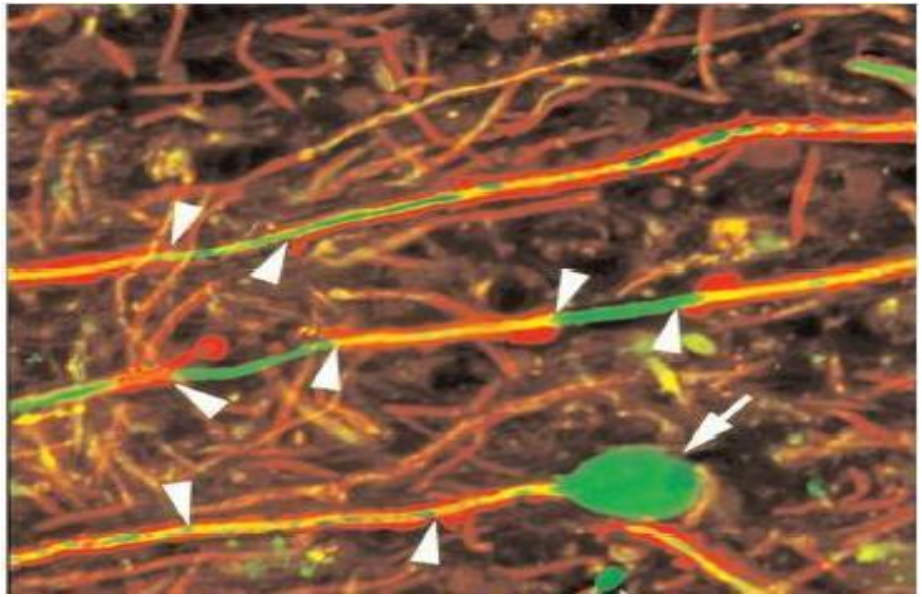
of inflammation in the MS brain is an inflammatory reaction, that accumulates in the large connective tissue spaces of the brain and spinal cord, dominantly *affecting the meninges and the large periventricular Virchow-Robin spaces*. In the B-cell lineage, CD20-positive cells are most frequent in active lesions, whereas *the majority of cells present in chronic lesions are plasma blasts and plasma cells*. In the meninges and perivascular space, this *inflammatory reaction is present diffusely or can form focal aggregates* or structures, which resemble *tertiary lymph follicles where* clearly separated T-cell, B-cell, and plasma cell areas can be seen.

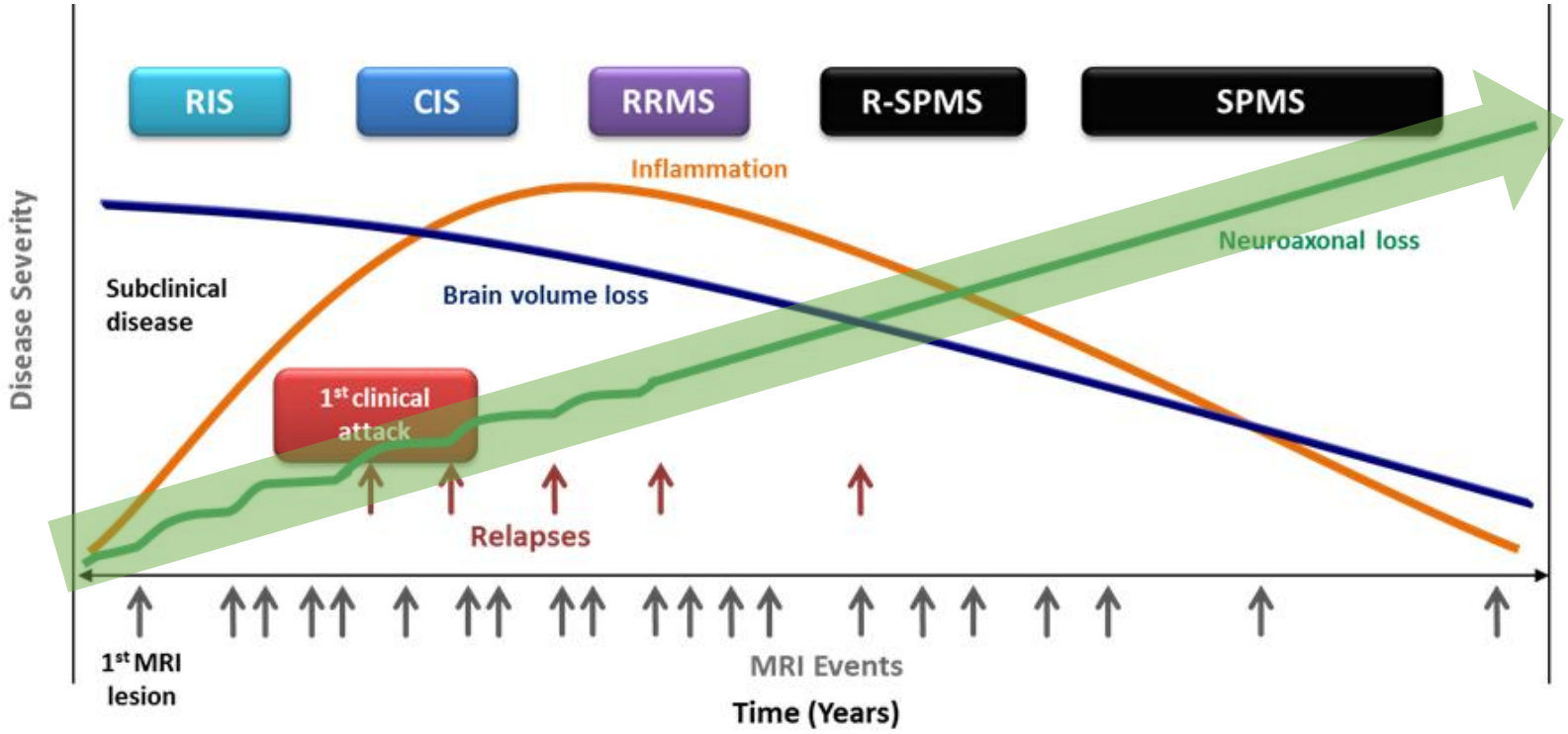


- In contrast to the inflammatory reaction in classical active white matter lesions, *blood-brain barrier damage is minor or absent in this compartmentalized inflammatory reaction* ***in chronic progressive MS***. The *meningeal and perivascular infiltrates are associated with slow expansion into the white and gray matter*. Tissue injury may be partly mediated by a cascade *involving microglia and macrophage activation, oxidative injury, and mitochondrial damage*. Soluble factors, produced by the inflammatory cells, may exert tissue damage either directly or indirectly through activation of microglia or macrophages as well as astrocytes.

Multiple Sclerosis- Chronic Neurodegenerative Disease







- Multiple Sclerosis (MS) is a chronic inflammatory demyelinating and degenerative disease of the Central Nervous System (CNS) affecting both the Brain and the Spinal Cord.

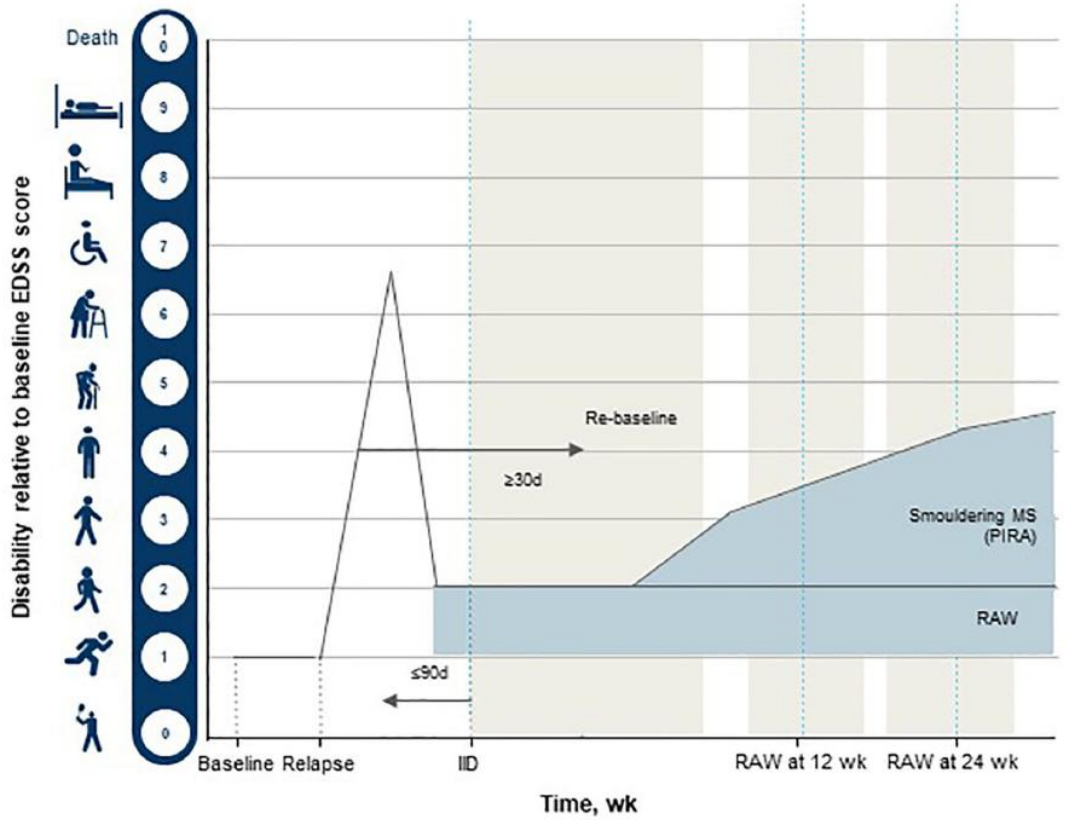
Therapeutic Advances in Neurological Disorders
2022, Vol. 15: 1–18
DOI: 10.1177/
17562864211066751

PIRA (progression independent of relapse activity)

Smouldering multiple sclerosis: the 'real MS'

Gavin Giovannoni, Veronica Popescu, Jens Wuerfel, Kerstin Hellwig, Ellen Iacobaeus, Michael B. Jensen, José Manuel García-Domínguez, Livia Sousa, Nicola De Rossi, Raymond Hupperts, Giuseppe Fenu, Benedetta Bodini, Hanna-Maija Kuusisto, Bruno Stankoff, Jan Lycke, Laura Airas, Cristina Granziera and Antonio Scalfari

A large proportion of people with multiple sclerosis (MS) continue to experience clinical deterioration despite a lack of overt ongoing inflammatory disease activity. To this end, such patients exhibit disability progression despite being relapse-free and exhibiting neither contrast-enhancing T1-weighted (T1w) lesions nor new or enlarging T2-weighted (T2w) lesions on magnetic resonance imaging (MRI). This is often referred to as progression independent of relapse activity (PIRA) or smouldering MS.



JAMA Neurol 2020; 77: 1132–1140

In relapsing-remitting MS (RRMS), the effective therapeutic suppression of relapses does not always correlate with the prevention of long-term disability accumulation, thus highlighting a disconnect between mechanisms underlying **inflammatory attacks** and those responsible for **disease progression**.

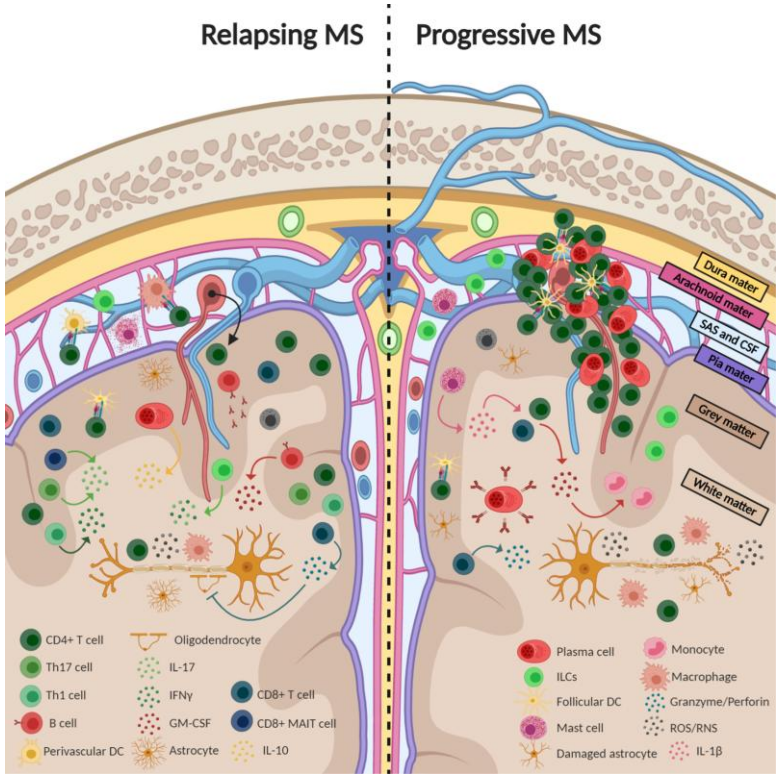
Kamma et al. Journal of Neuroinflammation (2022) 19:45
https://doi.org/10.1186/s12974-022-02408-y

Journal of Neuroinflammation

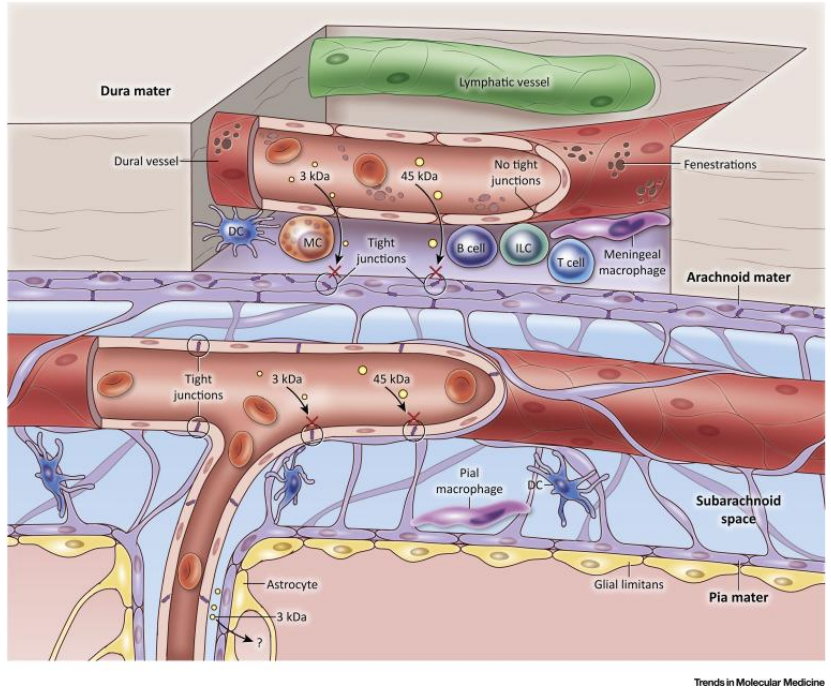
REVIEW Open Access

Central nervous system macrophages in progressive multiple sclerosis: relationship to neurodegeneration and therapeutics

Emily Kamma[1†], Wendy Lasisi[2†], Cole Libner[3†], Huah Shin Ng[4†] and Jason R. Plemel[5,6,7,8*]



Cellular & Molecular Immunology volume 18, pages1353–1374 (2021)

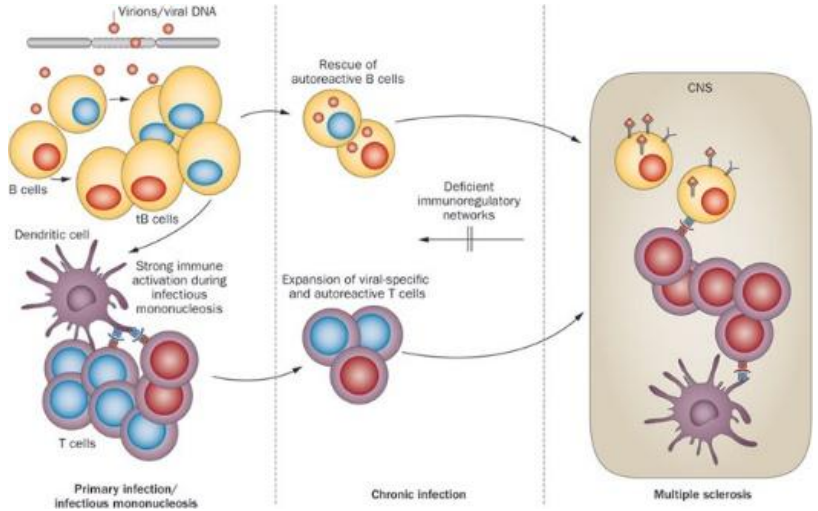


Trends in Molecular Medicine, June 2018, Vol. 24, No. 6

Lymphoid follicles, which are associated with more severe microglia activation and cortical demyelination, are found in large aggregates in the meninges and the perivascular Virchow–Robin spaces. They are typically found in 40–70% of people with SPMS, but not in people with PPMS; however, increased meningeal inflammation associated with more extensive cortical demyelination and neurite loss is present in PPMS, but without lymphoid follicles

ΠΕΡΙΒΑΛΛΟΝΤΙΚΟΙ ΠΑΡΑΓΟΝΤΕΣ ΚΑΙ ΠΟΛΛΑΠΛΗ ΣΚΛΗΡΥΝΣΗ

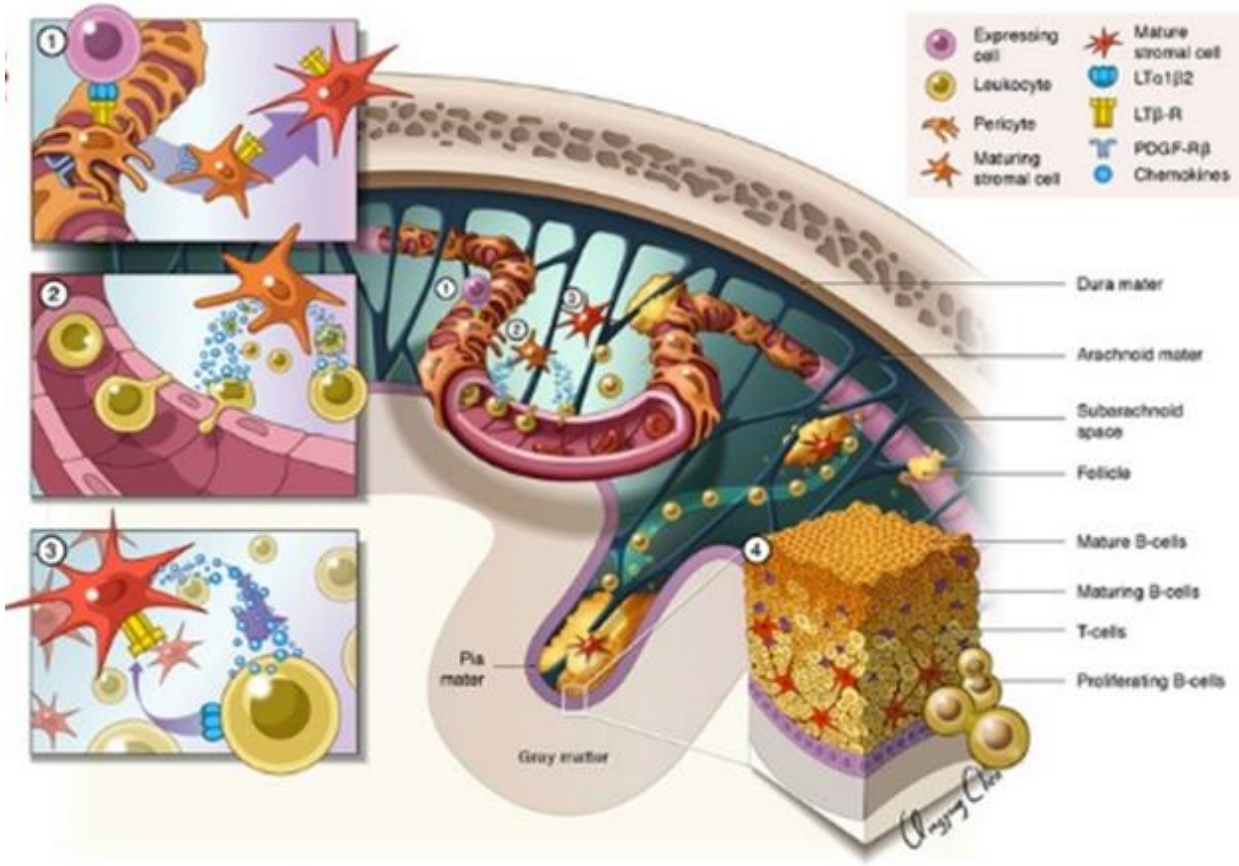
Ιός EBV



Compared with healthy individuals, patients with MS show higher frequencies and activation states of self-reactive B lymphocytes (cells with red nuclei), in addition to impaired functions of regulatory immune compartments, indicating a lower threshold for **breakdown of self-tolerance to CNS antigens**. Strong innate immune activation during primary EBV infection could facilitate activation and expansion of autoreactive and polyspecific (that is, both autoantigen-specific and viral-antigen-specific [cells with blue nuclei]) T and B cells. These cells could be maintained in the presence of continuous antigen exposure. In addition, latent EBV infection confers B-cell **(anti-EBNA-1-producing plasma cells)** survival advantages and could rescue autoreactive B cells from apoptotic deletion during B-cell development and differentiation. Homing of these rescued autoreactive lymphocytes, which can immuno-modulate and present antigens to T cells, to the inflamed CNS might contribute to the immunopathology of MS.

EBNA1-specific T cells from patients with multiple sclerosis cross react with myelin antigens and co-produce IFN-γ and IL-2

J. Exp. Med. Vol. 205 No. 8 1763-1773
www.jem.org/cgi/doi/10.1084/jem.20072397



Nature Reviews Neurology 8, 602-612 (November 2012)

Scientific Session 12: Viral infection and neuroinflammation

Track Pathogenesis

Room Lecture Hall 113

Date Thursday, 25 September 2025, 14:30 - 16:00 CEST

PRESENTATION ID O099

Unravelling the immune-pathological profile of proliferative B cells infected by Epstein-Barr virus in multiple sclerosis leptomeninges

Roberta Magliozzi (Italy)

ECTRIMS 2025

41st Congress of the European Committee for Treatment and Research in Multiple Sclerosis

30th Conference of Rehabilitation in Multiple Sclerosis

24-26 September 2025 | Barcelona, Spain

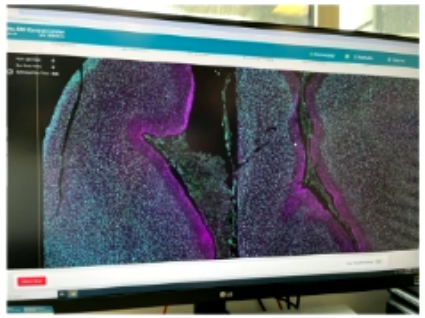
Conclusions

- **Persistent intrathecal presence of of EBNA2+ latently infected B cells** in all the examined MS brains but not in controls.
- The presence of meningeal EBNA2+ B cells is associated with specific immunopathological features and rapid disease progression.
- Advanced CSF profile of MS cases with high levels of meningeal EBNA2+ B cells reflects the key role of B cell signature possibly related to both cytotoxic/inflammatory activity and immunoglobulin production.

EBV latent infection as potential driver of continuous MS B cell intrathecal expansion and activaty

Ongoing: **Further molecular validation of the exact immuno- and molecular-phenotype of brain EBV latently infected B cells**

(Specific MS targets)



Single-cell viral and human genome spatial transcriptomic (Bruker/CosMX)

CING study on EBV genetic profile

frontiers in Immunology

REVIEW
published: 10 January 2019
doi: 10.3389/fimmu.2018.03116

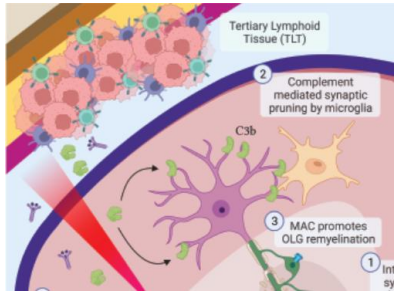
Pathogenic Mechanisms Associated With Different Clinical Courses of Multiple Sclerosis

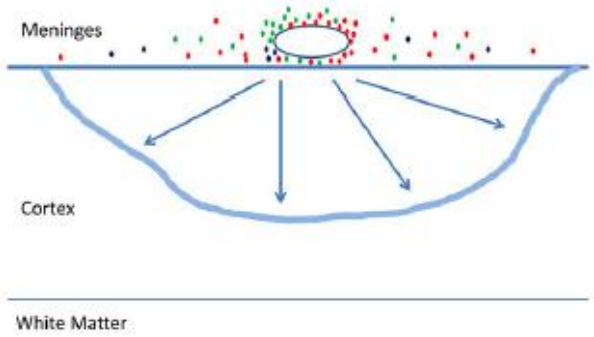
*Hans Lassmann**

Center for Brain Research, Medical University of Vienna, Vienna, Austria

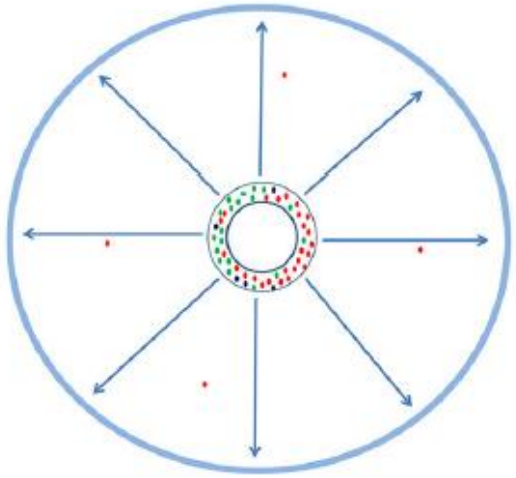
Activated microglial cells, which are full of Iron deposits

Slowly expanding lesions in progression of MS in the cortex and the white matter.





A



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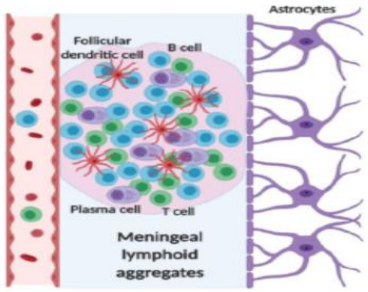


(A) ***Active cortical lesions*** are associated with inflammatory infiltrates in the meninges, which are composed of CD8+ T-cells (red), CD20+ B-cells (green) and plasma cells (blue). Active demyelination occurs at a distance of the inflammatory infiltrates and is associated with activated microglia (blue lesion rim). Th**e lesions gradually expand from the pial surface of the cortex toward the depth of the gray matter**. *Lymphocyte infiltrates are rare or completely absent in the cortical tissue and in particular at the zone of active demyelination*. It is suggested that the inflammatory infiltrates in the meninges produce a soluble factor, which induces demyelination and neurodegeneration either directly or indirectly through ***microglia activation*** (arrows).

(B) In ***slowly expanding lesions in the white matter*** T-cell, B-cell and plasma cell infiltrates are present in the large perivascular Virchow Robin spaces. **Active demyelination and neurodegeneration occurs at a distance and is associated with microglia activation**. Also in these lesions it is suggested that demyelination and neurodegeneration is driven by a soluble factor, produced by the perivascular lymphocytes or plasma cells (arrows).

The role of the complement system in Multiple Sclerosis: A review

Front. Immunol. 13:970486.
doi: 10.3389/fimmu.2022.970486

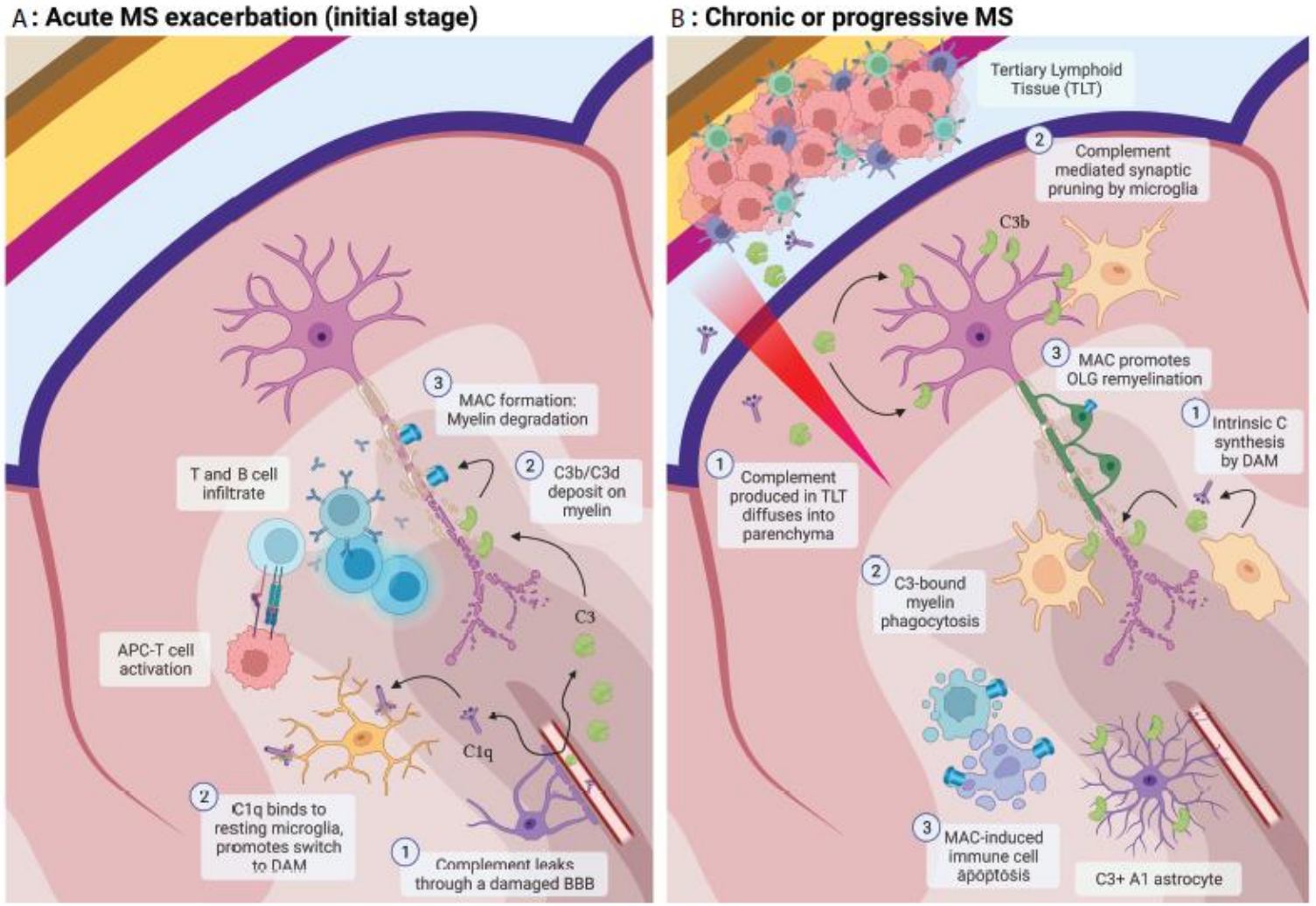
Nil Saez-Calveras[1] and Olaf Stuve[1,2*]

(A) Acute MS exacerbation:

1. Complement factors leak through a ***compromised BBB***. T and B cells infiltrate the parenchyma and are activated by myeloid APCs.
2. Activated C3b and C3d deposit on myelin promoting its opsonization. C1q binds resting microglia and modulates its phenotype switch to disease-associated microglia (DAM).
3. Downstream activation of complement leads to the formation of membrane attack complex (MAC) and damage to the myelin membrane.

(B) Progressive MS:

1. Complement and other factors are secreted by DAM and by the tertiary lymphoid tissue (TLT) and diffuse into the brain parenchyma.
2. C3-bound myelin products are opsonized by myeloid cells and activated microglia.
3. In this stage, MAC formation exerts protective effects through the apoptosis of inflammatory cells and prevention of OLG apoptosis



Hot Topic 7: Imaging chronic inflammation

Track	Imaging and non-imaging biomarkers
Room	Lecture Hall 111
Date	Thursday, 25 September 2025, 09:45 - 10:45 CEST

Iron, SEL and PRL

Alessandro Cagol (Switzerland)

ECTRIMS 2025

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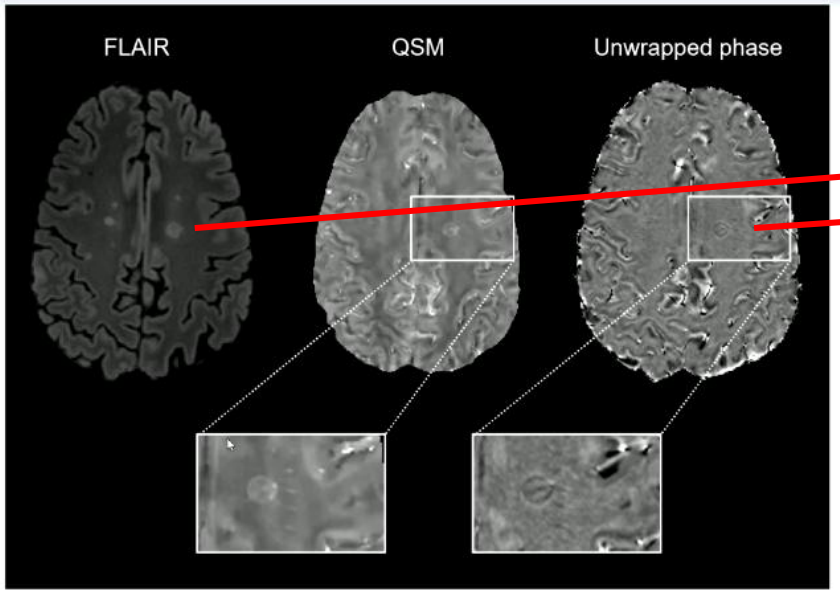
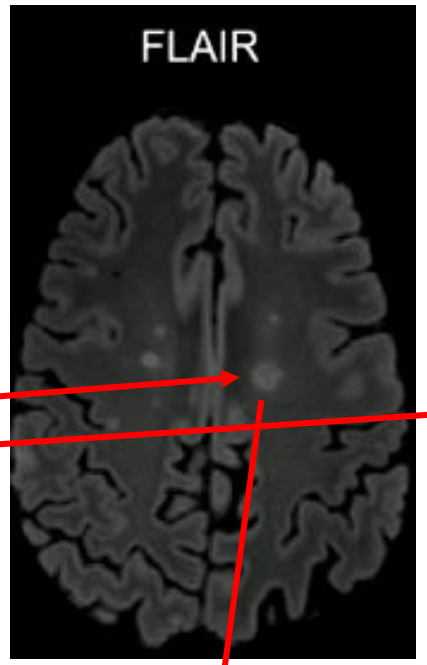
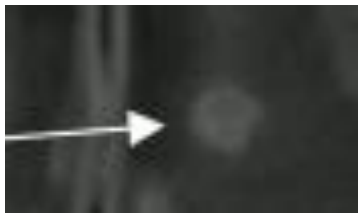
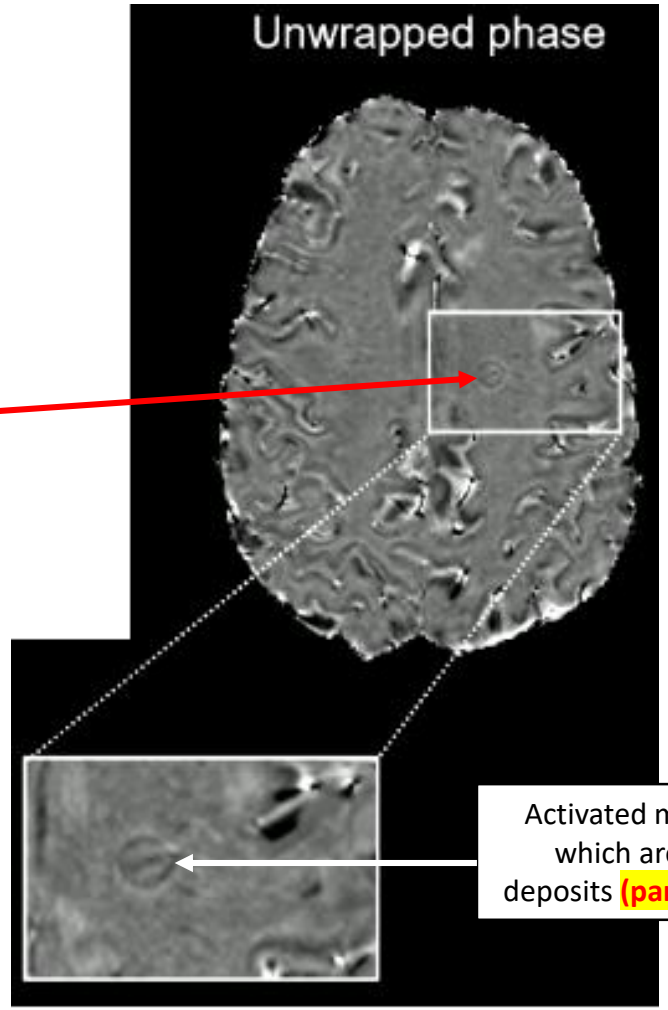
Paramagnetic Rim Lesions (PRLs)









Activated microglial cells, which are full of Iron deposits (**paramagnetic rim**)

European Charcot Foundation Symposium: MS update capsules

Track Clinical

Room Lecture Hall 111

Date Wednesday, 24 September 2025, 14:30 - 15:30 CEST

ECTRIMS 2025

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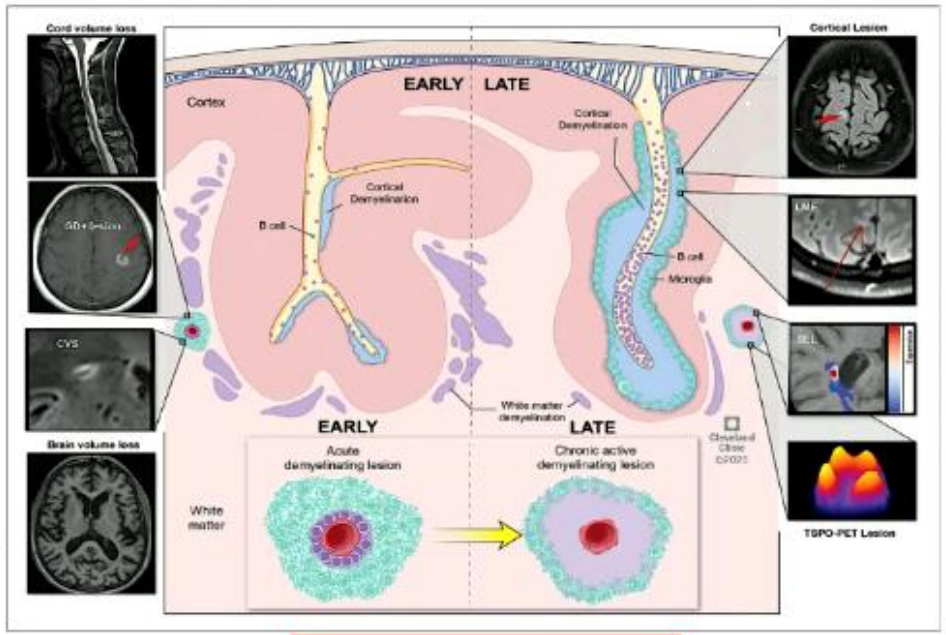
Key pathological mechanisms of progression across the continuum of MS

Focal inflammation

- Primarily driven by T and B lymphocytes. Perivenular inflammation. BBB damage

- Active Gd-enhancing demyelinating lesions prevalent in the white matter. 'Central vein sign' on FLAIR imaging



Smouldering chronic inflammation

-**Lymphocytic infiltrates of T and B lymphocytes, plasma cells, and macrophages** (lymphoid follicles in the meninges and the perivas. spaces)

-**Largely driven by macrophage/microglial activation**, (oxidative injury, mitochondrial dysfunction, energetic failure)

- **Chronic active demyelinating lesions** (slowly expanding lesions-**SELs**-Paramagnetic rim lesions –**PRLs**-)
-**Cortical lesions**
-**Leptomeningeal enhancement**

Failure of remyelination

neuro-axonal degeneration

brain and spinal atrophy

Biological substrate of Relapses and RAW

Biological substrate of PIRA and SAW

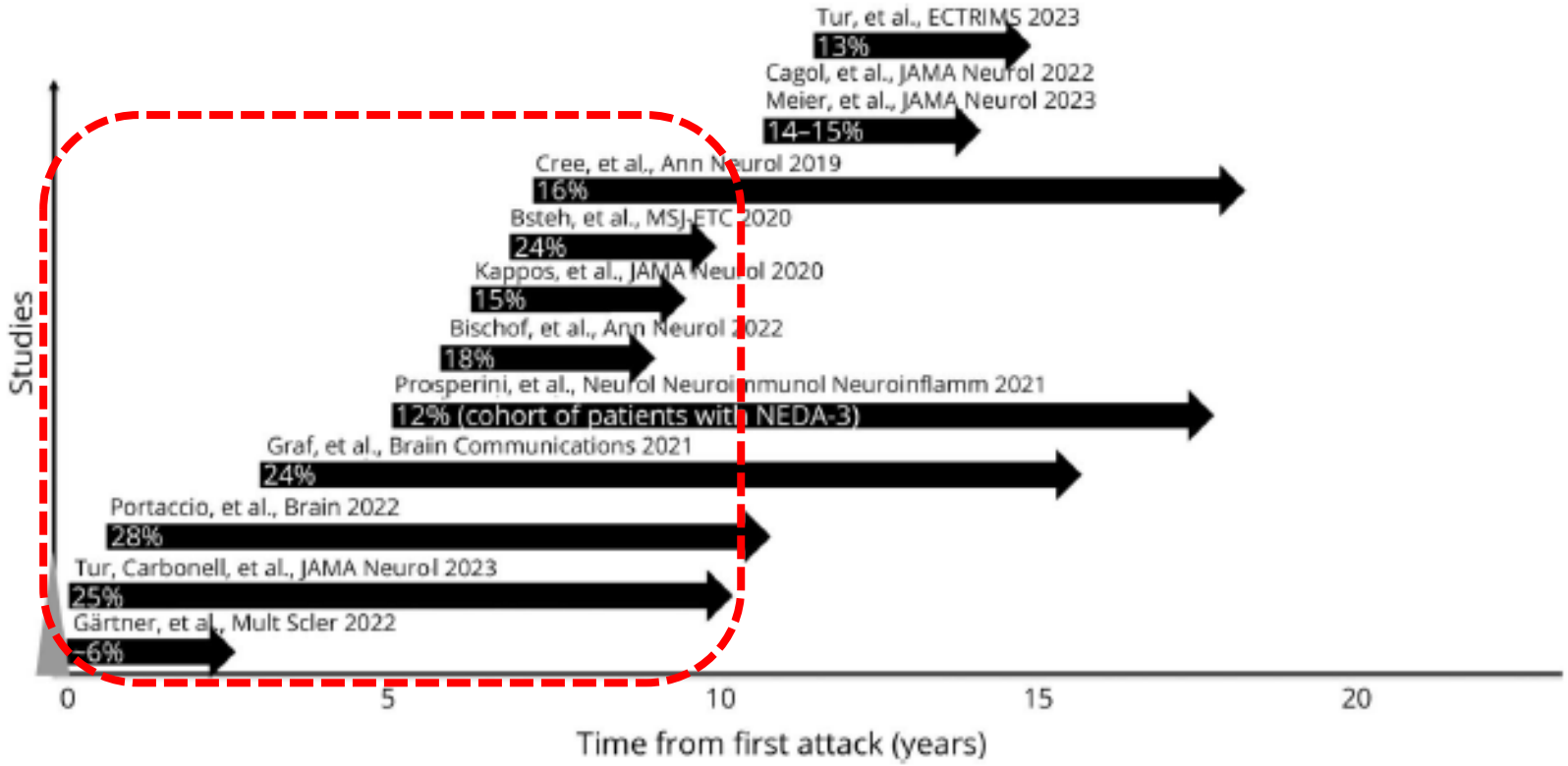
Lambe J. and Ontaneda D., Curr Opin Neurol 2025

ΠΡΟΒΛΗΜΑΤΙΣΜΟΙ (Ι)
ΠΟΙΑ Η ΣΗΜΜΑΣΙΑ ΤΗΣ PIRA/ Αργής Επιδείνωσης(?)

Using the Progression Independent of Relapse Activity Framework to Unveil the Pathobiological Foundations of Multiple Sclerosis

Neurology® 2024;103:e209444. doi:10.1212/WNL.0000000000209444

Figure 1 Annual Frequency of PIRA Events Reported by Previous Studies



This figure represents the percentage of people with MS who develop at least 1 PIRA event a year, as reported by previous studies. Each study is represented by an arrow, whose length indicates the median time of the study follow-up. The position of the start of the arrow along the x-axis represents the median/mean (as available) disease duration of the patients at study entry. The references are given in the eTable 1. MS = multiple sclerosis; NEDA = no evidence of disease activity; PIRA = progression independent of relapse activity.

JAMA Neurology | Original Investigation

Association of Early Progression Independent of Relapse Activity With Long-term Disability After a First Demyelinating Event in Multiple Sclerosis

JAMA Neurol. 2023;80(2):151-160. doi:10.1001/jamaneurol.2022.4655
Published online December 19, 2022.

Table 2. Prediction of Long-term Outcomes (N = 1128)

Outcome	All study patients (N = 1128)	PIRA (n = 277)	No PIRA (n = 851)	*P* value, PIRA vs no PIRA	Within 5 years: Early PIRA (n = 86)	Within 5 years: Late PIRA (n = 191)	*P* value, early PIRA vs late PIRA	Active PIRA (n = 73)	Nonactive PIRA (n = 71)	*P* value, active PIRA vs nonactive PIRA
Adjusted yearly EDSS increase rates (95% CI)	0.07 (0.06-0.09)	0.18 (0.16-0.20)	0.04 (0.02-0.05)	<.001	0.31 (0.26-0.35)	0.13 (0.10-0.16)	<.001	0.20 (0.15-0.25)	0.12 (0.06-0.18)	.05
Kaplan-Meier estimates (95% CI) of % patients reaching EDSS 6.0 from the first demyelinating event[a]										
5 y	0.48 (0.06-0.90)	1.09 (0-2.31)	0.24 (0-0.57)		2.41 (0-5.67)	0.52 (0-1.54)		1.37 (0-4.00)	1.52 (0-4.42)	
10 y	2.54 (1.41-3.65)	5.58 (2.69-8.39)	1.02 (0.18-1.86)	<.001	12.03 (3.71-19.63)	3.24 (0.65-5.76)	.07	9.11 (1.86-15.82)	4.86 (0-10.09)	.003
15 y	6.00 (3.97-7.98)	12.82 (8.18-17.23)	1.74 (0.42-3.03)		23.93 (11.01-34.98)	9.10 (4.55-3.42)		24.54 (12.18-35.15)	4.86 (0-10.09)	
20 y	9.25 (6.23-12.19)	18.49 (12.37-24.19)	2.45 (0.53-4.33)		23.93 (11.01-34.98)	16.41 (9.47-22.82)		38.32 (22.05-51.19)	10.46 (0-21.50)	
Adjusted HR (95% CI) for reaching confirmed EDSS 6.0 from the first demyelinating event[a]	NA	7.93 (2.25-27.96)	1 [Reference]	.001	26.21 (2.26-303.95)	1 [Reference]	.009	2.51 (0.58-10.85)	1 [Reference]	.22

MULTIPLE SCLEROSIS JOURNAL | MSJ

Original Research Paper

Cognitive progression independent of relapse in multiple sclerosis

Tom A Fuchs, Menno M Schoonheim, Robert Zivadinov, Michael G Dwyer, Elisa Colato, Zachary Weinstock, Bianca Weinstock-Guttman, Eva MM Strijbis and Ralph HB Benedict

Multiple Sclerosis Journal

2024, Vol. 30(11-12) 1468–1478

DOI: 10.1177/13524585241256540

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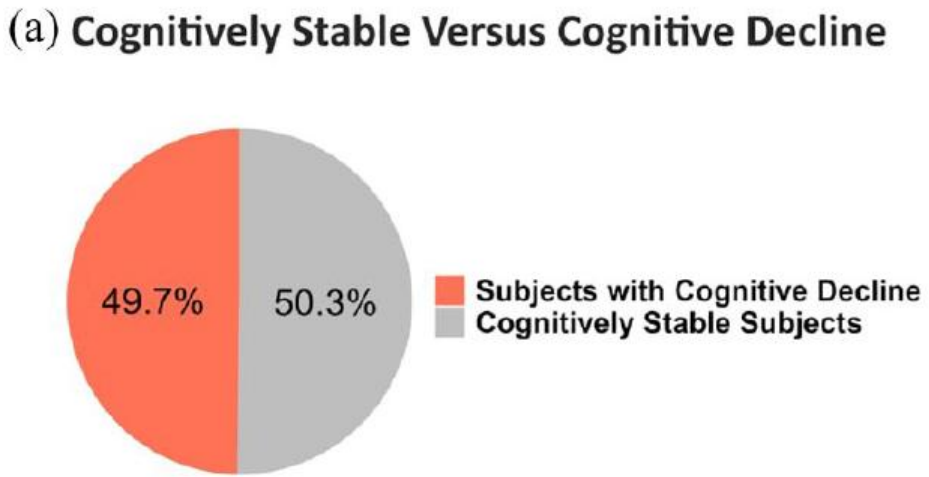

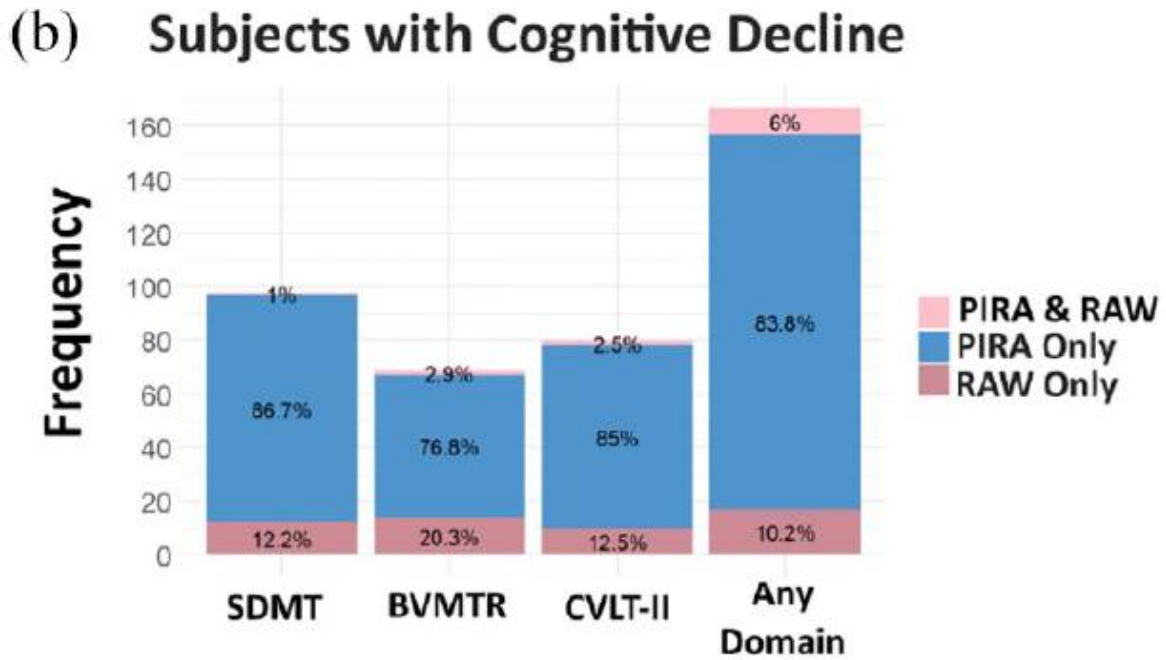

Hot Topic 7: Imaging chronic inflammation

Track Imaging and non-imaging biomarkers

Room Lecture Hall 111

Date Thursday, 25 September 2025, 09:45 - 10:45 CEST

Iron, SEL and PRL

Alessandro Cagol (Switzerland)

ECTRIMS 2025

41st Congress of the European Committee for Treatment and Research in Multiple Sclerosis

30th Conference of Rehabilitation in Multiple Sclerosis

24-26 September 2025 | Barcelona, Spain

Clinical Value of PRLs

Diagnosis

- Observed across all MS clinical phenotypes.
- Pooled prevalence: 51.3%.
- Rarely seen in non-MS conditions.
- In CIS: predict conversion to MS.
- **Can support the diagnosis of MS.**

2024 revisions of the McDonald criteria

Paramagnetic rim lesions (PRLs)

- Demonstrating one or more PRLs by MRI can be used to diagnose multiple sclerosis in specific situations
- Demonstrating one or more PRLs by MRI can increase the specificity of the diagnosis
- Demonstrating PRLs is not required for diagnosis
- In patients with typical symptoms and typical lesions in one region, the presence of one or more PRLs plus dissemination in time or positive CSF is sufficient for diagnosis

Montalban et al., Lancet, 2025

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Clinical Value of PRLs

Prognosis

Manifestation of chronic inflammation → contribution to disease progression.

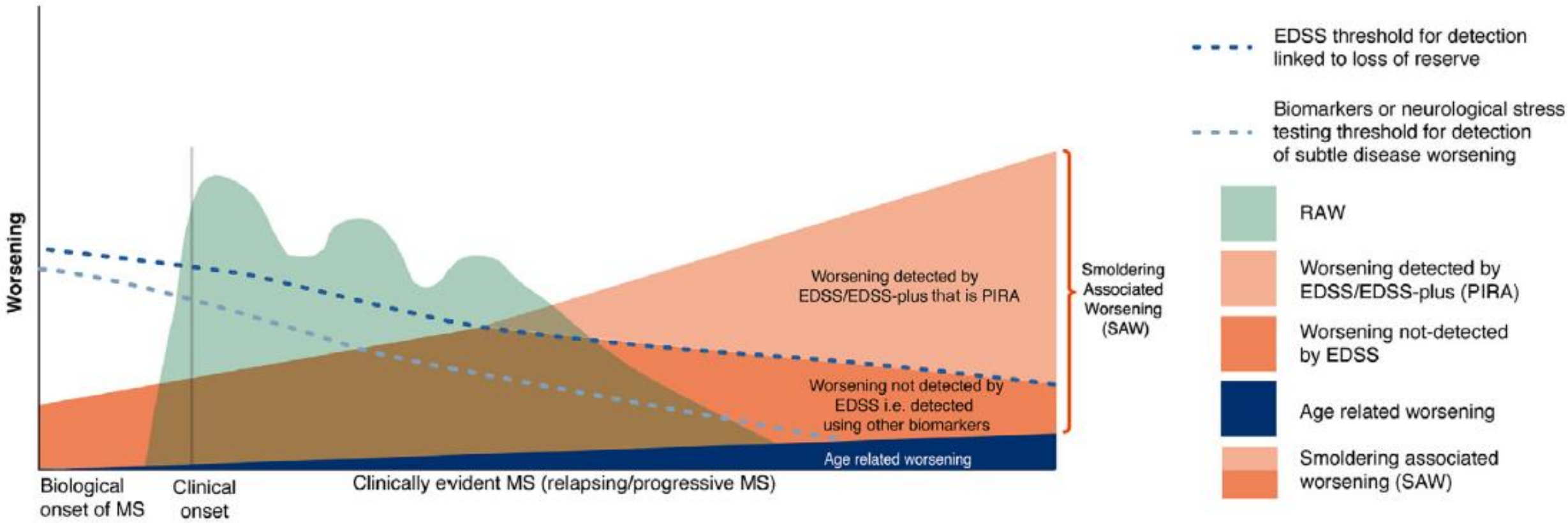
- PRL: more severe pathological changes.
- Associate with sNfL and brain atrophy.
- Correlate with higher physical and cognitive disability; predict worsening of disability/conversion to SPMS.
- **Associate with progression independent of relapse activity (PIRA).**

Table. Cohort Characteristics of 192 Patients With Multiple Sclerosis in the Cross-Sectional Cohort

Rim Category	No Detected Rims	1-3 Rims	≥4 Rims	Statistical Analysis[a]
Demographic and Clinical Data				
No. (%)	84 (44)	66 (34)	42 (22)	NA
Clinical phenotype, No. (%)				
CIS/RR	61 (73)	46 (70)	24 (57)	Fisher 2 × 3 P = .20, NS
SP	16 (19)	14 (21)	10 (24)	
PP	7 (8)	6 (9)	8 (19)	
Sex, Female, No. (%)	59 (70)	45 (68)	28 (67)	Fisher 2 × 3 P = .90, NS
Age, mean (SD), y	47.3 (14.5)	47.2 (11.4)	44.3 (11.1)	ANOVA P = .40, NS
Disease duration, mean (SD), y	13.4 (12.5)	12.9 (9.9)	12.2 (8.3)	ANOVA P = .80, NS
Patients never treated, No. (%)	27/84 (32)	11/66 (17)	5/42 (12)	Fisher 2 × 3 P = .01
African American, No. (%)	10 (12)	12 (18)	10 (24)	Fisher 2 × 3 P = .20, NS
HLA-DRB1*15:01, No. (%)	29/64 (45)	15/54 (28)	13/33 (41)	Fisher 2 × 3 P = .10, NS
EDSS score, median (range)	1.5 (0-7.5)[a]	2 (0-8)[b]	3 (1-7.5)[a,b]	ANOVA P = .002
MSSS score, mean (SD)	3.0 (2.5)[a]	3.4 (2.5)[b]	4.9 (2.5)[a,b]	ANOVA P < .001
PASAT score, mean (SD)	49.9 (8.6)[a]	48.4 (9.9)	44.6 (11.9)[a]	ANOVA P = .03
SDMT score, mean (SD)	53.4 (12.3)[a]	48.3 (13.4)	43.7 (17.8)[a]	ANOVA P = .001

Smouldering-Associated Worsening in Multiple Sclerosis: An International Consensus Statement on Definition, Biology, Clinical Implications, and Future Directions

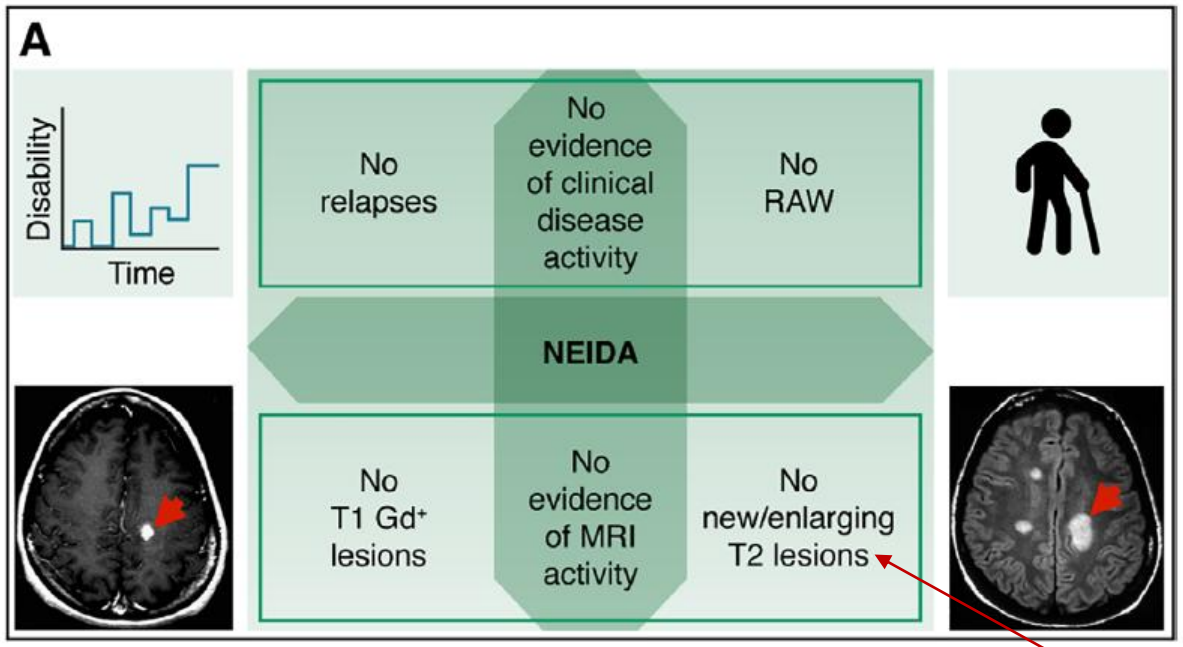
ANN NEUROL 2024;96:826–845

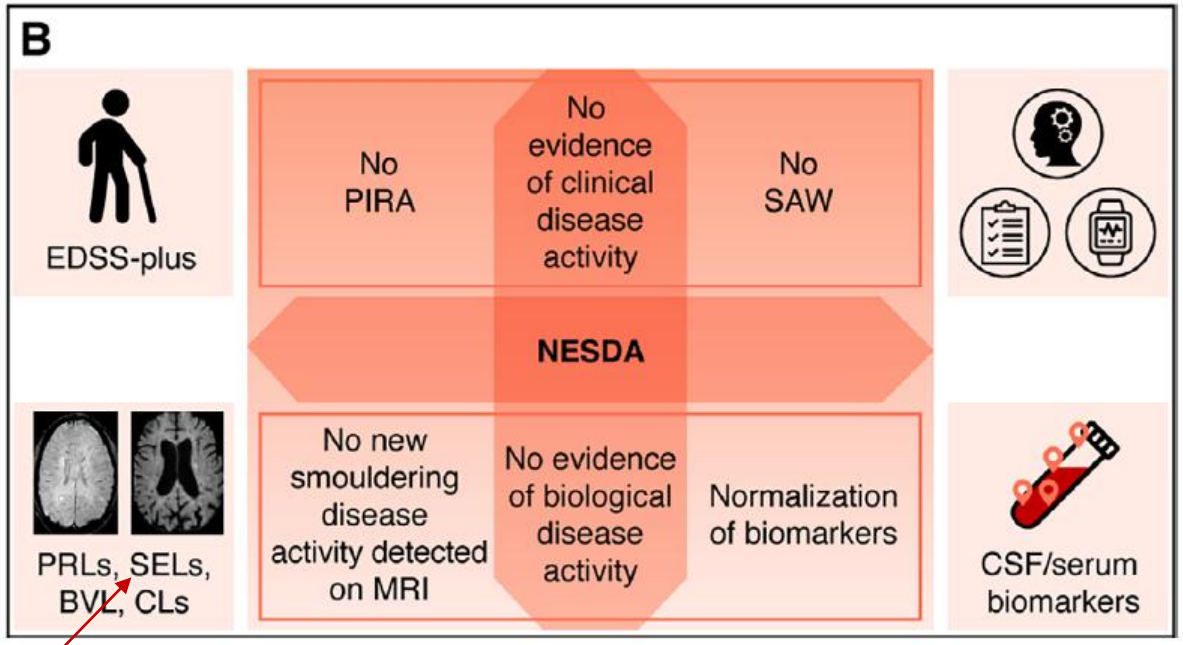


Smouldering-Associated Worsening in Multiple Sclerosis: An International Consensus Statement on Definition, Biology, Clinical Implications, and Future Directions

ANN NEUROL 2024;96:826–845

Remember NEDA??





D/D Enlarging T2 Vs Slowly expanding T1/T2 lesions

Hot Topic 7: Imaging chronic inflammation

Track	Imaging and non-imaging biomarkers
Room	Lecture Hall 111
Date	Thursday, 25 September 2025, 09:45 - 10:45 CEST

Iron, SEL and PRL

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Slowly Expanding Lesions (SEL)

Radiological biomarker of **chronic active lesions → steady, concentric, progressive expansion**

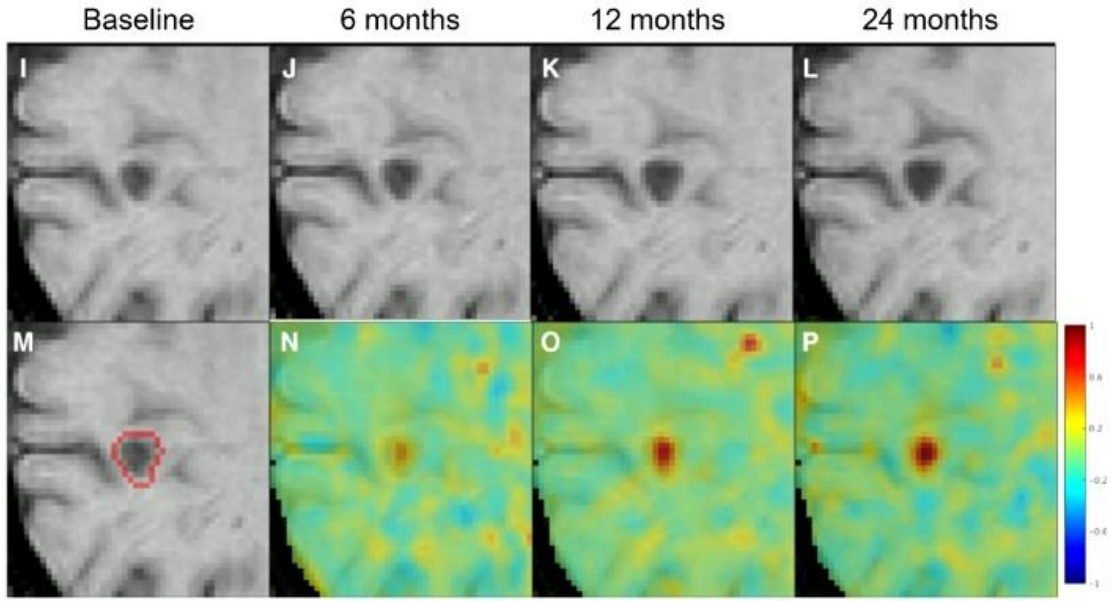

Image from: Bagnato et al, Brain, 2024

Prognosis

Manifestation of chronic inflammation → contribution to disease progression.

- In 99% of PMS cases and 86% of RMS cases.
- SEL: more severe pathological changes.
- Associated with brain atrophy.
- **Predict disease worsening.**

T 1 Black Holes/ T2 Lesions

Hot Topic 7: Imaging chronic inflammation

Track Imaging and non-imaging biomarkers

Room Lecture Hall 111

Date Thursday, 25 September 2025, 09:45 - 10:45 CEST

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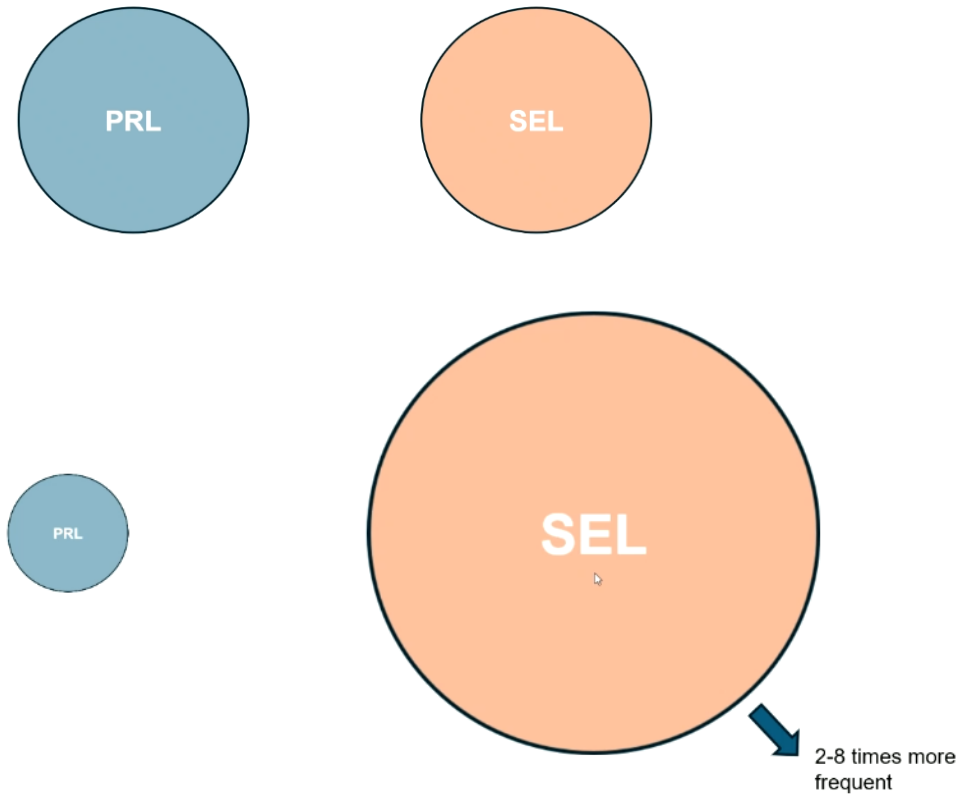
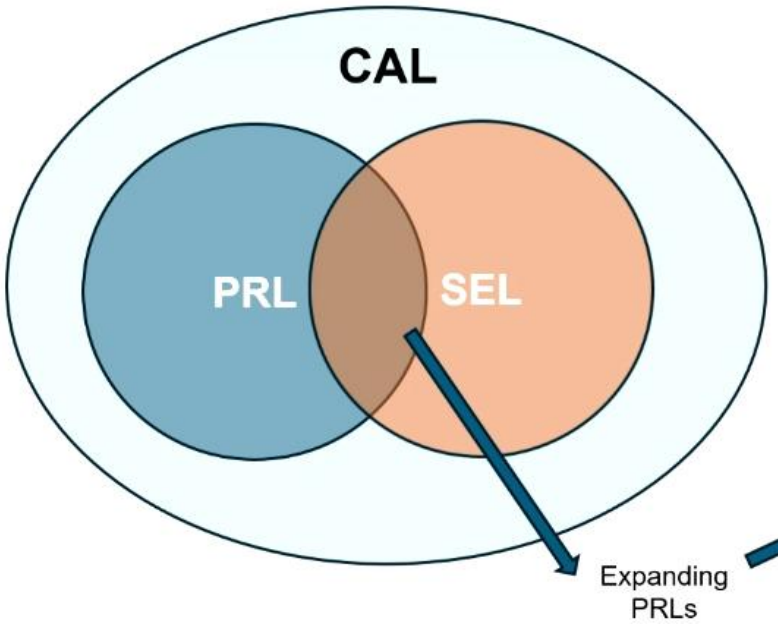
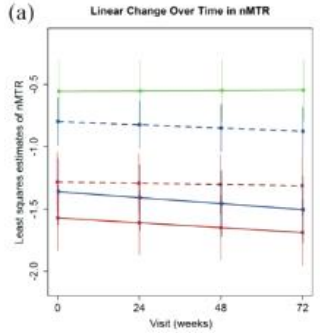
Relation Between PRLs and SELs





<20% SELs co-localize with PRLs.

Limited overlap:
- Different CAL types?
- Different developmental phases?



MULTIPLE SCLEROSIS JOURNAL | MSJ

Original Research Paper

Presence of slowly expanding lesions in multiple sclerosis predicts progressive demyelination within lesions and normal-appearing tissue over time

Multiple Sclerosis Journal
2025, Vol. 31(4) 418–432
DOI: 10.1177/13524585251316519
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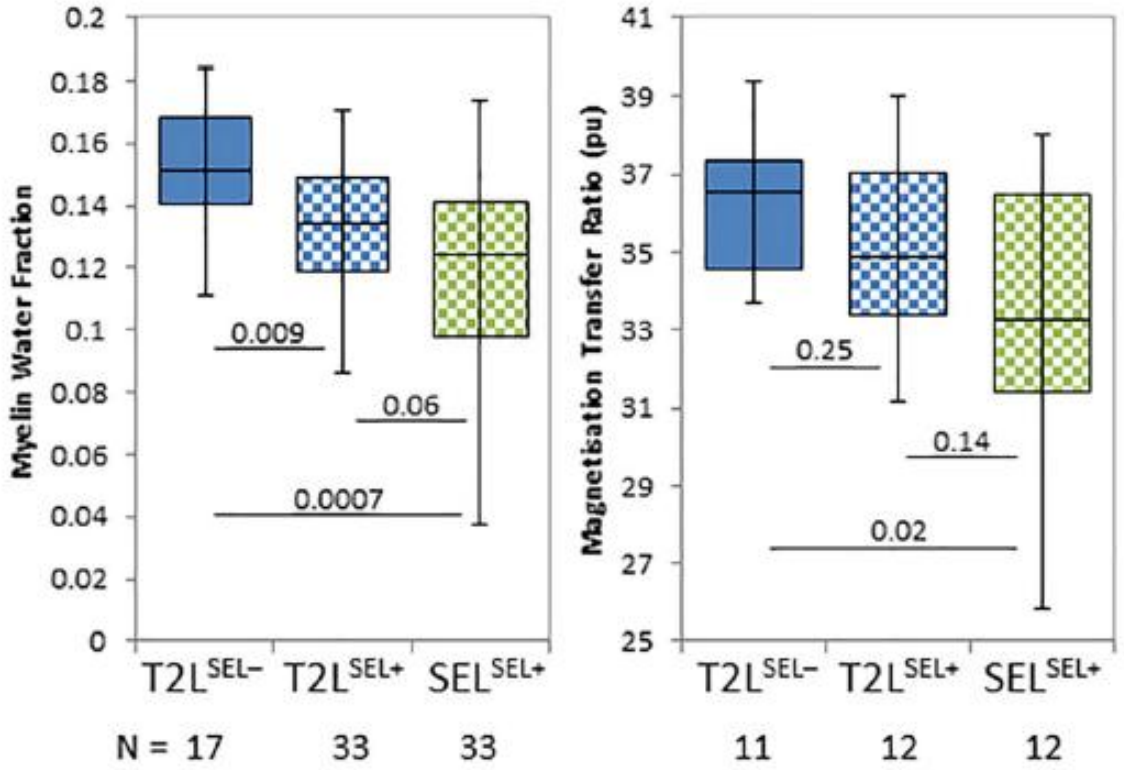

Our results indicate progressive focal and global demyelination in SEL+ participants, and that the presence of SELs might be a biomarker for ongoing diffuse or smouldering inflammation within the brain.

Free Communications 6: Imaging - barrier permeability and paramagnetic rim lesions

Track Imaging and non-imaging biomarkers

Room Lecture Hall 117

Date Thursday, 25 September 2025, 11:15 - 12:30 CEST

PRESENTATION ID O061

The Presence of Juxtacortical Paramagnetic Rims in People with MS is Associated with More Severe Disability

Riccardo Galbusera (Switzerland)

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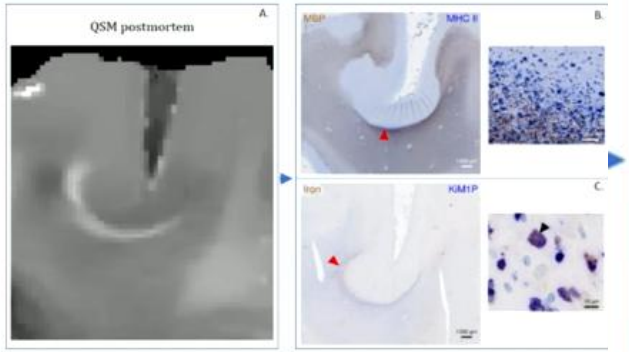
EVEN MORE COMPLICATED THINGS

Juxtacortical paramagnetic rims: a novel MR-biomarker in MS

Juxtacortical paramagnetic rims (JPR)

Background:

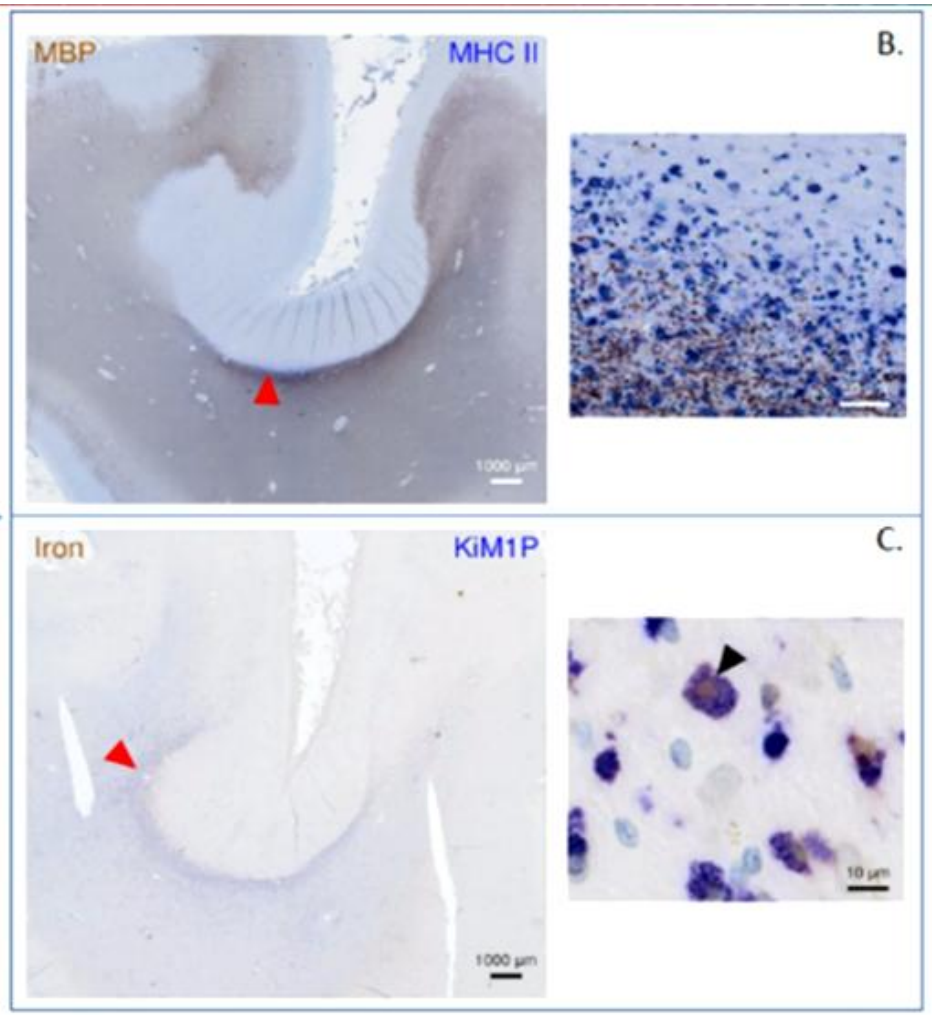
- Identified in ~10% of pwMS in vivo on 3T MRI (quantitative susceptibility mapping -QSM-)
- Histological correlate: cortical lesion type IV surrounded by iron-laden microglia at the gray-white matter boundary



Galbusera et al., *Neurology* 102.3 (2024): e207966.

- It is not surrounding a WML, but a cortical lesion
- Similarity to PRL: the rim is due to iron-laden phagocytes.

Research gap: clinical significance still unknown



Free Communications 6: Imaging - barrier permeability and paramagnetic rim lesions

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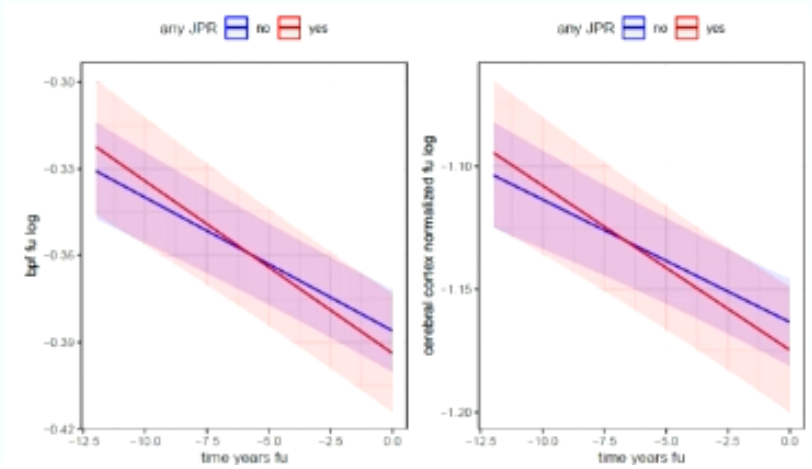
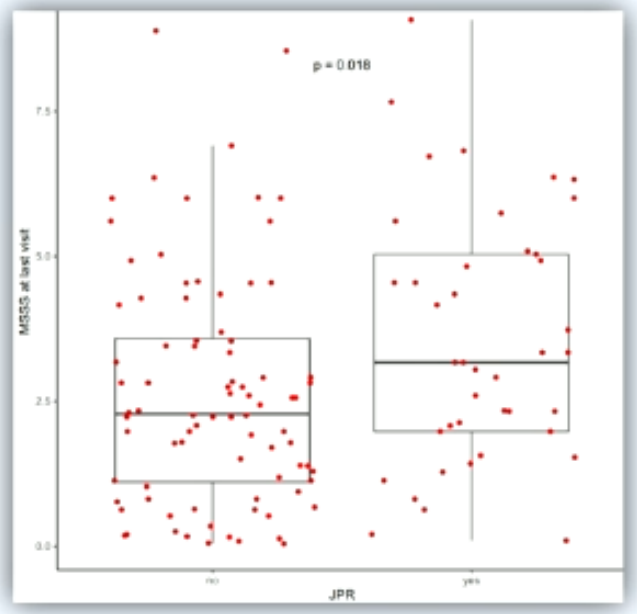
JPR are associated with more severe disability (MSSS)

- Juxtacortical paramagnetic rims (JPR), counterpart of the PRL in the cortex? -

Results:

PwMS with JPR have higher MSSS at last visit compared to matched pwMS without JPR (3.584 [2.955;4.213] vs 2.645 [2.206;3.085]; 95% CI 0.17-1.81, p = 0.018].





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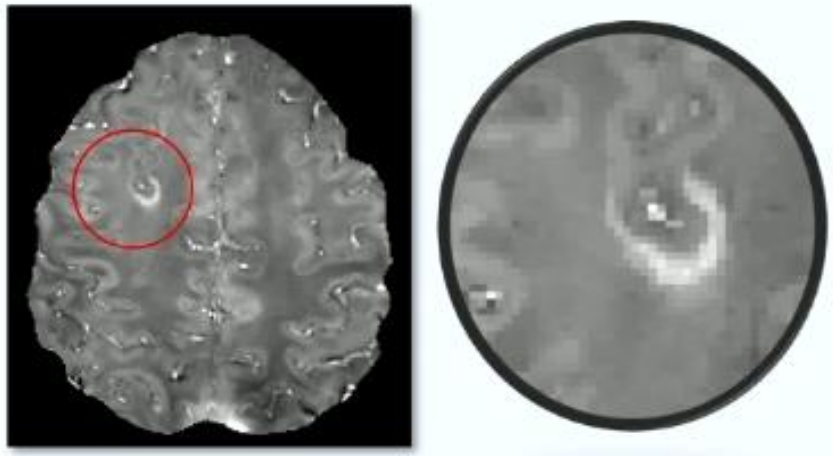
JPR are associated with more severe disability (MSSS)

- Juxtacortical paramagnetic rims (JPR), counterpart of the PRL in the cortex? -

Conclusions:

- Our data suggest that JPR may serve as a marker of disease severity
- Lack of correlation with relapse activity or sNfL levels indicates possible association with smouldering inflammation
- Future studies should confirm our results

Prototypical JPR on QSM in vivo



ΠΡΟΒΛΗΜΑΤΙΣΜΟΙ ΙΙ
ΒΙΟΔΕΙΚΤΕΣ- PIRA/ Αργής Επιδείνωσης

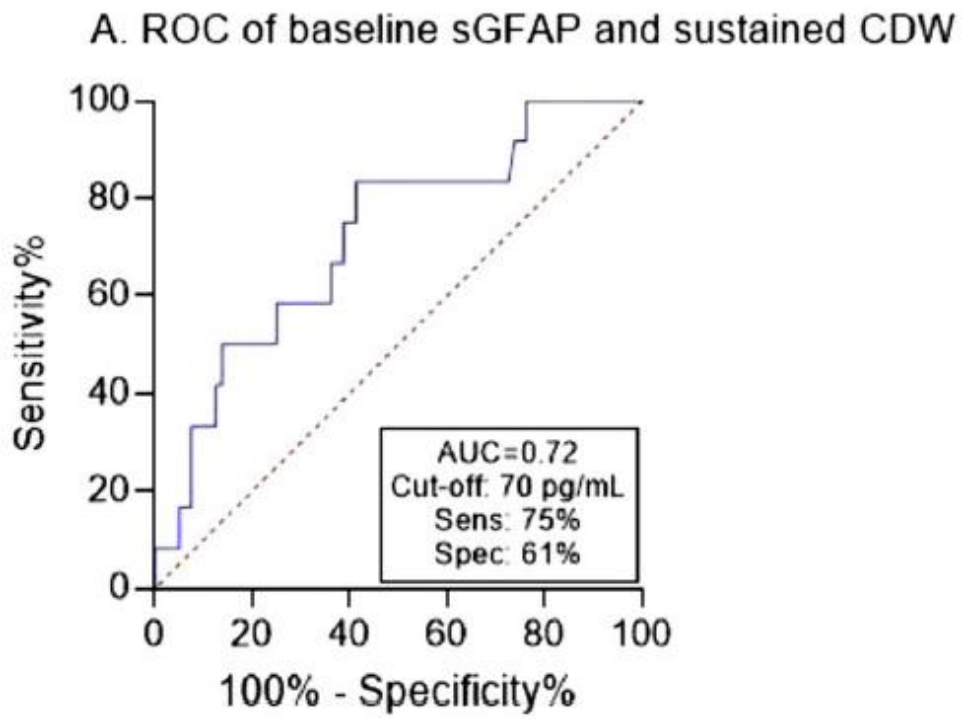
Journal of Neurology (2024) 271:4412–4422
https://doi.org/10.1007/s00415-024-12389-y

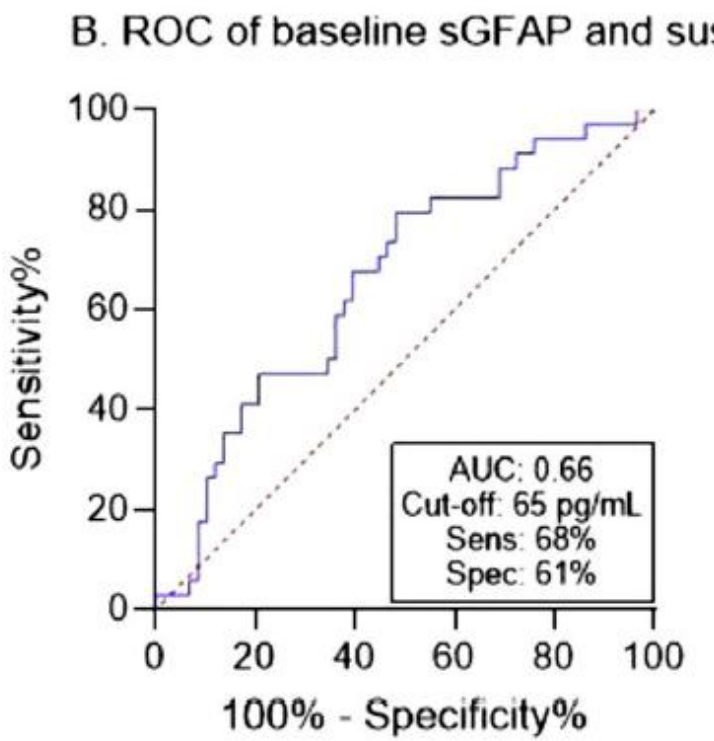
ORIGINAL COMMUNICATION

Association of serum glial fibrillary acidic protein with progression independent of relapse activity in multiple sclerosis

Igal Rosenstein[1,2] · Anna Nordin[1] · Hemin Sabir[2] · Clas Malmeström[1,2] · Kaj Blennow[3,4,5,6] · Markus Axelsson[1,2] · Lenka Novakova[1,2]

Glial fibrillary acidic protein (GFAP) constitutes the major component of astrocytic intermediate filaments implicated in the control of cell motility and morphology, providing structural stability to astrocyte processes.





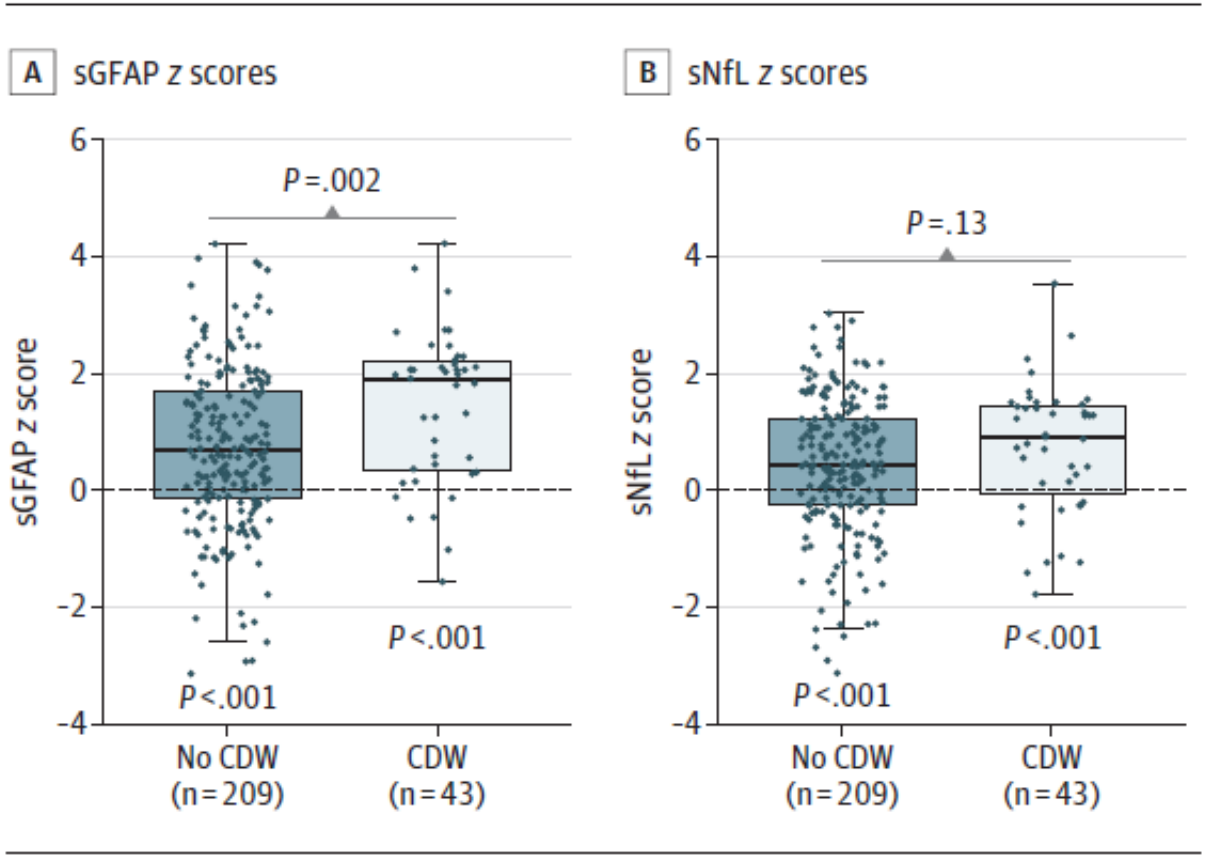
s-GFAP was significantly higher in PIRA at baseline (median [IQR] 73.9 [60.9–110.1] vs. 60.3 [45.2–79.9], p = 0.01).

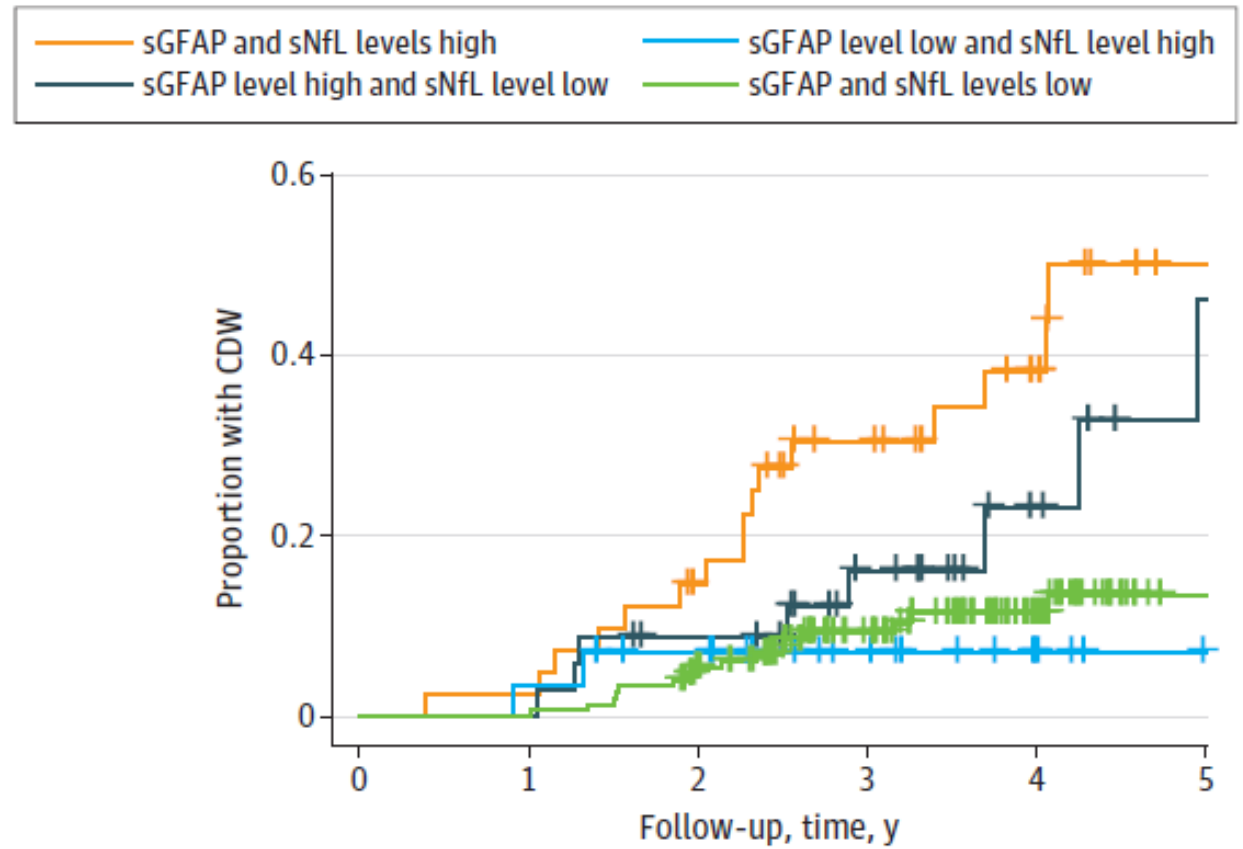
Repeated measures of s-GFAP levels showed that patients with PIRA during follow-up had higher levels of s-GFAP throughout the follow-up when compared to stable patients ($p < 0.001$).

JAMA Neurol. 2023;80(3):287-297. doi:10.1001/jamaneurol.2022.5250

JAMA Neurology | Original Investigation

Serum Glial Fibrillary Acidic Protein Compared With Neurofilament Light Chain as a Biomarker for Disease Progression in Multiple Sclerosis





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Emerging biomarkers: Guiding personalised treatment decisions

Enric Monreal (Spain)

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30th Conference of Rehabilitation in Multiple Sclerosis

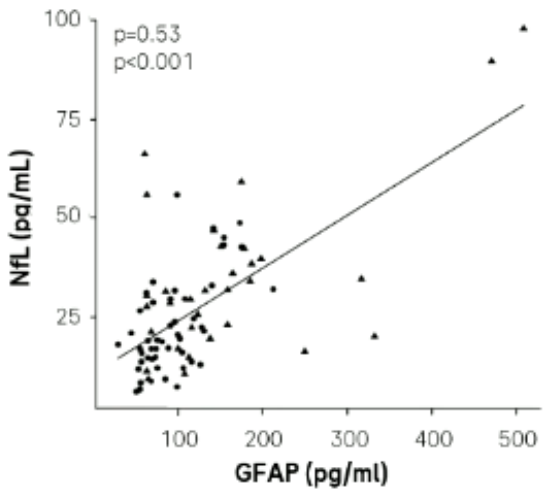
24-26 September 2025 | Barcelona, Spain

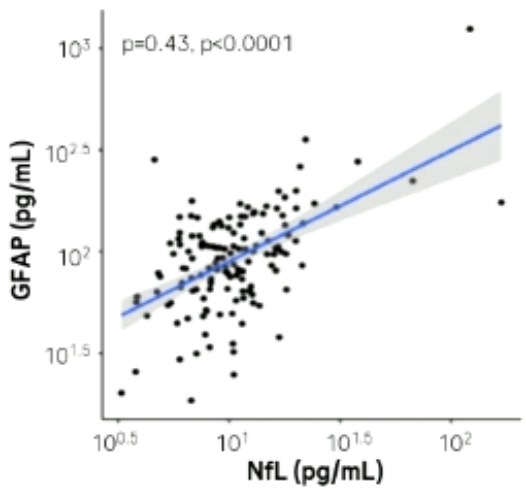
Satellite Symposium 2: How anti-CD20 therapies have shaped our understanding of MS and sparked future innovations

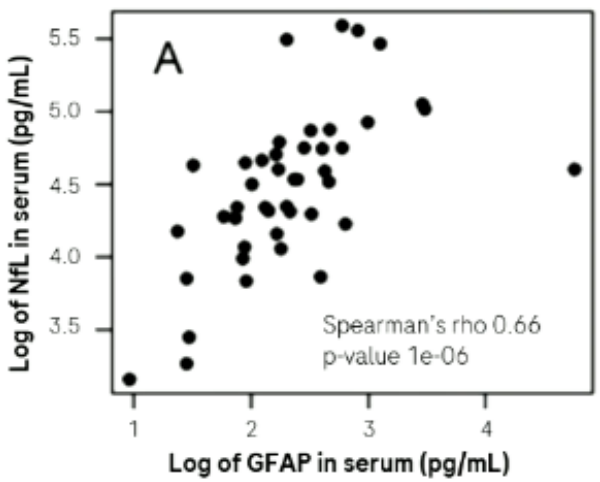
Track	Satellite Symposia
Room	Lecture Hall 7
Date	Wednesday, 24 September 2025, 13:15 - 14:15 CEST

The combination of elevated serum NfL and GFAP is indicative of ongoing acute inflammation and a disrupted blood–brain barrier

Association between elevated serum GFAP and NfL levels in MS[1–3]







Gd+/GE, gadolinium-enhancing; GFAP, glial fibrillary acidic protein; NfL, neurofilament light chain; sNfL, serum neurofilament light chain.
1. Högel H et al. *Mult Scler* 2020;26:210–9; 2. Fissolo N, et al. *J Neurol Neurosurg Psychiatry* 2024;95:410–8; 3. Ayrignac X, et al. *Sci Rep* 2020;10:10923.

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Emerging biomarkers: Guiding personalised treatment decisions

Enric Monreal (Spain)

Roche

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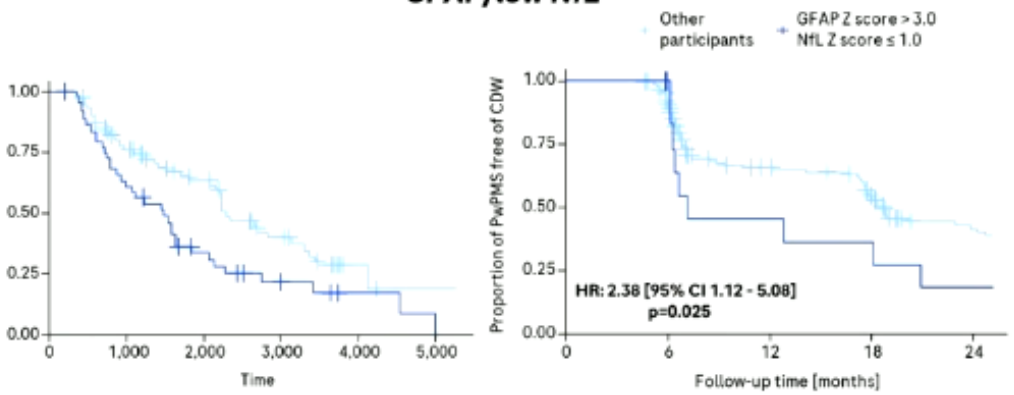
Satellite Symposium 2: How anti-CD20 therapies have shaped our understanding of MS and sparked future innovations

Track	Satellite Symposia
Room	Lecture Hall 7
Date	Wednesday, 24 September 2025, 13:15 - 14:15 CEST

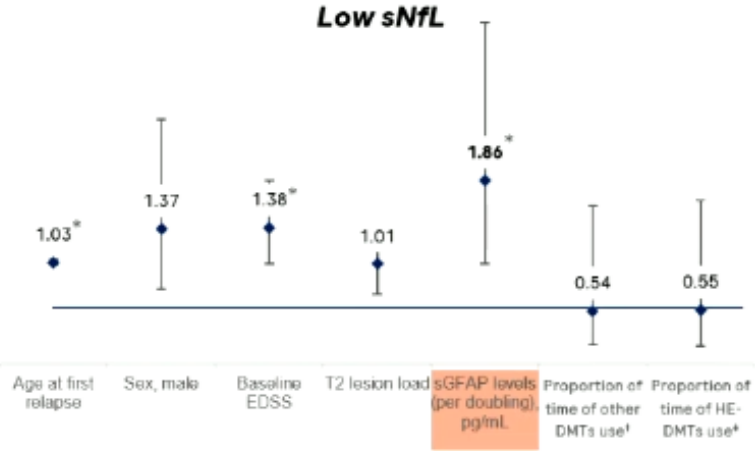
Elevated serum GFAP in the absence of NfL indicates compartmentalised inflammation through activated microglia

NfL ↓ **Chronic compartmentalised inflammation** ↑ **GFAP**

Serum GFAP-dependent risk of CDW in patients with low serum NfL[1,2]



Multivariable Cox regression models of associations between serum biomarker levels and the risk of PIRA[3]



* p<0.05; †Other DMTs: Subcutaneous or intramuscular interferon-β, glatiramer acetate, teriflunomide, dimethyl fumarate, fingolimod, oral cladribine, daclizumab and azathioprine; ‡HE-DMTs: natalizumab, alemtuzumab, ocrelizumab, rituximab and ofatumumab.

CDW, confirmed disability worsening; CI, confidence interval; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; GFAP, glial fibrillary acidic protein; HE-DMT, high-efficacy DMT; HR, hazard ratio; NfL, neurofilament light chain; PIRA, progression independent of relapse activity; PwPMS, people with progressive MS; sGFAP, serum glial fibrillary acidic protein; sNfL, serum neurofilament light chain.

1. Barro C, et al. *Neurol Neuroimmunol Neuroinflamm* 2022;10:e200052; 2. Abdelhak A, et al. *Ann Clin Transl Neurol* 2024;11:477–85; 3. Monreal E, et al. *Brain* 2024;147:4084–93.

Scientific Session 6: Body fluid biomarkers 2 - treatment monitoring

Track Imaging and non-imaging biomarkers

Room Lecture Hall 7

Date Thursday, 25 September 2025, 11:15 - 12:45 CEST

Other body fluid biomarkers as surrogate marker in clinical trials
Tanuja Chitnis (United States)

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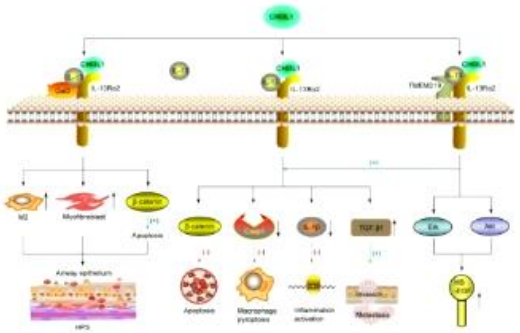
Chitinase 3-like 1 protein (CHI3L1 or YKL40)

- CHI3L1 is a member of glycoside hydrolase family Secreted by macrophages, neutrophils, varied stromal and epithelial cells and by astrocytes
- Is upregulated by variety of inflammatory stimuli and other stressors



Zhao, Nature Signal Transduction and Targeted Therapy, 2020

CHI3L1 and MS

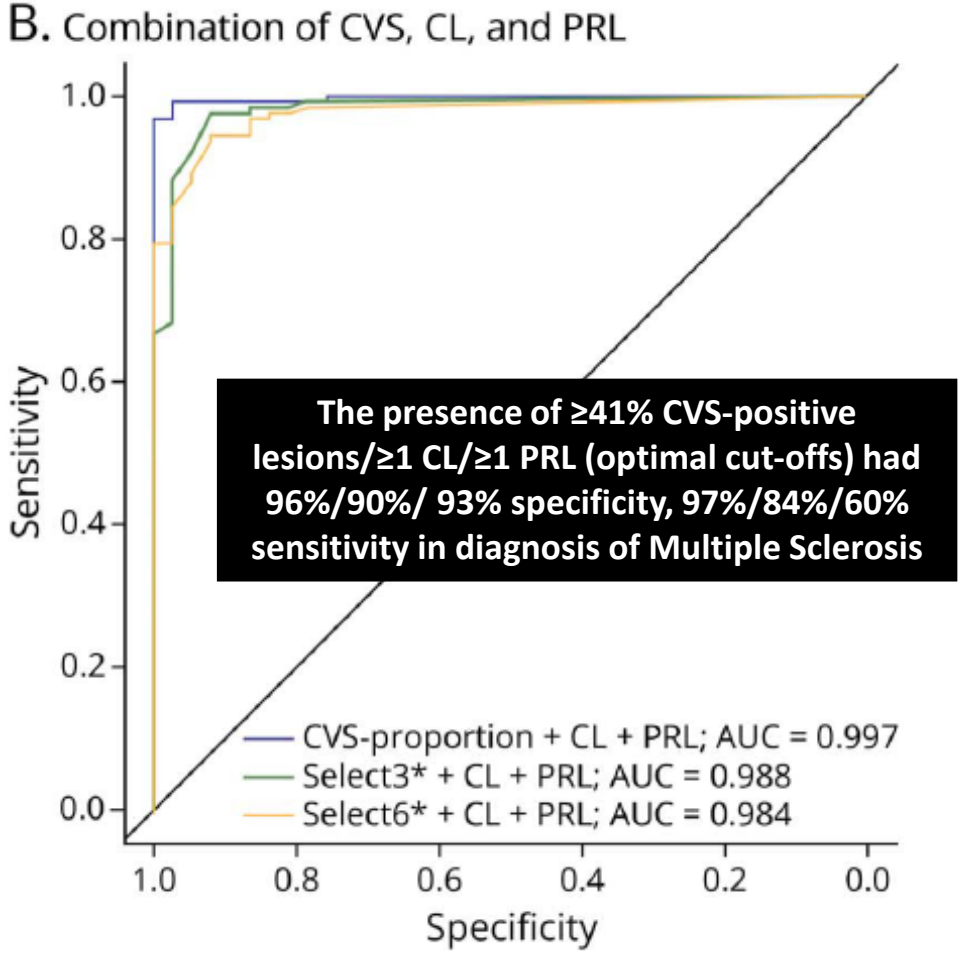
- CHI3L1 in the CSF was found to be a risk factor for conversion to multiple sclerosis HR 1.6; $p=3.7x10^6$ by the 2005 McDonald criteria *(Canto, Brain 2015)*
- Increased concentrations of CHI3L1 in CSF correlated with higher scores EDSS scores *(Canto, Brain 2015)*
- CHI3L1 was associated with cognitive impairment *(Modvig, MSJ 2015; Quintana EJN, 2018)*
- CHI3L1 associated with iron rim lesions in CIS *(Comabella, MSJ 2021)*

- Serum CHI3L1 was reduced in Beta-IFN but not GA-treated patients
- CSF CHI3L1 protein was reduced after 4-12 months in fingolimod-treated patients
- CHI3L1 was the most important predictor of NEDA status in Cladribine-treated patients

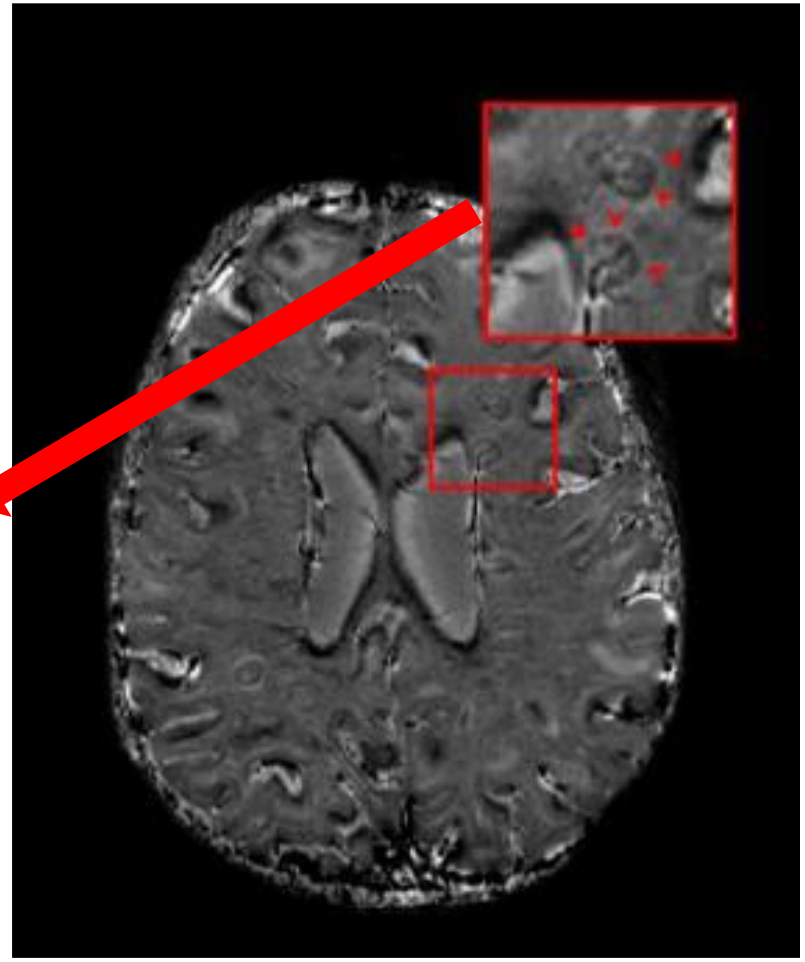
RESEARCH ARTICLE OPEN ACCESS

Central Vein Sign, Cortical Lesions, and Paramagnetic Rim Lesions for the Diagnostic and Prognostic Workup of Multiple Sclerosis

Neurol Neuroimmunol Neuroinflamm 2024;11:e200253.



The presence of ≥41% CVS-positive lesions/≥1 CL/≥1 PRL (optimal cut-offs) had 96%/90%/ 93% specificity, 97%/84%/60% sensitivity in diagnosis of Multiple Sclerosis



Longitudinal analysis (n = 61) showed that MS cases with >4 PRL at baseline were more likely to experience PIRA at 2-year follow-up (odds ratio 17.0, 95% confidence interval: 2.1–138.5; p = 0.008), whereas no association was observed between other baseline MRI measures and PIRA, including the number of CL.

Clin Transl Imaging (2015) 3:461–473
DOI 10.1007/s40336-015-0147-6

REVIEW ARTICLE

TSPO: Translocator Protein located in the outer surface of mitochondria

Imaging neuroinflammation in multiple sclerosis using TSPO-PET

Laura Airas[1,2] · Eero Rissanen[1,2] · Juha O. Rinne[1,2]

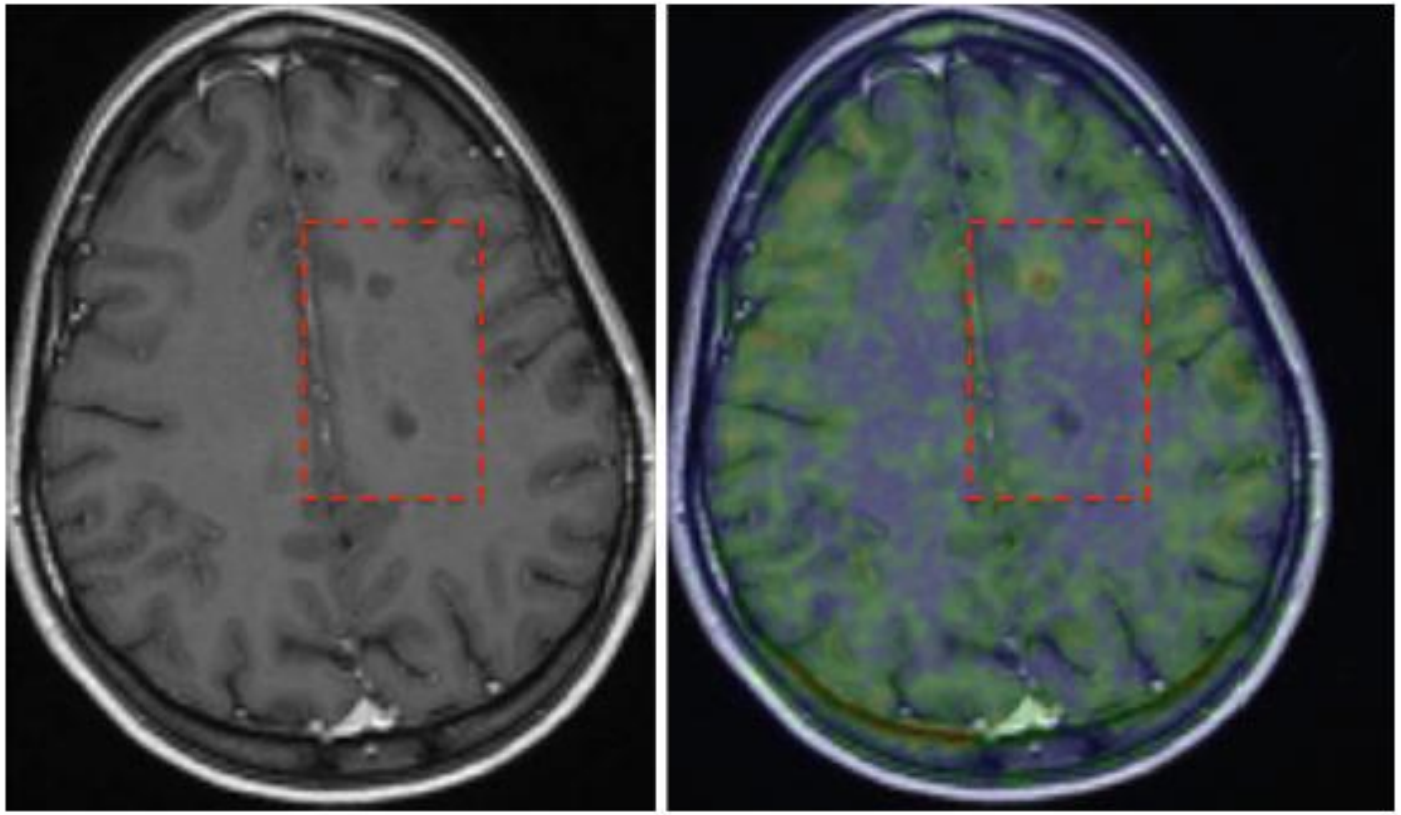
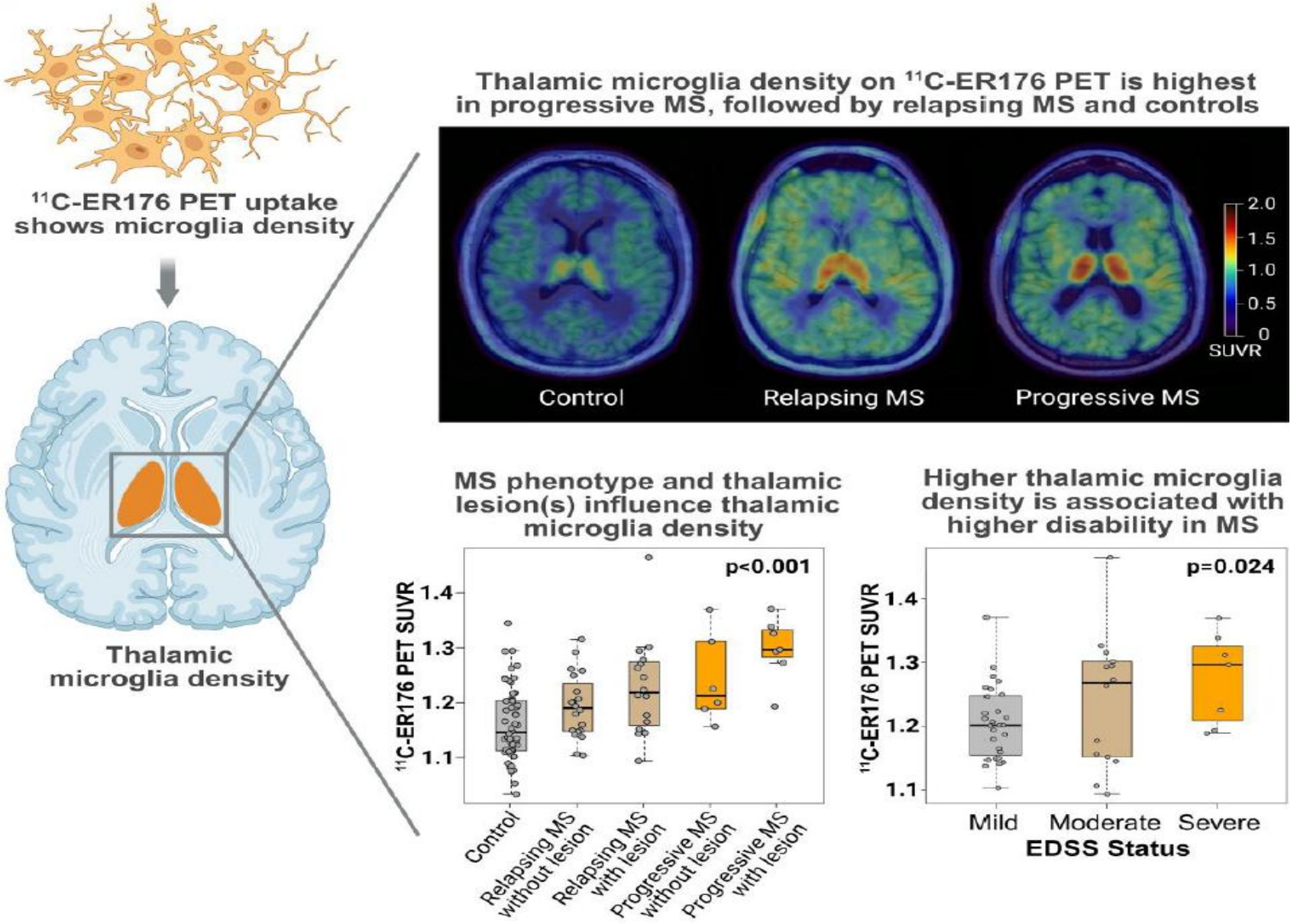


Fig. 1 In vivo differentiation of chronic T1 lesions using TSPO-PET. *Left image* a T1-weighted MRI image with two similar-looking (non-gadolinium-enhancing) T1 black holes. TSPO-PET (on the *right*) shows that in the upper lesion there is microglial activation, confirming this lesion to be a chronic active lesion, whereas in the lower lesion there is no radioligand uptake, confirming this lesion to be a chronic inactive lesion

BRAIN COMMUNICATIONS
https://doi.org/10.1093/braincomms/fcaf141 BRAIN COMMUNICATIONS 2025: fcaf141 | 1

Microglia positron emission tomography and progression in multiple sclerosis: thalamus on fire



Microglia density in the thalamus is highest in patients with progressive multiple sclerosis and is associated with imaging biomarkers of neurodegeneration and clinical disease severity. As a signature imaging biomarker of progression in multiple sclerosis, effectively reflecting the global disease burden, 11C-ER176 PET may aid development and efficacy evaluation of therapeutics targeting microglia.

Hot Topic 7: Imaging chronic inflammation

Track	Imaging and non-imaging biomarkers
Room	Lecture Hall 111
Date	Thursday, 25 September 2025, 09:45 - 10:45 CEST

Iron, SEL and PRL

Alessandro Cagol (Switzerland)

ECTRIMS 2025

41st Congress of the European Committee for Treatment and Research in Multiple Sclerosis

30th Conference of Rehabilitation in Multiple Sclerosis

24-26 September 2025 | Barcelona, Spain

Slowly Expanding Lesions (SEL)

Radiological biomarker of **chronic active lesions → steady, concentric, progressive expansion**

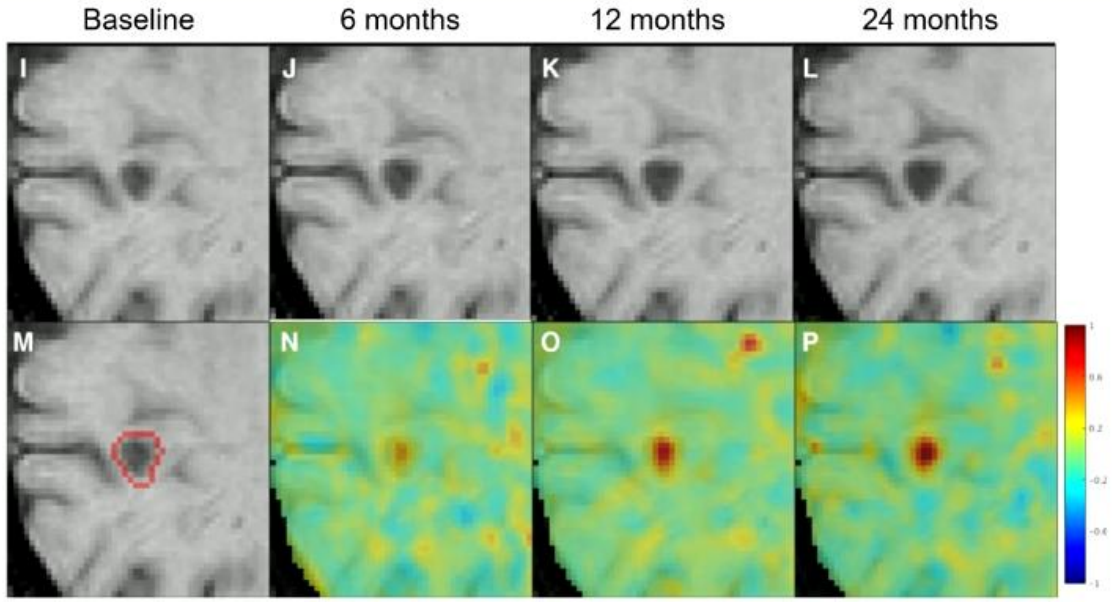


Image from: Bagnato et al, Brain, 2024

Prognosis

Manifestation of chronic inflammation → contribution to disease progression.

- In 99% of PMS cases and 86% of RMS cases.
- SEL: more severe pathological changes.
- Associated with brain atrophy.
- **Predict disease worsening.**

Free Communications 6: Imaging - barrier permeability and paramagnetic rim lesions

Track Imaging and non-imaging biomarkers

Room Lecture Hall 117

Date Thursday, 25 September 2025, 11:15 - 12:30 CEST

PRESENTATION ID O061

The Presence of Juxtacortical Paramagnetic Rims in People with MS is Associated with More Severe Disability

Riccardo Galbusera (Switzerland)

ECTRIMS 2025

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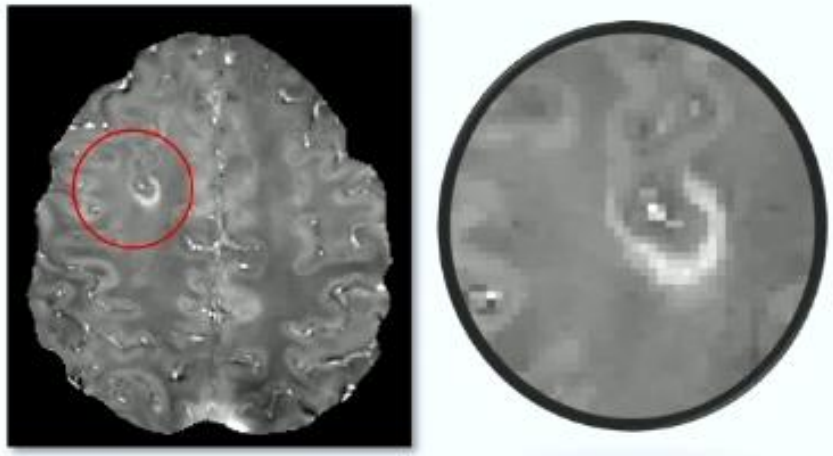
JPR are associated with more severe disability (MSSS)

- Juxtacortical paramagnetic rims (JPR), counterpart of the PRL in the cortex? -

Conclusions:

- Our data suggest that JPR may serve as a marker of disease severity
- Lack of correlation with relapse activity or sNfL levels indicates possible association with smouldering inflammation
- Future studies should confirm our results

Prototypical JPR on QSM in vivo



Hot Topic 7: Imaging chronic inflammation

Track	Imaging and non-imaging biomarkers
Room	Lecture Hall 111
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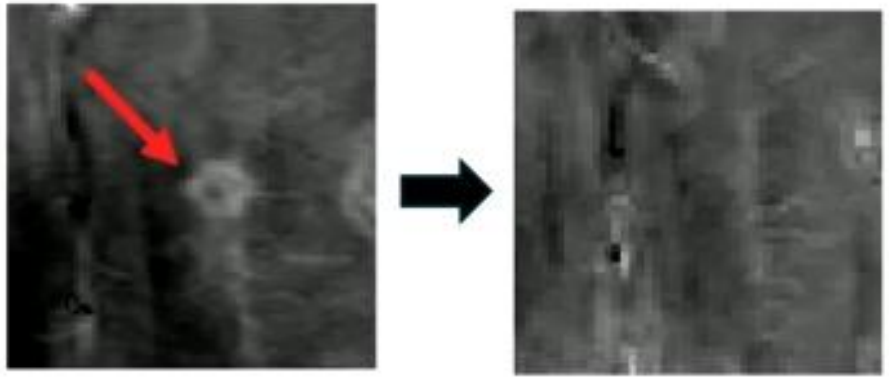
Clinical Value of PRLs

Disease/Treatment Monitoring

- PRL appearance/disappearance is related to clinical outcomes.
- No evidence of treatments inducing PRL resolution so far.

Treatment Effectiveness Evaluation



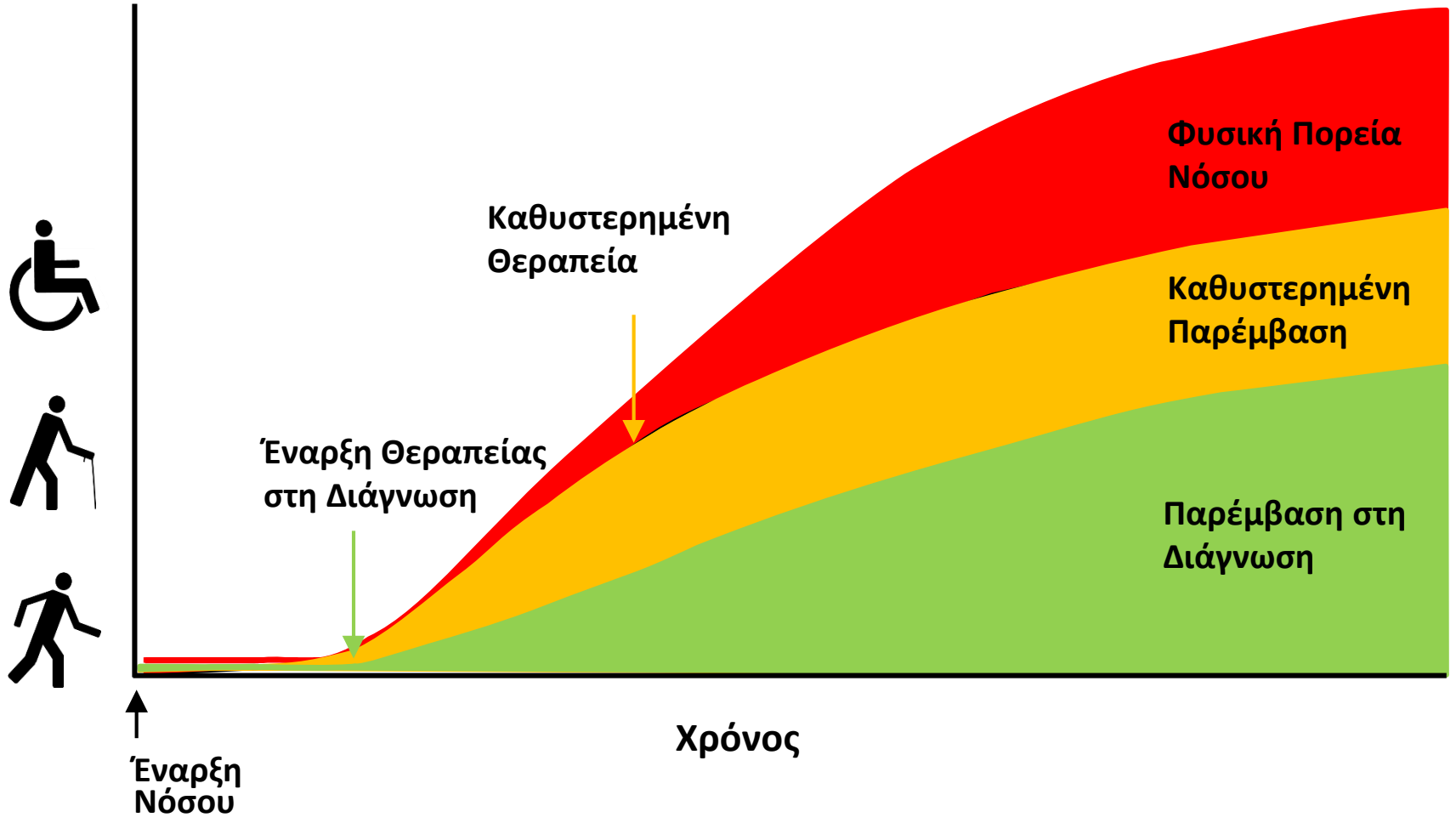
- Resolution of existing rims
- Absence of new PRLs

↓

Reduced risk of progression

ΠΡΟΒΛΗΜΑΤΙΣΜΟΙ (IV)
ΘΕΡΑΠΕΙΑ- ΕΝΑΡΞΗ

Έγκαιρη έναρξη της θεραπείας



J Manag Care Pharm. 2004;10(3)(suppl S-b):S4-S11

JAMA Neurology | Original Investigation

Association of Early Progression Independent of Relapse Activity With Long-term Disability After a First Demyelinating Event in Multiple Sclerosis

JAMA Neurol. 2023;80(2):151-160. doi:10.1001/jamaneurol.2022.4655
Published online December 19, 2022.

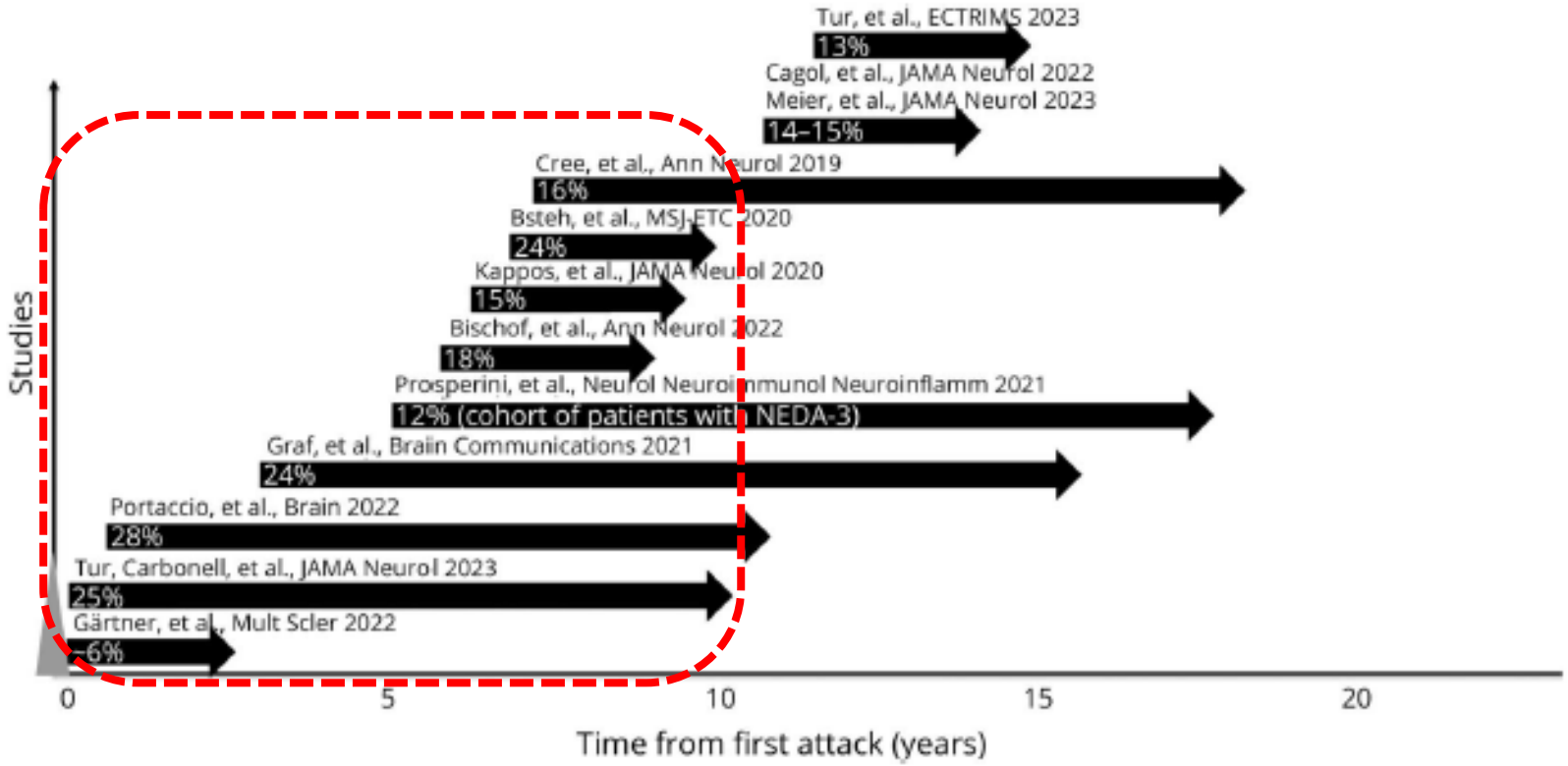
Table 2. Prediction of Long-term Outcomes (N = 1128)

Outcome	All study patients (N = 1128)	PIRA (n = 277)	No PIRA (n = 851)	*P* value, PIRA vs no PIRA	Early PIRA (n = 86)	Late PIRA (n = 191)	*P* value, early PIRA vs late PIRA	Active PIRA (n = 73)	Nonactive PIRA (n = 71)	*P* value, active PIRA vs nonactive PIRA
Adjusted yearly EDSS increase rates (95% CI)	0.07 (0.06-0.09)	0.18 (0.16-0.20)	0.04 (0.02-0.05)	<.001	0.31 (0.26-0.35)	0.13 (0.10-0.16)	<.001	0.20 (0.15-0.25)	0.12 (0.06-0.18)	.05
Kaplan-Meier estimates (95% CI) of % patients reaching EDSS 6.0 from the first demyelinating event[a]										
5 y	0.48 (0.06-0.90)	1.09 (0-2.31)	0.24 (0-0.57)	<.001	2.41 (0-5.67)	0.52 (0-1.54)	.07	1.37 (0-4.00)	1.52 (0-4.42)	.003
10 y	2.54 (1.41-3.65)	5.58 (2.69-8.39)	1.02 (0.18-1.86)		12.03 (3.71-19.63)	3.24 (0.65-5.76)		9.11 (1.86-15.82)	4.86 (0-10.09)	
15 y	6.00 (3.97-7.98)	12.82 (8.18-17.23)	1.74 (0.42-3.03)		23.93 (11.01-34.98)	9.10 (4.55-3.42)		24.54 (12.18-35.15)	4.86 (0-10.09)	
20 y	9.25 (6.23-12.19)	18.49 (12.37-24.19)	2.45 (0.53-4.33)		23.93 (11.01-34.98)	16.41 (9.47-22.82)		38.32 (22.05-51.19)	10.46 (0-21.50)	
Adjusted HR (95% CI) for reaching confirmed EDSS 6.0 from the first demyelinating event[a]	NA	7.93 (2.25-27.96)	1 [Reference]	.001	26.21 (2.26-303.95)	1 [Reference]	.009	2.51 (0.58-10.85)	1 [Reference]	.22

Using the Progression Independent of Relapse Activity Framework to Unveil the Pathobiological Foundations of Multiple Sclerosis

Neurology® 2024;103:e209444. doi:10.1212/WNL.0000000000209444

Figure 1 Annual Frequency of PIRA Events Reported by Previous Studies



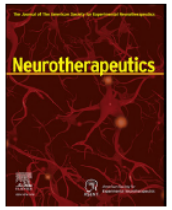
This figure represents the percentage of people with MS who develop at least 1 PIRA event a year, as reported by previous studies. Each study is represented by an arrow, whose length indicates the median time of the study follow-up. The position of the start of the arrow along the x-axis represents the median/mean (as available) disease duration of the patients at study entry. The references are given in the eTable 1. MS = multiple sclerosis; NEDA = no evidence of disease activity; PIRA = progression independent of relapse activity.

Neurotherapeutics 22 (2025) e00552

Contents lists available at ScienceDirect

Neurotherapeutics

journal homepage: www.sciencedirect.com/journal/neurotherapeutics



Original Article

First-year treatment response predicts the following 5-year disease course in patients with relapsing-remitting multiple sclerosis

Multivariate survival model for all outcomes.

Explanatory variable	Category	First relapse	Disability progression	EDSS 3.0[c]	EDSS 6.0[d]	Conversion to SPMS	New brain MRI lesions	New spine MRI lesions
Sub-optimal response in first year of treatment[a]	**Yes[b]**	3.84 (3.51, 4.19)	1.74 (1.56, 1.93)	3.01 (2.58, 3.51)	1.77 (1.43,2.20)	1.20 (0.87, 1.66)	2.33 (2.04, 2.66)	1.65 (1.29, 2.09)
		<0.001	**<0.001**	**<0.001**	**<0.001**	0.258	**<0.001**	**<0.001**
	No	Reference	Reference	Reference	Reference	Reference	Reference	Reference
First DMT - high efficacy	**Yes**	0.78 (0.67, 0.91)						
		0.002						
	No	Reference						

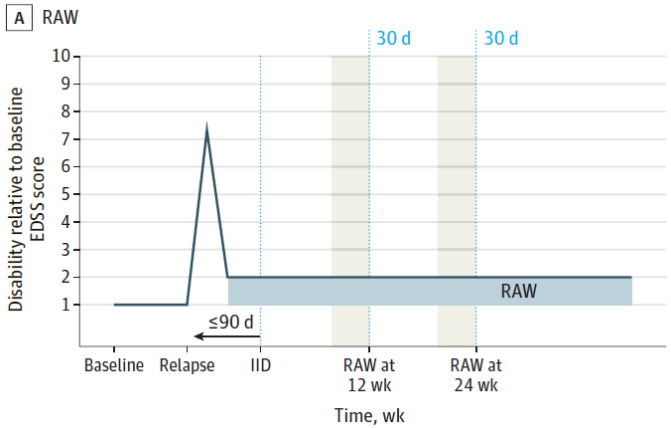
We recruited patients from the MSBase Registry covering the period between 1996 and 2022. All patients were diagnosed with RRMS and actively followed up for at least 5 years to explore the following outcomes: clinical relapses, confirmed disability worsening (CDW) and improvement (CDI), EDSS 3.0, EDSS 6.0, conversion to secondary progressive MS (SPMS), new MRI lesions, Progression Independent of Relapse Activity (PIRA). Predictors included demographic, clinical, and radiological data, as well as sub-optimal response (SR) within the first year of treatment.

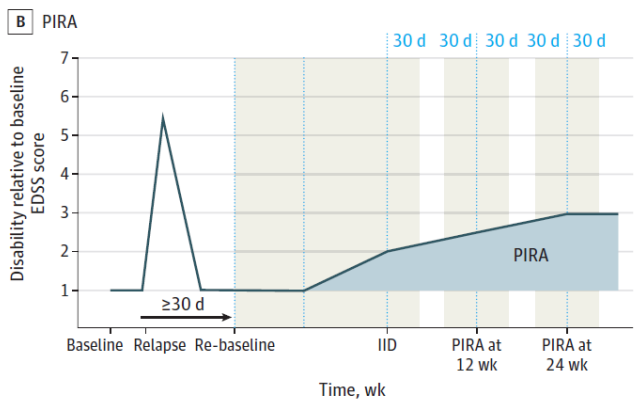
JAMA Neurology | Original Investigation

Contribution of Relapse-Independent Progression vs Relapse-Associated Worsening to Overall Confirmed Disability Accumulation in Typical Relapsing Multiple Sclerosis in a Pooled Analysis of 2 Randomized Clinical Trials

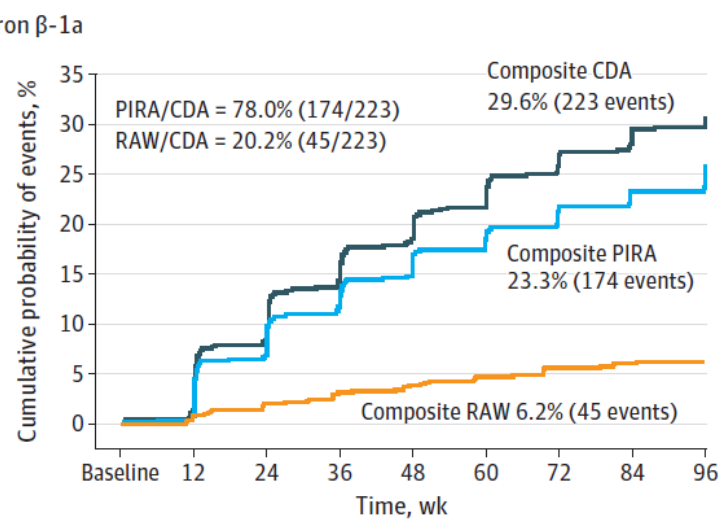
Ludwig Kappos, MD; Jerry S. Wolinsky, MD; Gavin Giovannoni, PhD; Douglas L. Arnold, MD; Qing Wang, PhD; Corrado Bernasconi, PhD; Fabian Model, PhD; Harold Koendgen, MD; Marianna Manfrini, MD; Shibeshih Belachew, MD; Stephen L. Hauser, MD

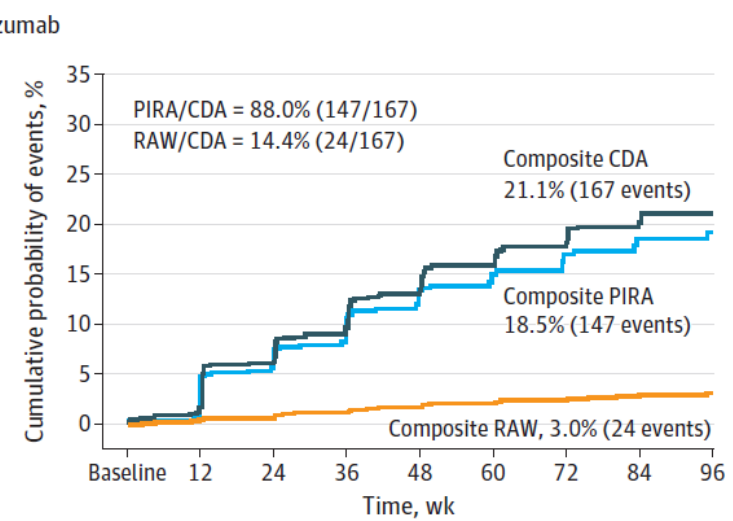
JAMA Neurol. 2020;77(9):1132-1140. doi:10.1001/jamaneurol.2020.1568
Published online June 8, 2020.





CONCLUSIONS AND RELEVANCE Most disability accumulation in RMS is not associated with overt relapses. This indicates an underlying progression in this typical RMS population and challenges the current clinical distinction of relapsing and progressive forms of multiple sclerosis. Ocrelizumab was superior to interferon β-1a in preventing both RAW and PIRA.





This session is sponsored by: **F. Hoffmann-La Roche**

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Paving the way: Lessons from anti-CD20 therapies towards a better understanding of MS
Amit Bar-Or (United States)

ECTRIMS 2025

41st Congress of the European Committee for Treatment and Research in Multiple Sclerosis

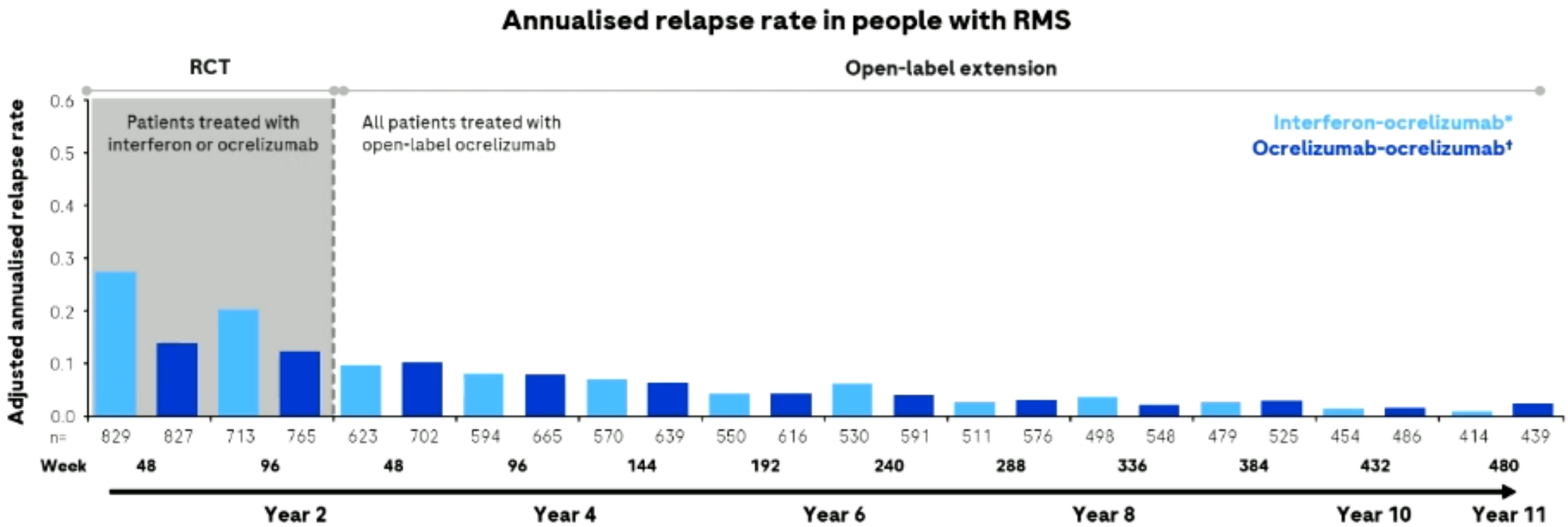
30th Conference of Rehabilitation in Multiple Sclerosis

24-26 September 2025 | Barcelona, Spain

Satellite Symposium 2: How anti-CD20 therapies have shaped our understanding of MS and sparked future innovations

Track	Satellite Symposia
Room	Lecture Hall 7
Date	Wednesday, 24 September 2025, 13:15 - 14:15 CEST

Anti-CD20 therapies result in long-term reduction of annualised relapse rates



This session is sponsored by: **F. Hoffmann-La Roche**

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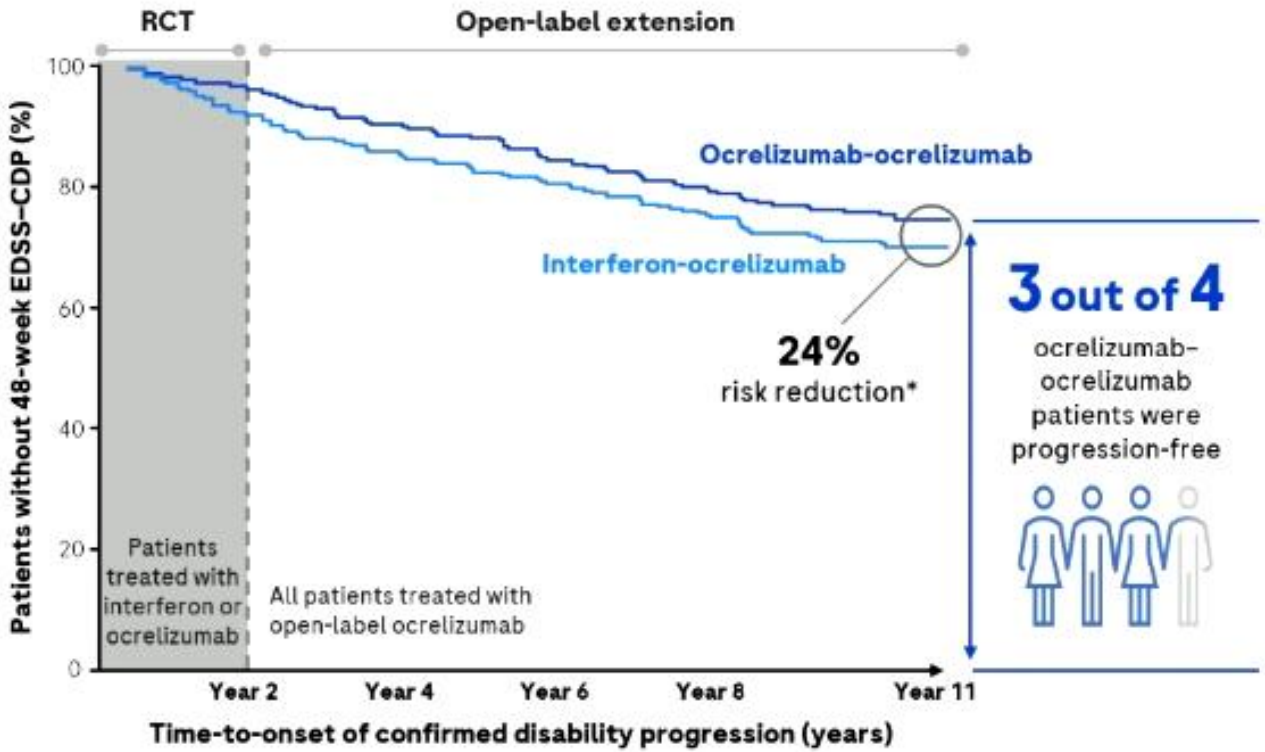
Satellite Symposium 2: How anti-CD20 therapies have shaped our understanding of MS and sparked future innovations

Track	Satellite Symposia
Room	Lecture Hall 7
Date	Wednesday, 24 September 2025, 13:15 - 14:15 CEST

Anti-CD20 therapies result in a long-term reduction of risk of disability progression



8 years
delay

until next disability event for people with RMS starting ocrelizumab two years earlier†

Research

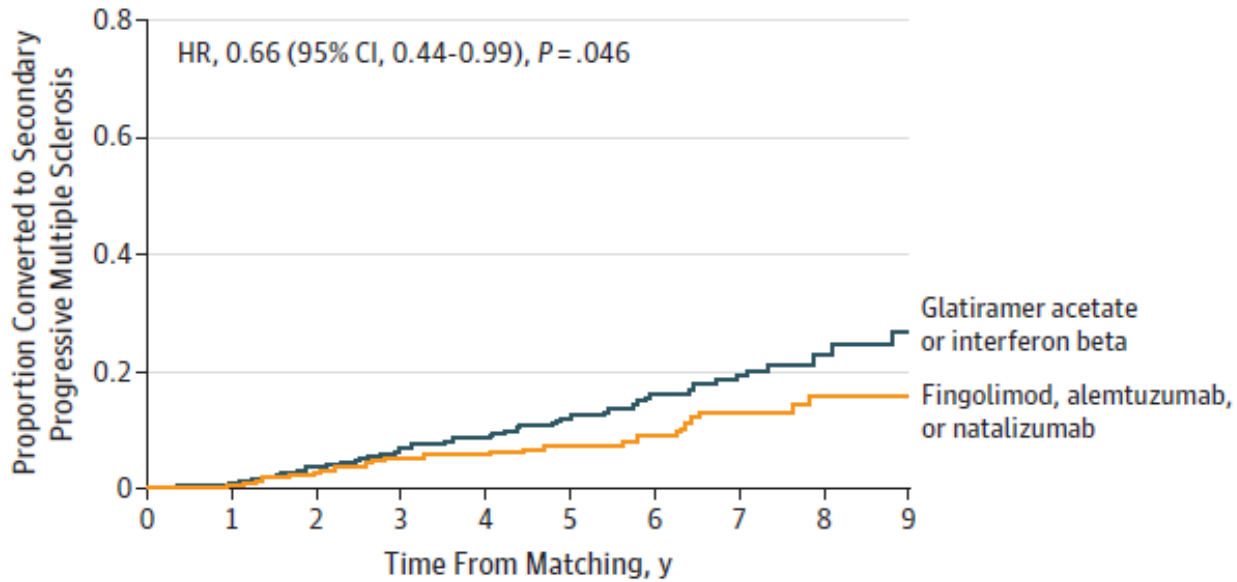
JAMA. 2019;321(2):175-187. doi:10.1001/jama.2018.20588
Last corrected on April 7, 2020.

JAMA | Original Investigation

Association of Initial Disease-Modifying Therapy With Later Conversion to Secondary Progressive Multiple Sclerosis

DESIGN, SETTING, AND PARTICIPANTS Cohort study with prospective data from 68 neurology centers in 21 countries examining patients with relapsing-remitting MS commencing DMTs (or clinical monitoring) between 1988-2012 with minimum 4 years' follow-up.

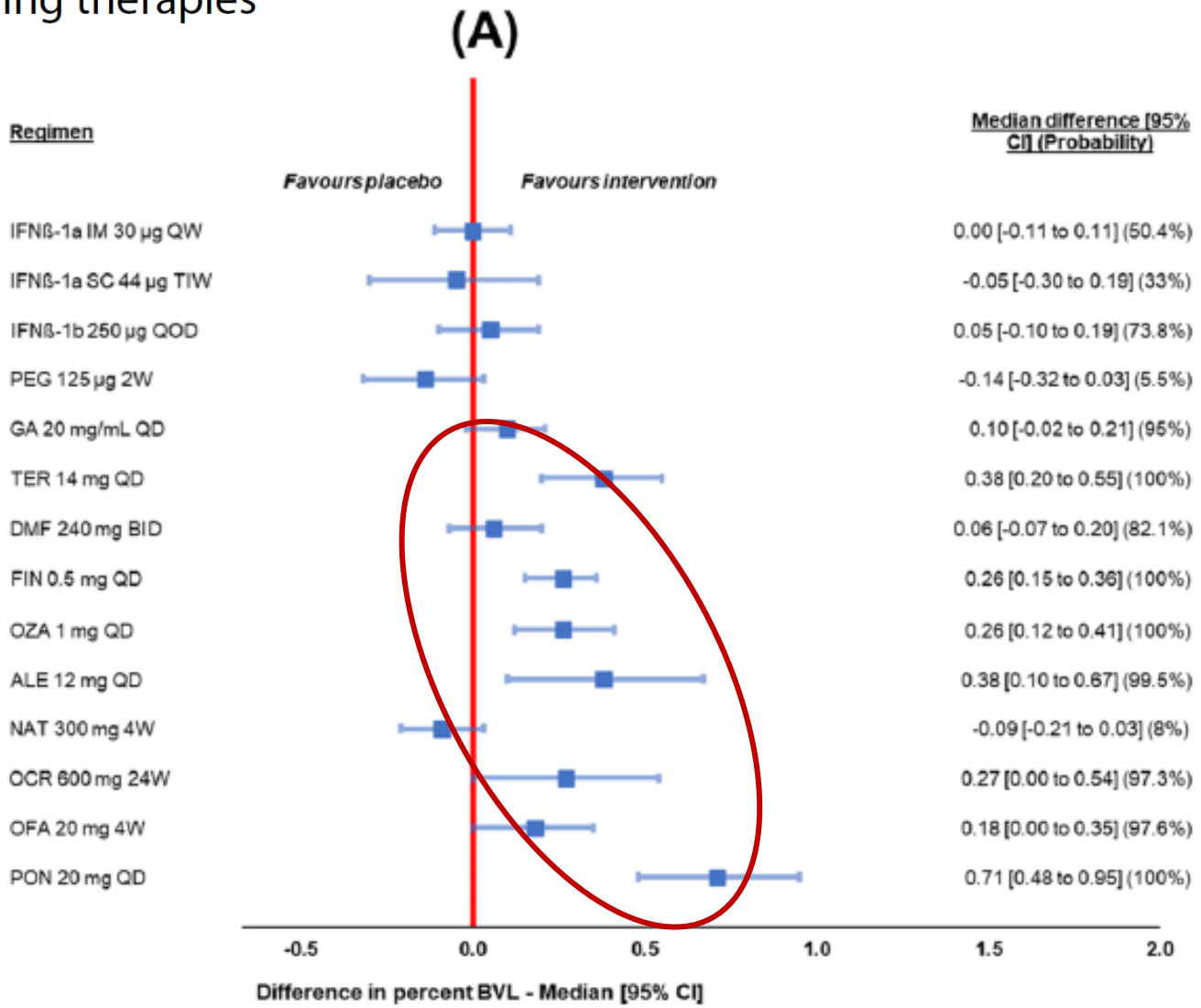
Figure 4. Comparison of Cumulative Hazard of Conversion to Secondary Progressive Multiple Sclerosis for Initial Treatment With Glatiramer Acetate or Interferon Beta vs Fingolimod, Alemtuzumab, or Natalizumab



Zivadinov *et al. BMC Neurology* (2024) 24:378
https://doi.org/10.1186/s12883-024-03888-6

RESEARCH Open Access

Brain volume loss in relapsing multiple sclerosis: indirect treatment comparisons of available disease-modifying therapies



Journal of Neurology (2024) 271:105–115
https://doi.org/10.1007/s00415-023-11969-8

REVIEW

Multiple sclerosis: time for early treatment with high-efficacy drugs

Krzysztof Selmaj[1,2] · Bruce A. C. Cree[3] · Michael Barnett[4] · Alan Thompson[5] · Hans-Peter Hartung[4,6,7,8]

Table 1 Short-term randomized HETA studies vs. LETA

Study	HETA	Comparator	Duration	Reduction					NEDA
				ARR	3mCDW	Gd+	T2	BV	T2
Transforms [55]	Fingolimod	IM Interferon beta-1a	12 months	52%	ns	59%	30%	27%	63.4% v.44.3%
CARE MS I [56]	Alemtuzumab	SC Interferon beta-1a	24 months	54.9%	ns (27.3%)[a]	51.5%	27%	42%	38.6% v.26.7
CARE MS-II [57]	Alemtuzumab	SC Interferon beta-1a	24 months	49.4%	42%[a]	71%	57.5%	23%	32.2% v.13.6
Opera I [29]	Ocrelizumab	IM Interferon beta-1a	24 months	46%	43%	94%	77%	23.5%	48 v.29%
Opera II [29]	Ocrelizumab	IM Interferon beta-1a	24 months	47%	37%	95%	83%	23.8%	48 v.25%
Radiance [60]	Ozanimod	IM Interferon beta-1a	24 months	38%	ns	53%	42%	27%	24.2% v. 17%
Sunbeam [59]	Ozanimod	IM Interferon beta-1a	12 months	48%	ns	63%	48%	31%	NA
Optimum [61]	Ponesimod	Teriflunomide	24 months	30.5%	ns (17%)	56%[b]		34%	25 v.16.5%
Asclepios I [30]	Ofatumumab	Teriflunomide	24 months	50.5%	34.4[c]	97.5%	82%	ns (7%)	44.6 v. 17.7%
Asclepios II [30]	Ofatumumab	Teriflunomide	24 months	58.5%		93.8%	84.5%	ns (7%)	
Ultimate I [50]	Ublituximab	Teriflunomide	24 months	59.4%	ns	96.7%	92.4%	NA	44.6 v. 15.0%
Ultimate II [50]	Ublituximab	Teriflunomide	24 months	49.1%	ns	96.5%	90%	NA	43.0 v. 11.4%

ARR annual relapse rate, *ns* non significant, *3mCDW* 3-month confirmed disability worsening, *BV* brain volume, *ns* not significant

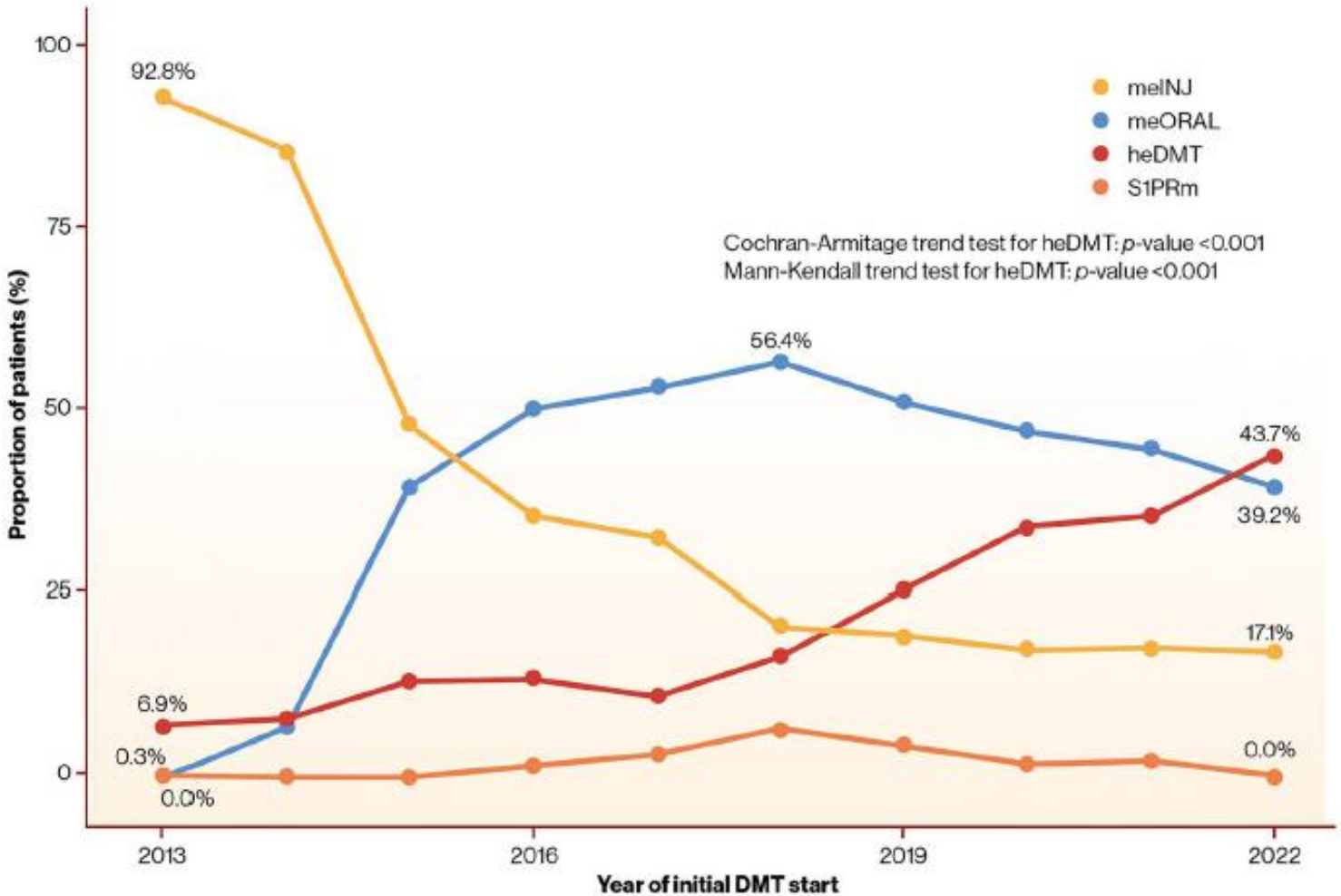
WILEY
Brain and Behavior
Open Access

ORIGINAL ARTICLE OPEN ACCESS

Evolving Patterns of Initial RRMS Treatment in Finland (2013–2022): Insights From a Nationwide Multiple Sclerosis Register

Henrik Ahvenjärvi[1] | Elina Jokinen[2] | Matias Viitala[3] | Henri Autio[2] | Anne M. Portaankorva[1,4,5] | Merja Soilu-Hänninen[6,7] | Johanna Krüger[1,4,8] | Mervi Ryytty[1,4,8]

Brain and Behavior, 2025; 15:e70326
https://doi.org/10.1002/brb3.70326



Shifting from the treat-to-target to the early highly effective treatment approach in patients with multiple sclerosis – real-world evidence from Germany

Ther Adv Neurol Disord
2024, Vol. 17: 1–13
DOI: 10.1177/17562864241237857

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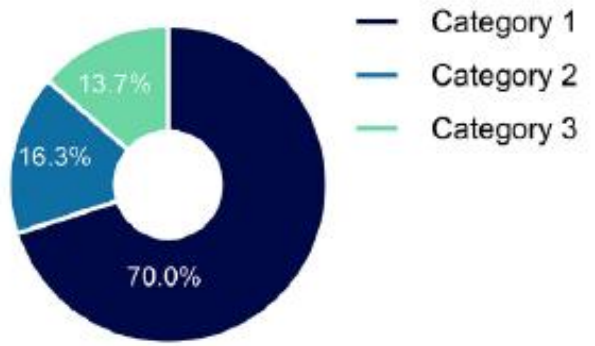
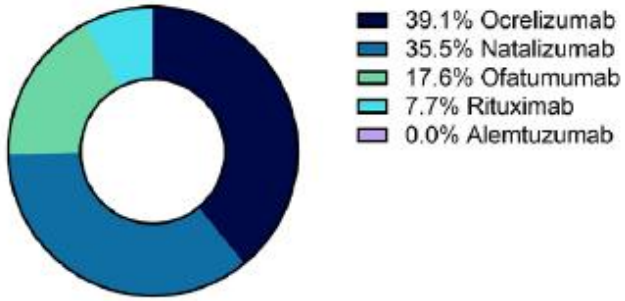
Category 1 (dimethyl fumarate, Diroximel fumarate, glatiramer acetate, teriflunomide, and interferons),

Category 2 (cladribine, S1P-modulators) and

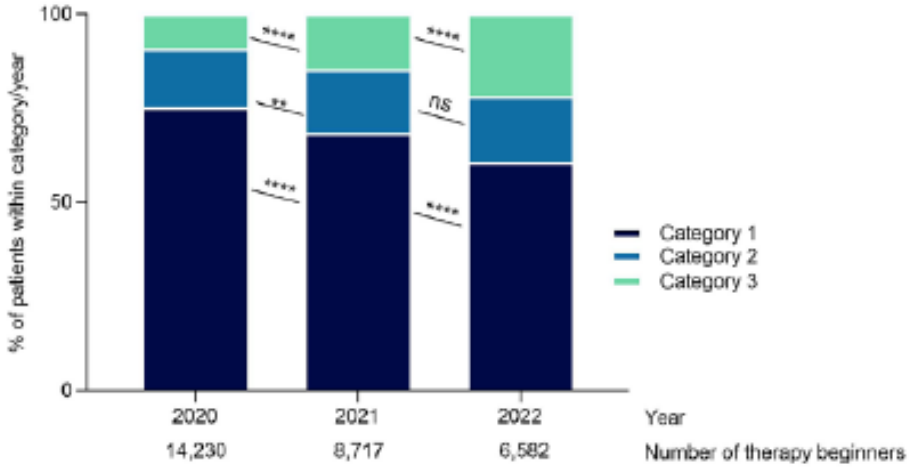
Category 3 (alemtuzumab, natalizumab, ocrelizumab, ofatumumab and rituximab).

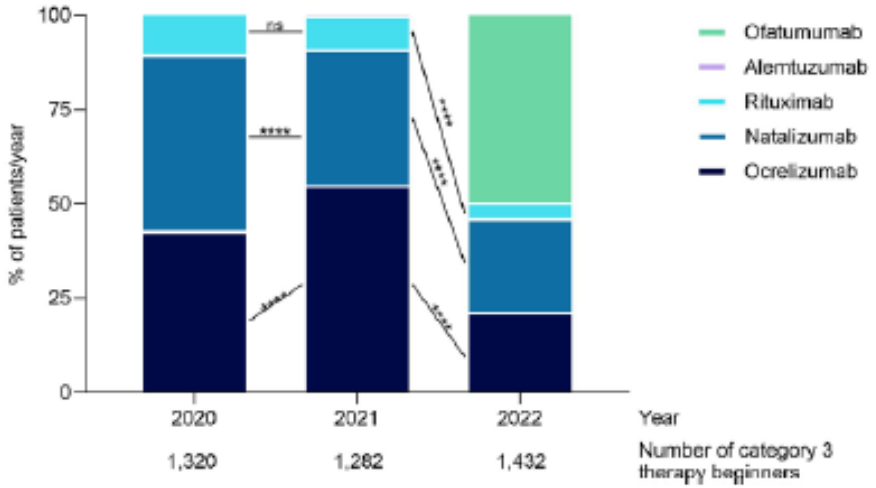


Total number of therapy beginners = 29,529



Total number of category 3 therapy beginners = 4,034





Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria

Lancet Neurol 2025; 24: 850–65

Diagnostic criteria

- Allison and Millar (1954)
- Schumacher (1965)
- McAlpine (1972)
- Rose (1976)
- McDonald and Holliday (1977)
- Poser (1983)
- McDonald 2001, 2005, 2010, 2017, 2024

➢ ~~Symptoms suggestive of MS~~

➢ Dissemination in ~~time~~ and ~~space~~

➢ Exclusion of other diseases

➢ Diagnosis can be made by clinical assessment alone

The following diagnostic features can substitute for dissemination in time in the diagnosis of multiple sclerosis, as they have equivalent diagnostic value:

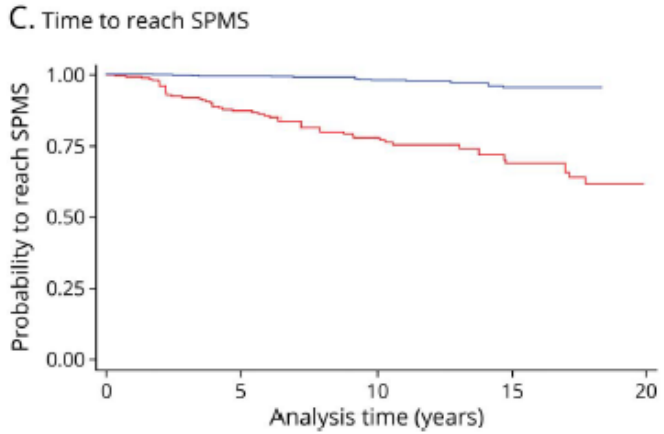
- Oligoclonal bands (since 2017)
- Kappa free light chain index
- Central vein sign
- Paramagnetic rim lesions in some situations
- Dissemination in space — characteristic lesions in four or five typical topographies

Papolla A et al. Nat Rev Neurol 2025

RESEARCH ARTICLE

Association of Very Early Treatment Initiation With the Risk of Long-term Disability in Patients With a First Demyelinating Event

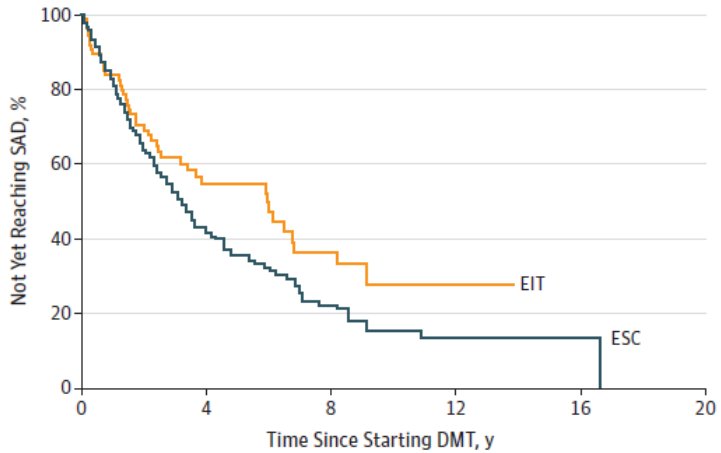
Neurology® 2023;101:e1280-e1292.



JAMA Neurology | Original Investigation

Clinical Outcomes of Escalation vs Early Intensive Disease-Modifying Therapy in Patients With Multiple Sclerosis

JAMA Neurol. 2019;76(5):536-541.



Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria

Lancet Neurol 2025; 24: 850–65

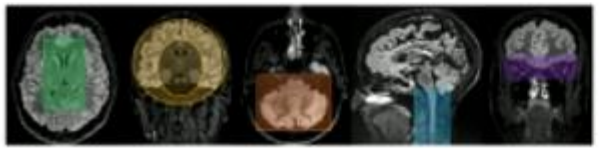
Definition of optic nerve lesion

- By use of OCT: inter-eye differences in pRNFL thickness of 6 µm or greater, or GCIPL thickness of 4 µm or greater
- By use of VEPs: delayed latency or interocular asymmetry in VEP latencies (based on normative data specific to the centre where the test is done)

Lancet Neurol 2025; 24: 880–92

5 TOPOGRAPHIES

Peri-Ventricular
Cortico-Juxta-Cortical
Infra Tentorial
Spinal Cord
Optic nerve



4 Additional features

DIT
≥ 6 CVS
≥ 1 PRL
CSF ≥2 OCB or Kappa

DIT CSF
6CVS 1PRL

NEW
1 Topography
+ 2 add F

≥ 2 Topographies
+ 1 add

4 ou 5 Topographies
Nothing else
If ø red flag!

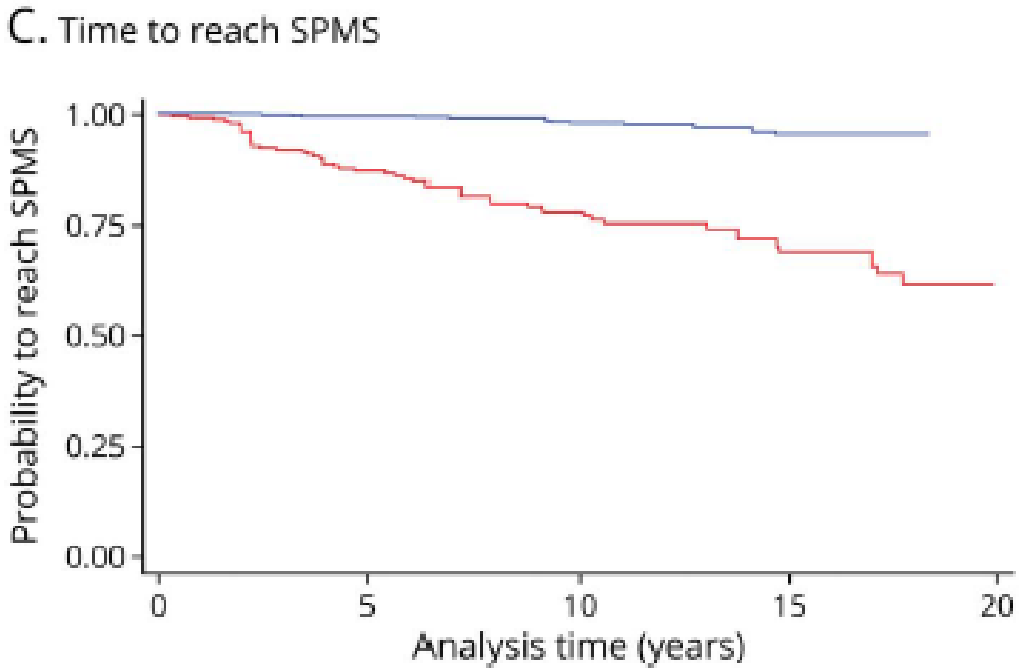
C Lebrun-Frénay, ECTRIMS Barcelona 2025

RESEARCH ARTICLE

Association of Very Early Treatment Initiation With the Risk of Long-term Disability in Patients With a First Demyelinating Event

Neurology® 2023;101:e1280-e1292.

< 6 months



JAMA Neurology | Original Investigation

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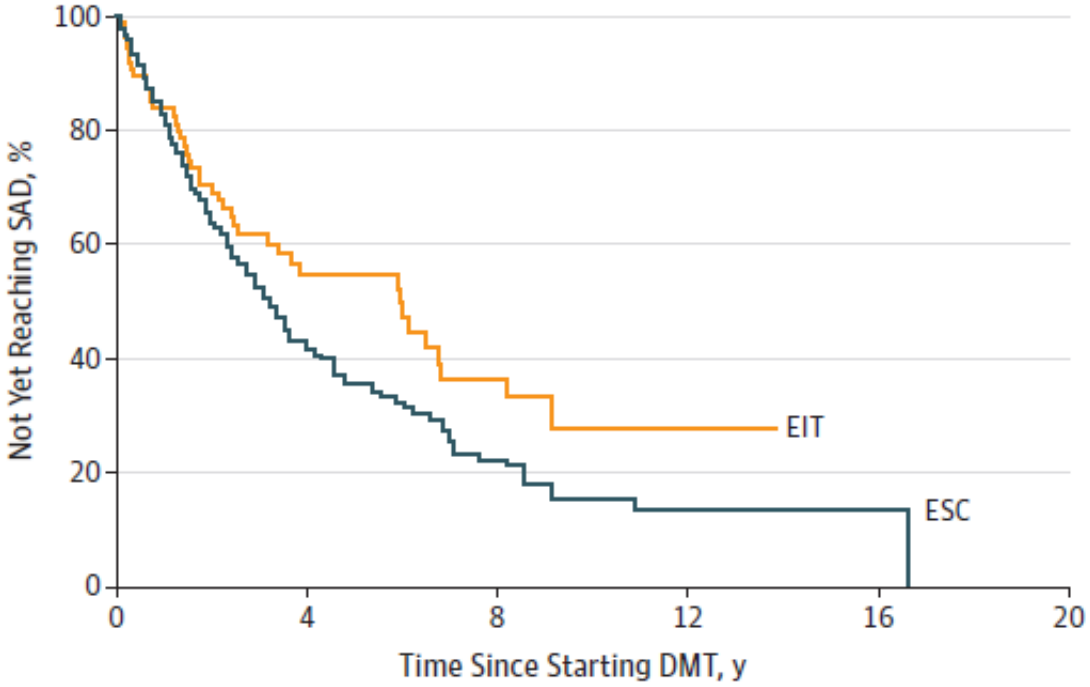
JAMA Neurol. 2019;76(5):536-541.



ΠΡΟΒΛΗΜΑΤΙΣΜΟΙ (V) ΘΕΡΑΠΕΙΑ- ΕΝ ΕΞΕΛΙΞΗ ΘΕΡΑΠΕΙΕΣ

Neurotherapeutics 22 (2025) e00554

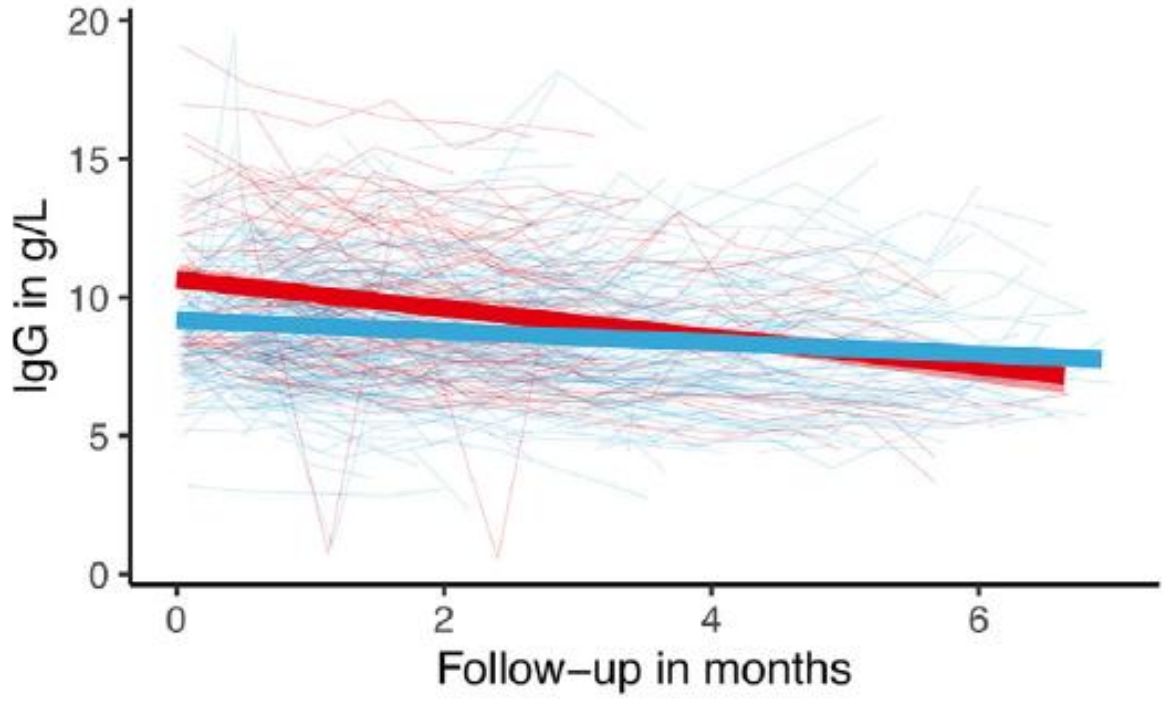
Contents lists available at ScienceDirect

Neurotherapeutics

journal homepage: www.sciencedirect.com/journal/neurotherapeutics

Original Article

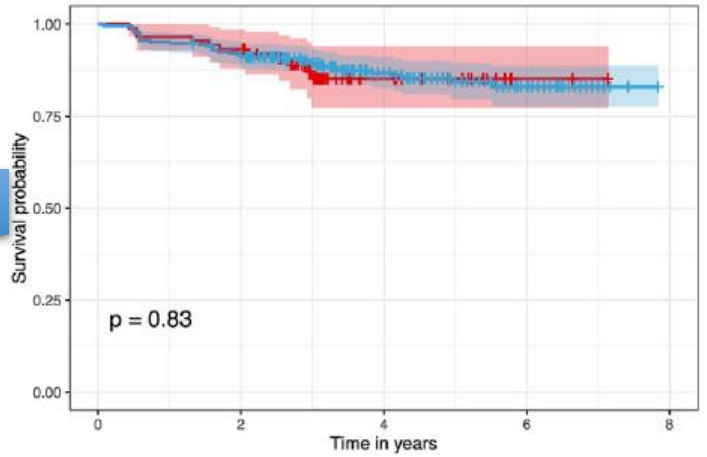
Extended-interval dosing of rituximab/ocrelizumab is associated with a reduced decrease in IgG levels in multiple sclerosis



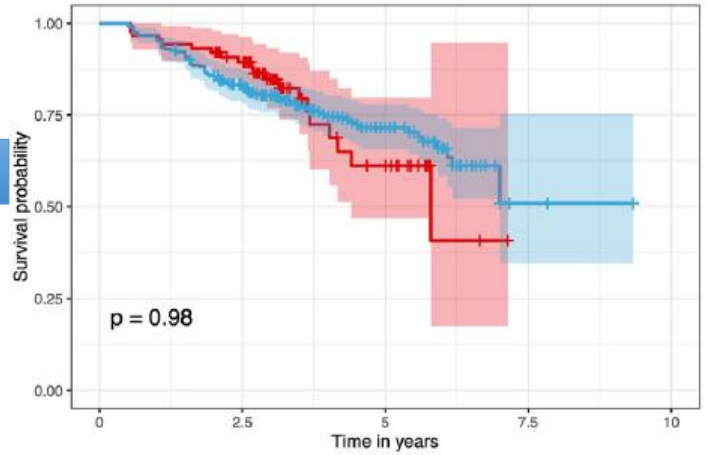
6 months

Extended

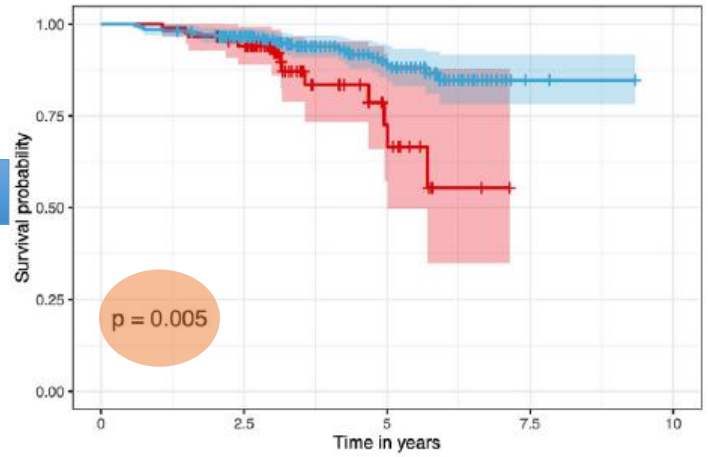
Relapse



Disability



Severe infection



Scientific Session 9: Managing HET-associated risks in demyelinating disorders

Track Therapy

Room Lecture Hall Auditorium

Date Thursday, 25 September 2025, 14:30 - 16:00 CEST

RItuximab long-term DOSE trial in Multiple Sclerosis – RIDOSE-MS. A rater-blinded randomized phase 3 trial comparing standard with extended dosing intervals of rituximab in relapsing-remitting MS

Anders Svenningsson (Sweden)

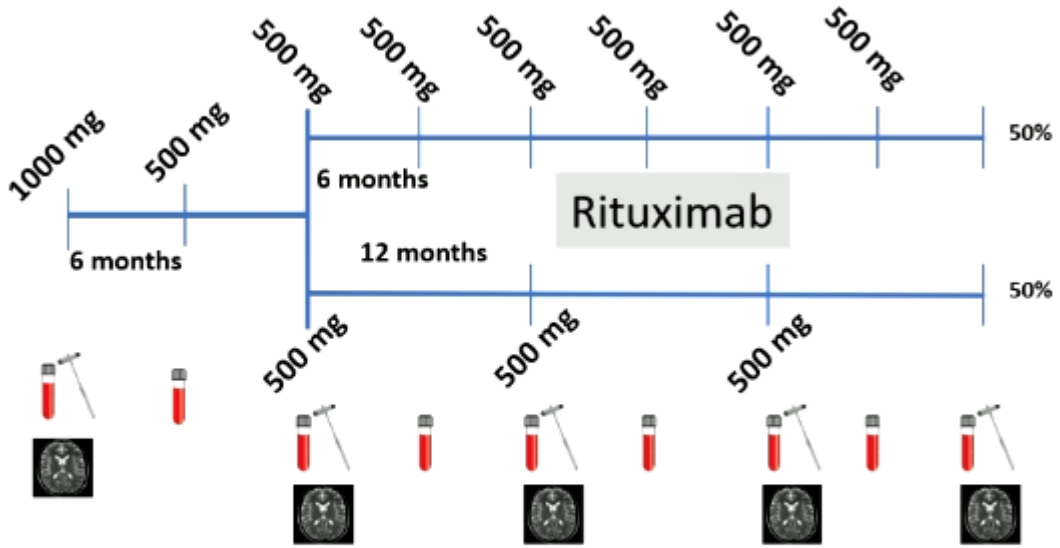
ECTRIMS 2025

41st Congress of the European Committee for Treatment and Research in Multiple Sclerosis

30th Conference of Rehabilitation in Multiple Sclerosis

24-26 September 2025 | Barcelona, Spain

RIDOSE study outline



Design:
- Randomised rater-blinded
- After 1 year 6-monthly treatment 1:1 randomisation to 500 mg RTX every 6 months or 500 mg RTX every 12 months
- Swedish multicenter
- 200 patients

Assessments: EDSS and MRI 12-monthly, blinded relapse evaluations, biomarkers 6-monthly

Hypothesis: *Extended dose regimen (500 mg 12-monthly) is equally effective to maintain NEDA-3 as 500 mg 6-monthly during year 2 – 4 in the trial*

Patients:
- Relapsing-remitting MS or CIS
- Naive to RTX or previous up to 2 years of RTX treatment

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Track Therapy

RItuximab long-term DOSE trial in Multiple Sclerosis – RIDOSE-MS. A rater-blinded randomized phase 3 trial comparing standard with extended dosing intervals of rituximab in relapsing-remitting MS

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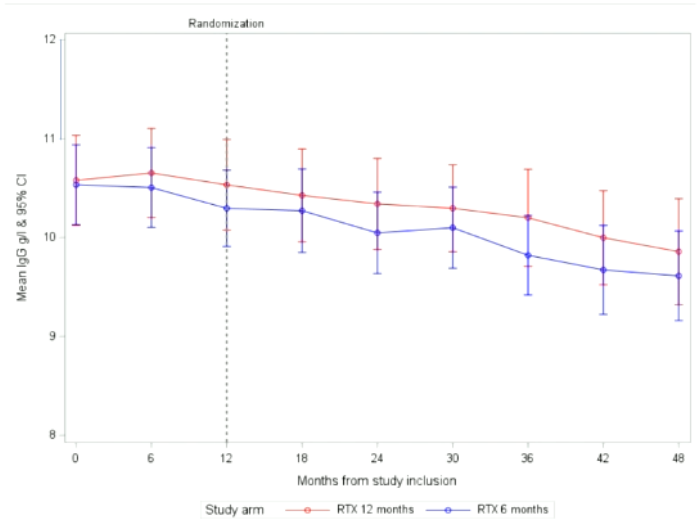
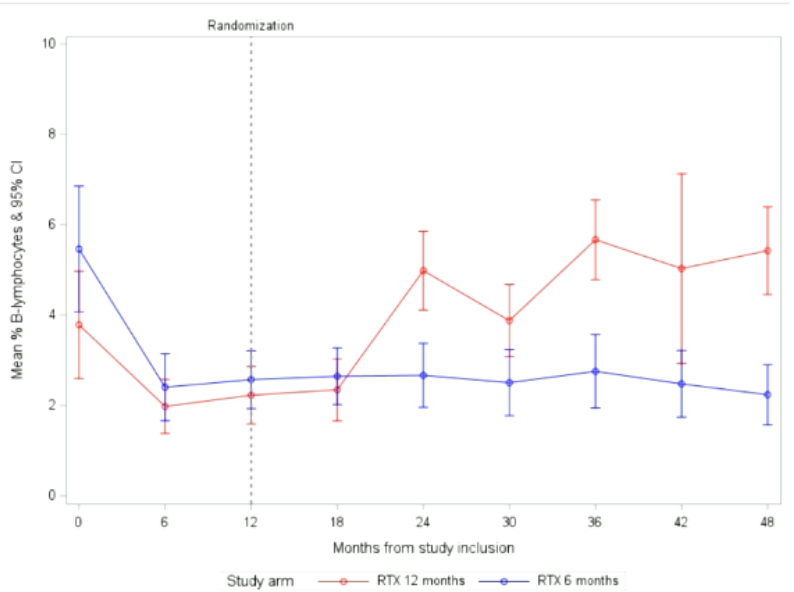
Mean IgG-levels during RIDOSE



Approx 0.17 g/L per year in 12-month arm

Mean CD19+ B-ymphocyte levels in RIDOSE



Scientific Session 9: Managing HET-associated risks in demyelinating disorders

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RItuximab long-term DOSE trial in Multiple Sclerosis – RIDOSE-MS. A rater-blinded randomized phase 3 trial comparing standard with extended dosing intervals of rituximab in relapsing-remitting MS

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Karolinska Institutet

Danderyds Sjukhus

RIDOSE-MS conclusions safety

Conclusions:

- Extending dose interval did *not* appear to improve safety of rituximab in MS
- Crude figures from the RIDOSE trial *might* indicate slighly lower rate of s-IgG decline with no significant difference between dose arms
- The longer dose interval allowed more repopulation of B-cells before the next dose, apparently not affecting neither efficacy or safety during a 4-year period
- Compared with other studies, incidence of severe infections *might* be lower than in previous Swedish cohorts
- Inflammatory bowel disorder may be a specific side effect of rituximab in MS to look out for

ΠΡΟΒΛΗΜΑΤΙΣΜΟΙ (VI)
ΘΕΡΑΠΕΙΑ-ΑΝΟΣΟΓΗΡΑΝΣΗ/ ΔΙΑΚΟΠΗ ΘΕΡΑΠΕΙΑΣ

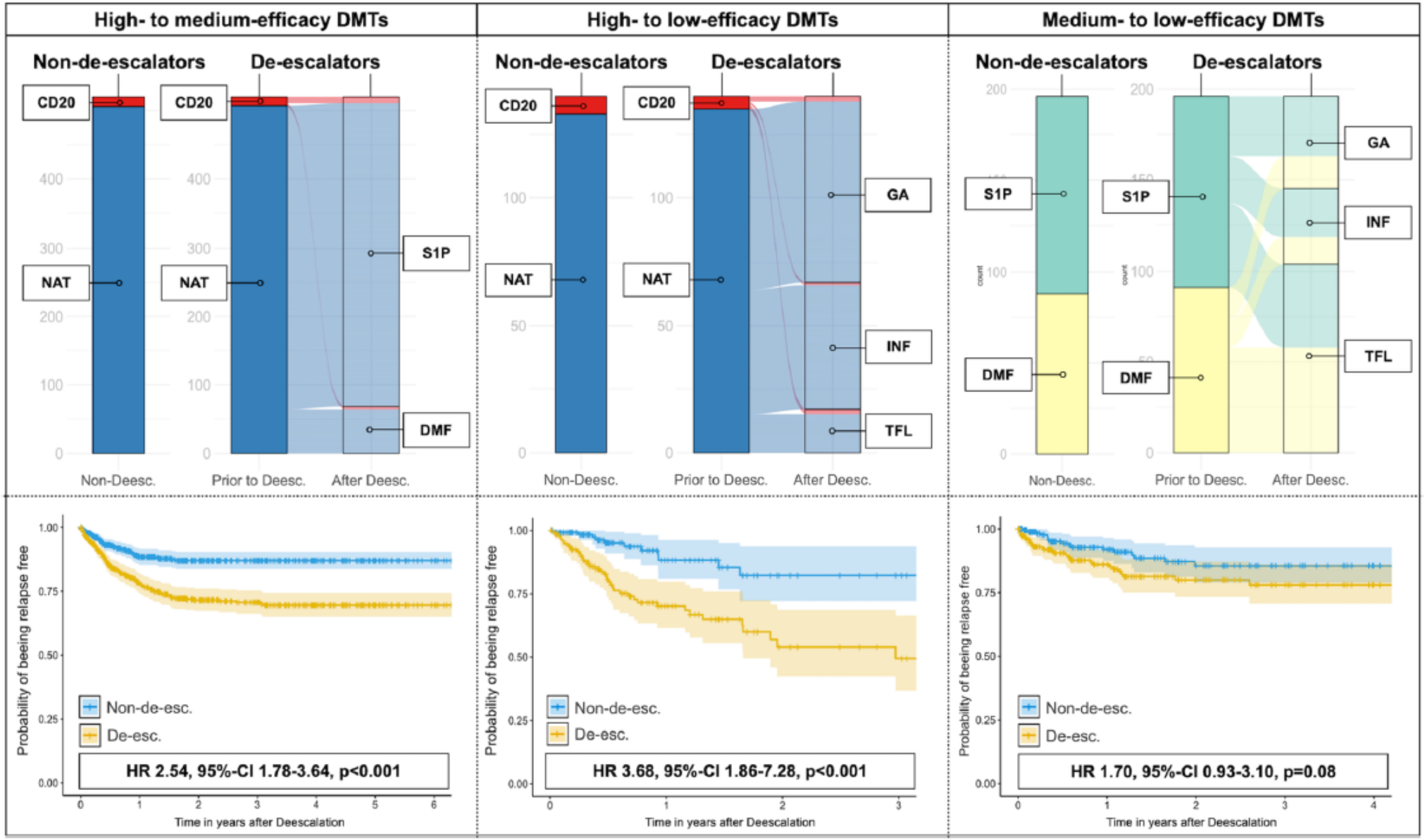
CNS Drugs (2025) 39:403–416
https://doi.org/10.1007/s40263-025-01164-w

ORIGINAL RESEARCH ARTICLE

Treatment De-escalation in Relapsing-Remitting Multiple Sclerosis: An Observational Study

Jannis Müller · Sifat Sharmin · Johannes Lorscheider · Dana Horakova · Eva Kubala Havrdova · Sara Eichau, et al. *[full author details at the end of the article]*

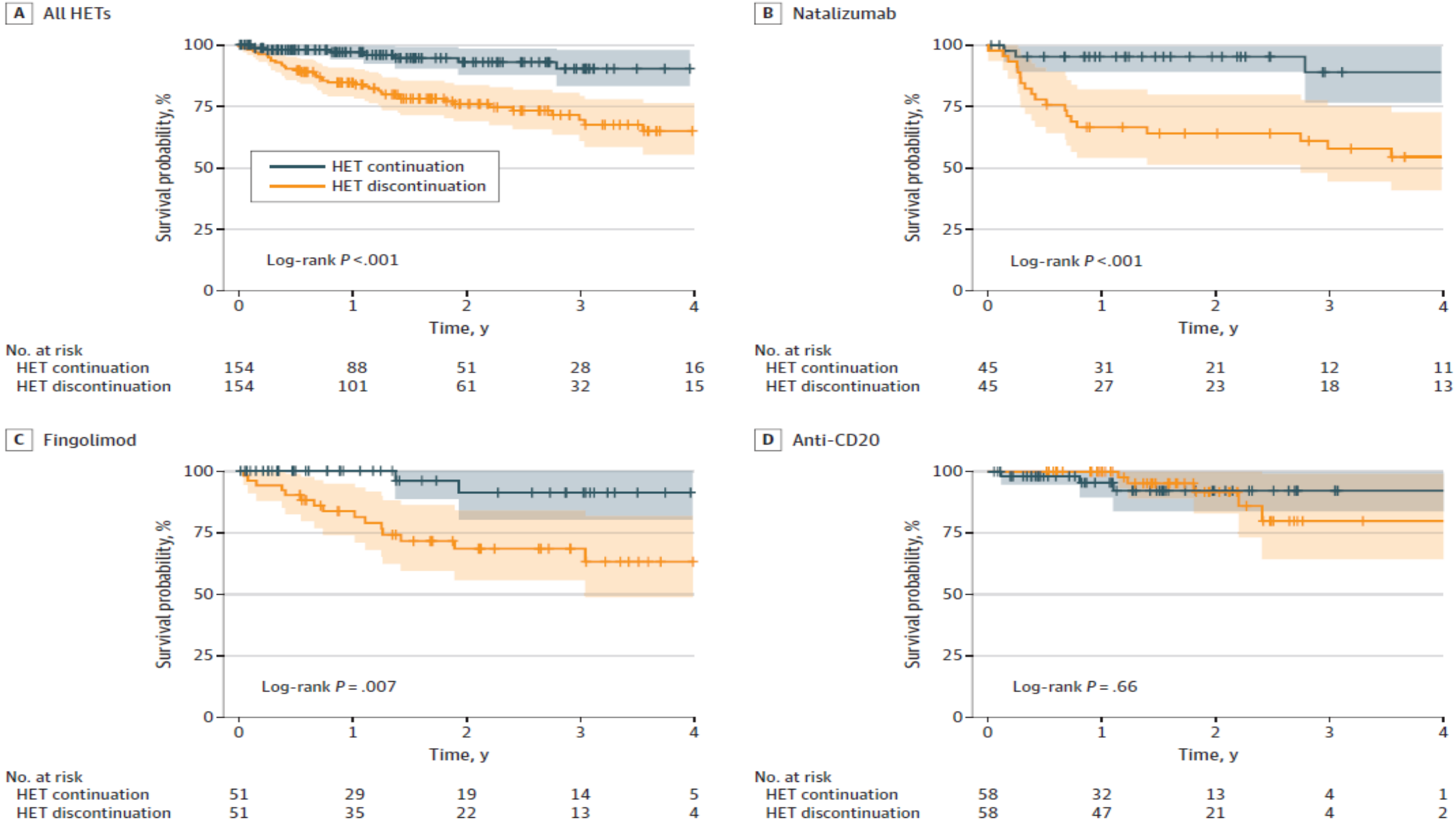
Relapse Free



JAMA Neurol. 2024;81(5):490-498. doi:10.1001/jamaneurol.2024.0395

High-Efficacy Therapy Discontinuation vs Continuation in Patients 50 Years and Older With Nonactive MS

Figure 2. Time to First Relapse in the High-Efficacy Therapy (HET) Treatment Discontinuation vs HET Continuation Groups After Propensity Score Matching

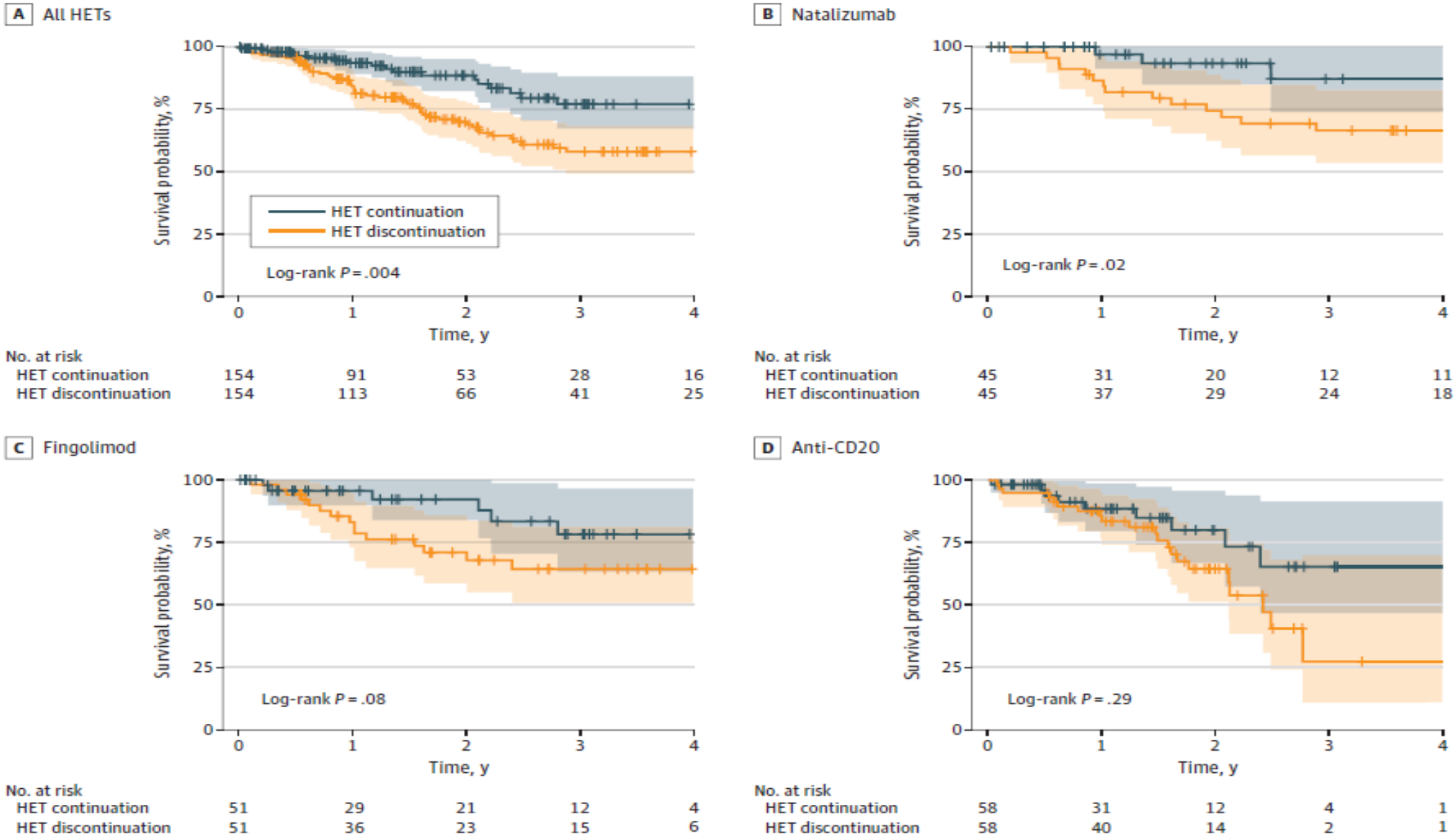


Rituximab and ocrelizumab were grouped together as anti-CD20 therapies. The shaded area indicates 95% CIs.

JAMA Neurol. 2024;81(5):490-498. doi:10.1001/jamaneurol.2024.0395

High-Efficacy Therapy Discontinuation vs Continuation in Patients 50 Years and Older With Nonactive MS

Figure 4. Time to Confirm Disability Progression in the High-Efficacy Therapy (HET) Treatment Discontinuation vs HET Continuation Groups After Propensity Score Matching



Rituximab and ocrelizumab were grouped together as anti-CD20 therapies. The shaded area indicates 95% CIs.

ΠΡΟΒΛΗΜΑΤΙΣΜΟΙ (V)
ΝΕΩΤΕΡΕΣ ΘΕΡΑΠΕΙΕΣ

ΑΥΤΟΛΟΓΗ ΜΕΤΑΜΟΣΧΕΥΣΗ ΑΙΜΟΠΟΙΗΤΙΚΩΝ ΒΛΑΣΤΟΚΥΤΤΑΡΩΝ

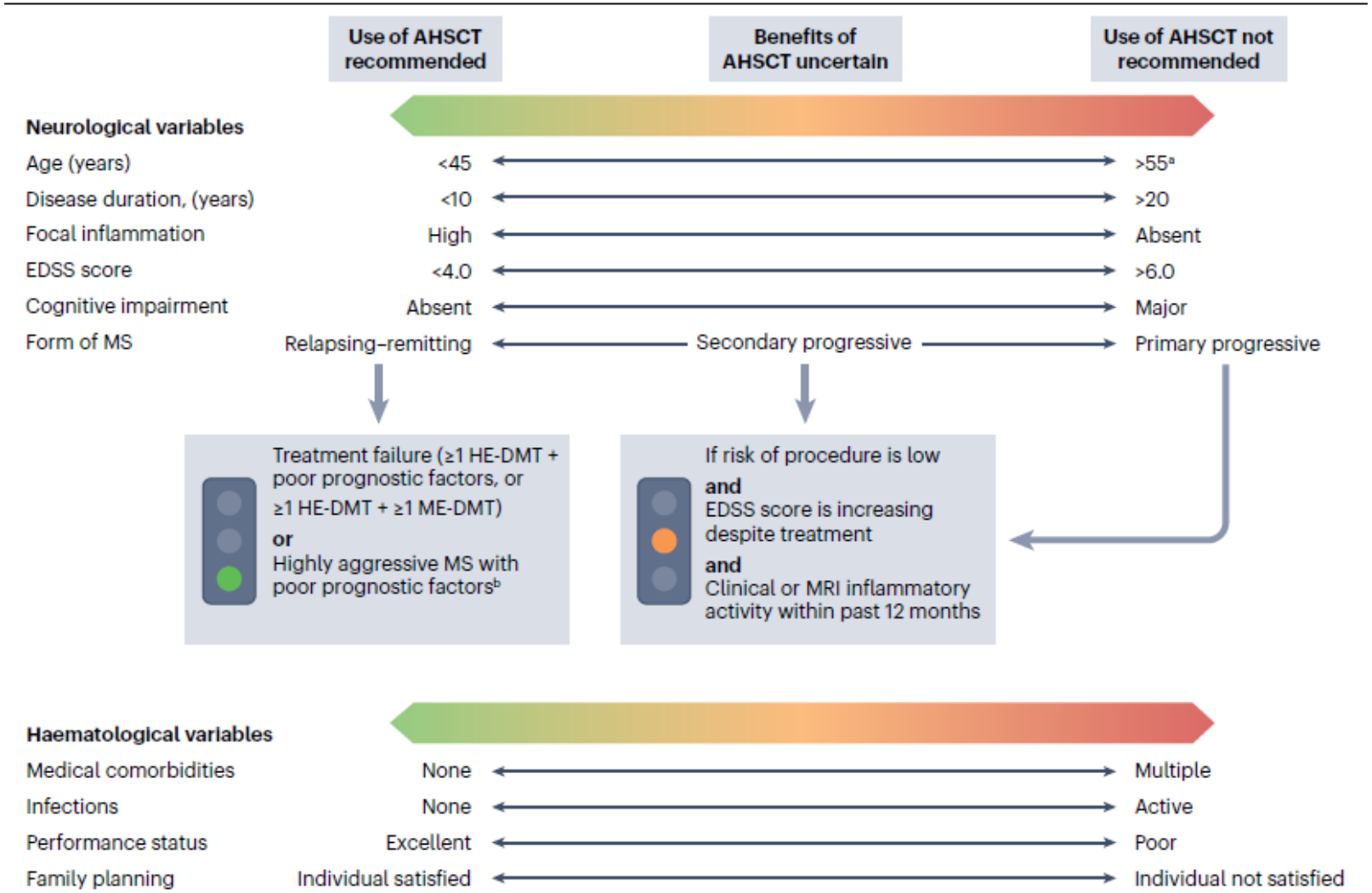
nature reviews neurology
https://doi.org/10.1038/s41582-024-01050-x

Consensus statement

Check for updates

Nature Reviews Neurology | Volume 21 | March 2025 | 140–158

Autologous haematopoietic stem cell transplantation for treatment of multiple sclerosis and neuromyelitis optica spectrum disorder — recommendations from ECTRIMS and the EBMT



nature reviews neurology https://doi.org/10.1038/s41582-024-01050-x

Consensus statement Check for updates

Nature Reviews Neurology | Volume 21 | March 2025 | 140–158

Autologous haematopoietic stem cell transplantation for treatment of multiple sclerosis and neuromyelitis optica spectrum disorder — recommendations from ECTRIMS and the EBMT

Box 1 | Recommendations for selection of people with multiple sclerosis for haematopoietic stem cell transplantation

Neurological assessment

General suitability profile

- Age <45 years
- Disease duration <10 years
- Rapidly evolving severe and/or treatment-refractory inflammatory active MS
- EDSS <6.0[a]
- Capacity to give informed consent and to adhere to HSCT schedule
- Markers of disease aggressiveness: frequent relapses, incomplete recovery from relapses, high frequency of new MRI lesions, rapid accumulation of disability

Additional profile for suitability in relapsing–remitting MS

- After failure of any one high-efficacy DMT
- Regardless of previous DMT failure: rapidly evolving severe MS with poor prognostic factors (highly restricted indication, should be offered only in a clinical trial or study)

Additional profile for suitability in progressive MS (primary or secondary)

- Early, active disease forms
- Recent (<12 months) evidence of inflammatory activity (confirmed relapse and MRI)
- Clinical progression with rapid worsening of disability despite treatment with DMT
- Favourable risk profile (young age, no relevant comorbidities)

Haematological assessment required

- Renal and bladder function, liver and bone profiles
- Screening for infective diseases
- Lung function test and plain radiography of the chest (additional respiratory work-up, including chest CT and respiratory review, as needed)
- Cardiac assessment with electrocardiography and echocardiography (additional cardiological work-up and cardiological referral, as needed)
- Dental check-up
- Fertility discussion and referral if appropriate
- Performance status
- Psychological and mental health evaluation

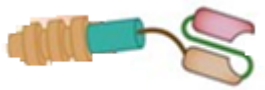
Major contraindications for AHSCT in MS

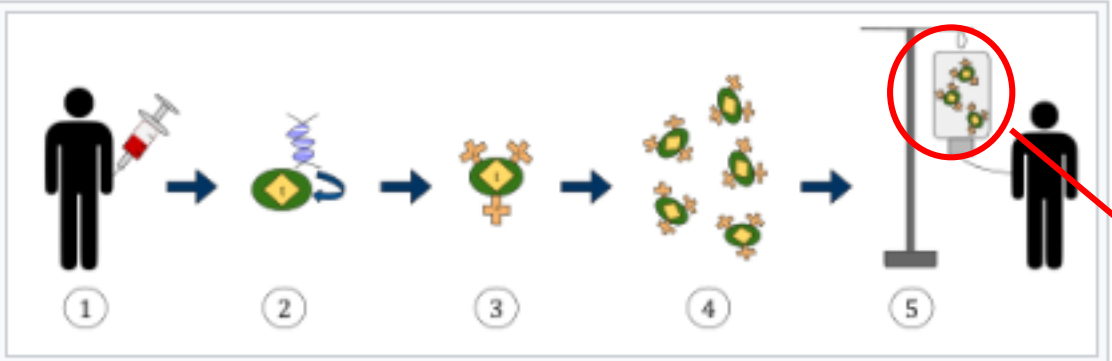
- Active neoplasia or concomitant myelodysplasia
- Acute or chronic uncontrolled infection
- Uncontrolled psychiatric disease or any other condition that raises the risk of poor adherence to treatment regimen

[a]Some people with an EDSS score of >6.0 might be suitable for AHSCT if the increase above EDSS 6.0 was caused by an MS relapse in the previous few months, suggesting acute inflammatory activity rather than chronic neurodegenerative processes. AHSCT, autologous HSCT; DMT, disease-modifying therapy; EDSS, expanded disability status scale; HSCT, haematopoietic stem cell transplantation; MS, multiple sclerosis.

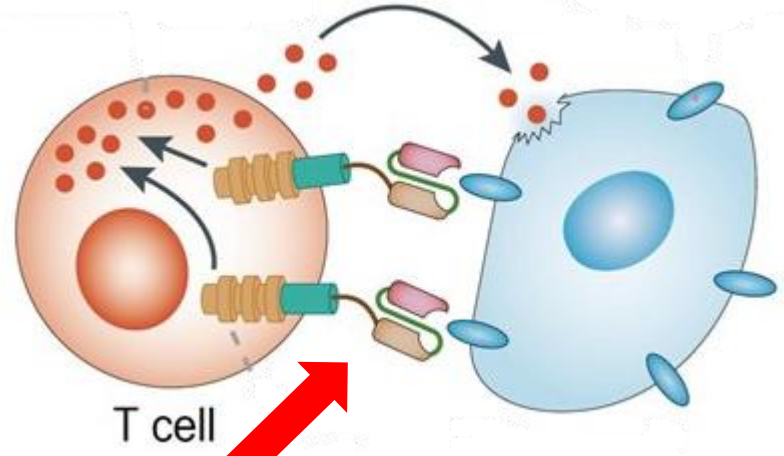
CAR T-cells

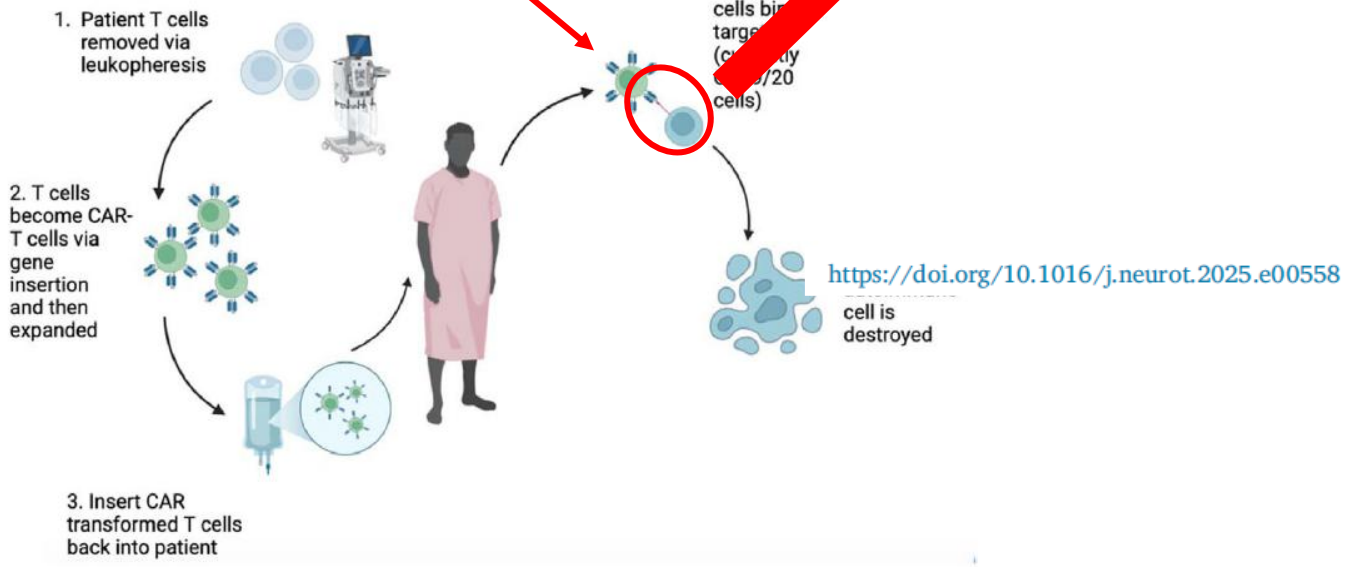
Chimeric Antigen Receptor





Chimeric antigen receptor T cell production and infusion:
1. T cells are isolated from a patient's blood
2. A new gene encoding a chimeric antigen receptor is incorporated into the T cells
3. Engineered T cells are now specific to a desired target antigen
4. Engineered T cells are expanded in tissue culture
5. Engineered T cells are infused back into the patient





https://doi.org/10.1016/j.neurot.2025.e00558

[CAR T cell - Wikipedia]

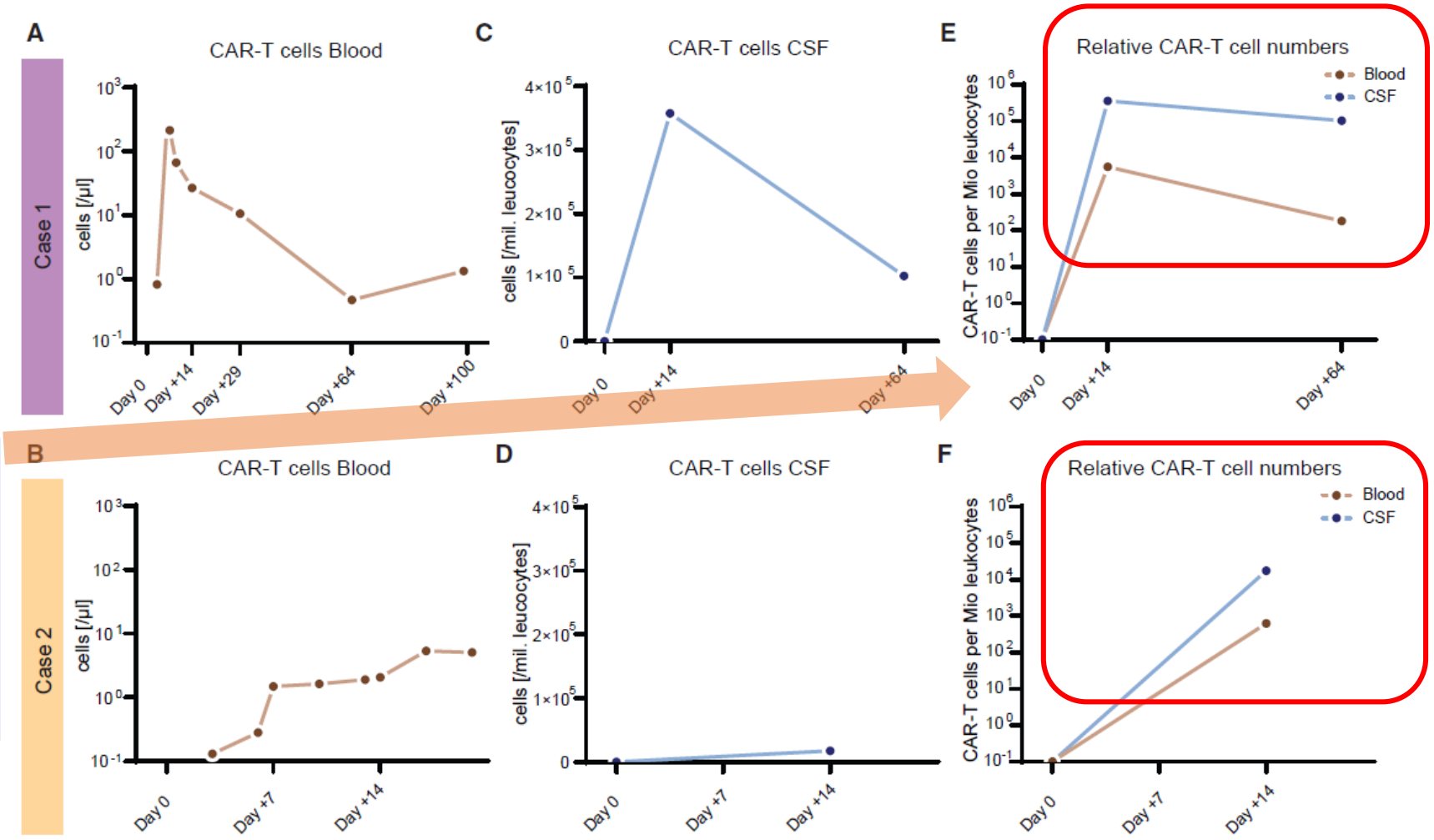
Med

CellPress
OPEN ACCESS

Case Report

CD19-targeted chimeric antigen receptor T cell therapy in two patients with multiple sclerosis

Med 5, 550–558, June 14, 2024



The presence of CAR-T cells in CSF underlines the benefit of CAR-T cell therapy in penetrating immune compartments, which have not been accessible to systemic application of B-cell-depleting monoclonal antibodies.

CAR-driven expansion of pathogenic T cells could theoretically lead to severe worsening of MS symptoms and ICANS, which would be expected to occur during the expansion phase of the CAR-T cells. However, we did not observe CAR-T cell-related neurological toxicity, which is especially notable given the substantial expansion of CAR-T cells in the CSF of the patients. This finding is particularly noteworthy since CAR-T cell expansion in the CSF has only been reported concurrently with the clinical presentation of Immune effector cell-associated neurotoxicity syndrome (ICANS) in patients with lymphoma.

Hot Topic 4: Novel monoclonal antibodies and CAR-T cells

Track Therapy

Room Lecture Hall 113

Date Wednesday, 24 September 2025, 14:30 - 15:30 CEST

CAR-T cell-mediated B-cell depletion in MS and other autoimmune diseases
Scott Zamvil (United States)

ECTRIMS 2025

41st Congress of the European Committee for Treatment and Research in Multiple Sclerosis

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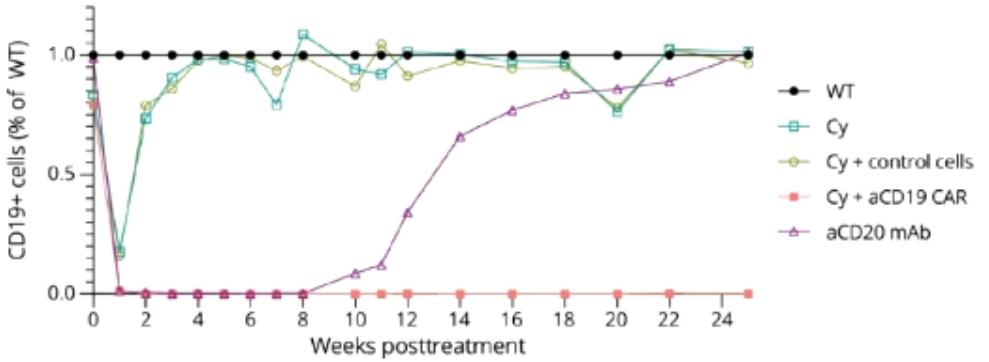
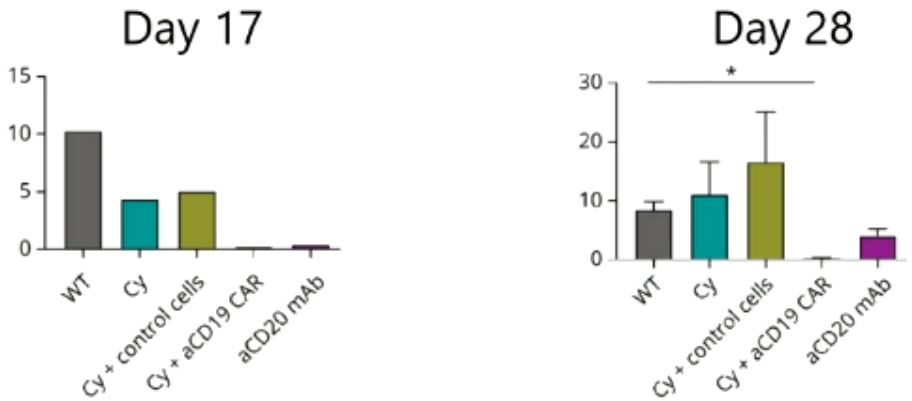
24-26 September 2025 | Barcelona, Spain

Anti-CD19 CAR-T treatment in mice causes more sustained B cell depletion than does anti-CD20 antibody

Periphery



CNS



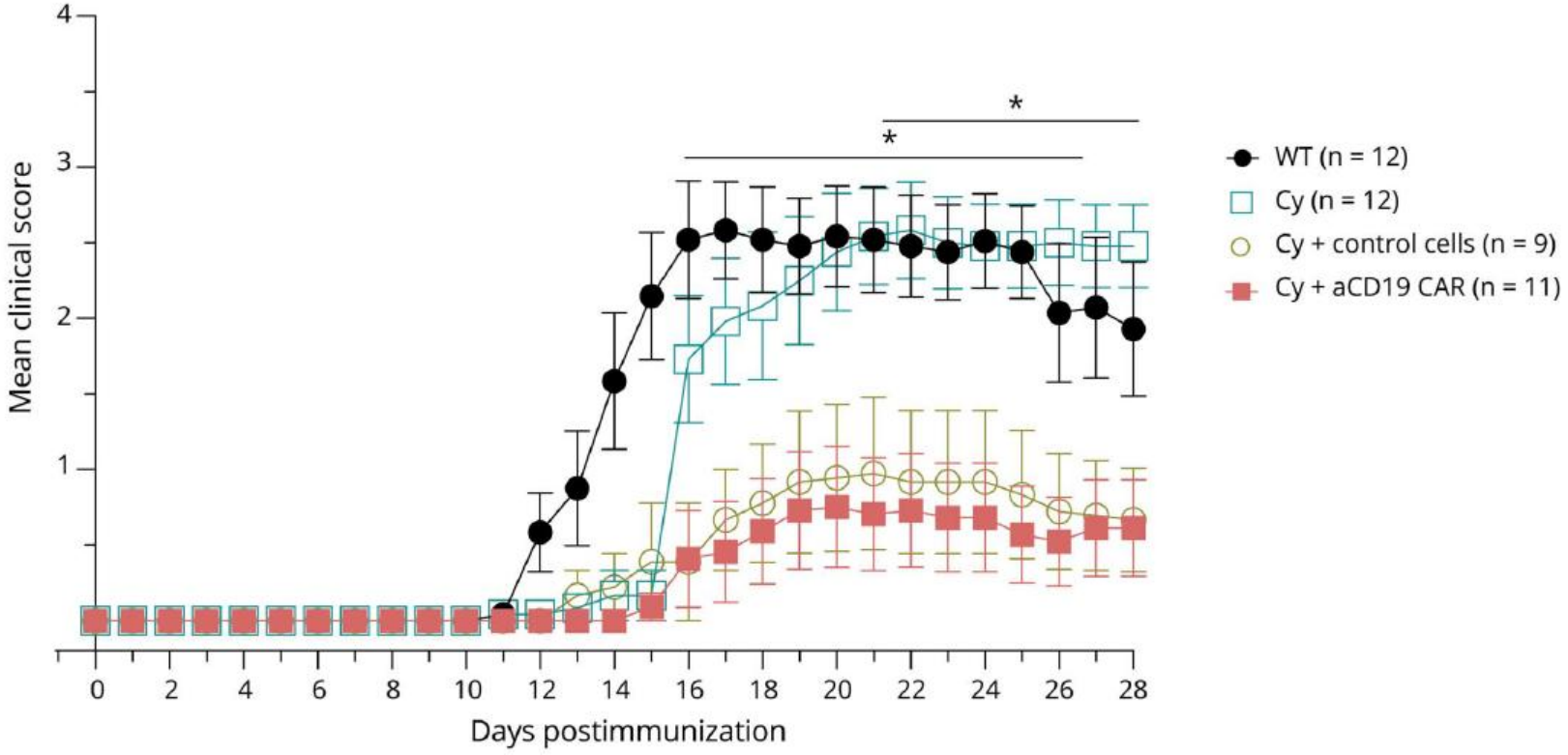
RESEARCH ARTICLE OPEN ACCESS

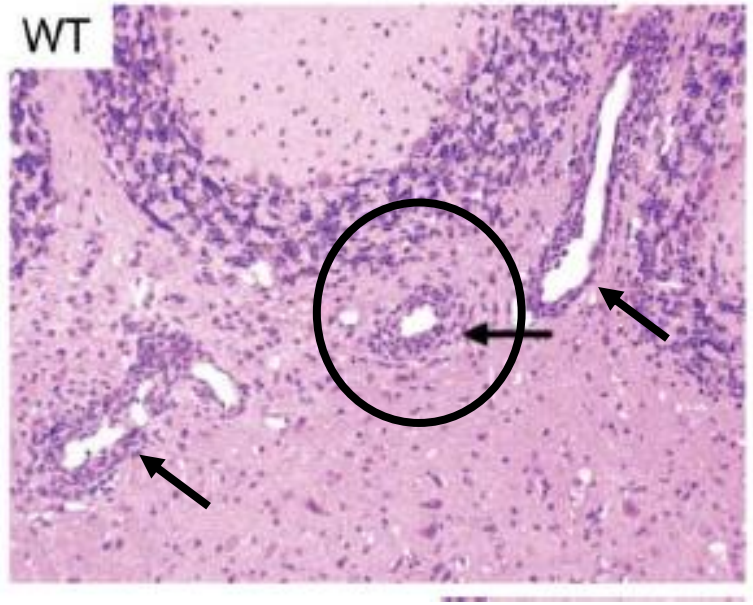
CAR-T Cell–Mediated B-Cell Depletion in Central Nervous System Autoimmunity

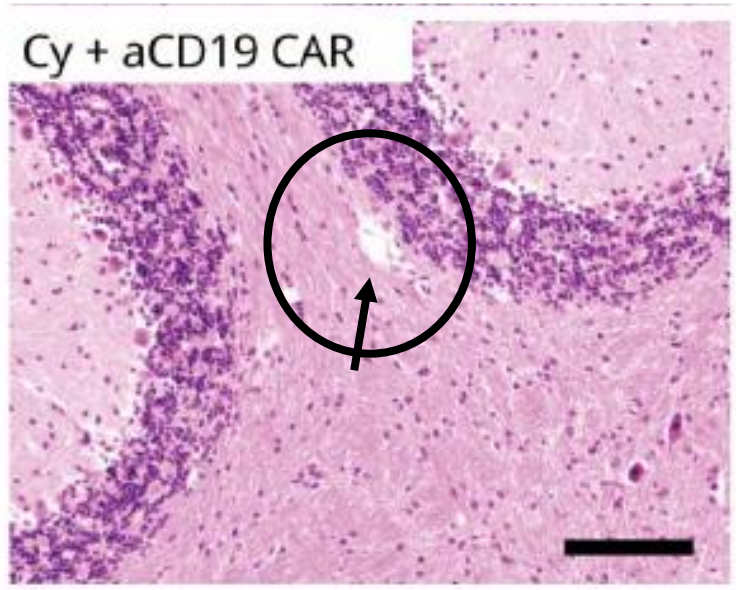
Sasha Gupta, MD, Milos Simic, PhD, Sharon A. Sagan, BS, Chanelle Shepherd, BS, Jason Duecker, BS, Raymond A. Sobel, MD, Ravi Dandekar, MS, Gregory F. Wu, MD, PhD, Wesley Wu, PhD, John E. Pak, PhD, Stephen L. Hauser, MD, Wendell Lim, PhD, Michael R. Wilson, MD,* and Scott S. Zamvil, MD, PhD*

Correspondence
Dr. Zamvil
zamvil@ucsf.neuroimmunol.org

Neurol Neuroimmunol Neuroinflamm 2023;10:e200080. doi:10.1212/NXI.0000000000200080







aCD19 CAR as anti-CD19 CAR-T cell.

Scientific Session 19: Neuroregeneration strategies and cellular therapies

Track	Pathogenesis
Room	Lecture Hall 211
Date	Friday, 26 September 2025, 10:30 - 12:00 CEST

PRESENTATION ID O152

Anti-BCMA CAR T cell therapy in patients with Multiple Sclerosis

Chuan Qin (China)

ECTRIMS 2025

41st Congress of the European Committee for Treatment and Research in Multiple Sclerosis

30th Conference of Rehabilitation in Multiple Sclerosis

24-26 September 2025 | Barcelona, Spain

Anti-BCMA CART T-cells: T-cells to target the B-cell maturation antigen (BCMA) protein found on myeloma cells

Anti-BCMA CAR T cell therapy in patients with Multiple Sclerosis

Chuan Qin, M.D., Ph.D. [1], Ke Shang, M.D.[1], Dai-Shi Tian, M.D., Ph.D.[1], Huan Ye, M.D.[2], and Wei Wang, M.D., Ph.D.[1].

[1]Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [2]Nanjing IASO Biotherapeutics Ltd, Nanjing, China

Scientific Session 19: Neuroregeneration strategies and cellular therapies

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Characteristics of MS patients

- Five MS patients (4 SPMS and 1 PPMS) were enrolled, the mean follow-up post-infusion was 5.1 months.
- The mean EDSS at baseline was 6.2 (range: 6-7). All patients had received biologic drug treatment.

Characteristics	MS-1	MS-2	MS-3	MS-4	MS-5
Type of MS	PPMS	SPMS	SPMS	SPMS	SPMS
Race	East Asian	East Asian	East Asian	East Asian	White
Sex	Male	Female	Male	Male	Male
Age at baseline; years	53	43	48	55	36
Follow-up; months	9	6	6	3	3
EDSS at baseline	7	6	6	6	6
Number of lesions on T2-weighted images (> 3mm)	21	42	115	28	19
Previous treatment	corticosteroid Siponimod Fampridine	corticosteroid Siponimod Ozanimod Teriflunomide Ofatumumab Fampridine	corticosteroid Siponimod Ozanimod Teriflunomide	corticosteroid Siponimod Ozanimod Teriflunomide Ofatumumab	corticosteroid Ofatumumab Rituximab

EDSS: expanded disability status scale; SPMS: secondary progressive MS; PPMS: primary progressive MS.

Scientific Session 19: Neuroregeneration strategies and cellular therapies

Track Pathogenesis

Room Lecture Hall 211

Date Friday, 26 September 2025, 10:30 - 12:00 CEST

PRESENTATION ID O152

Anti-BCMA CAR T cell therapy in patients with Multiple Sclerosis

Chuan Qin (China)

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30th Conference of Rehabilitation in Multiple Sclerosis

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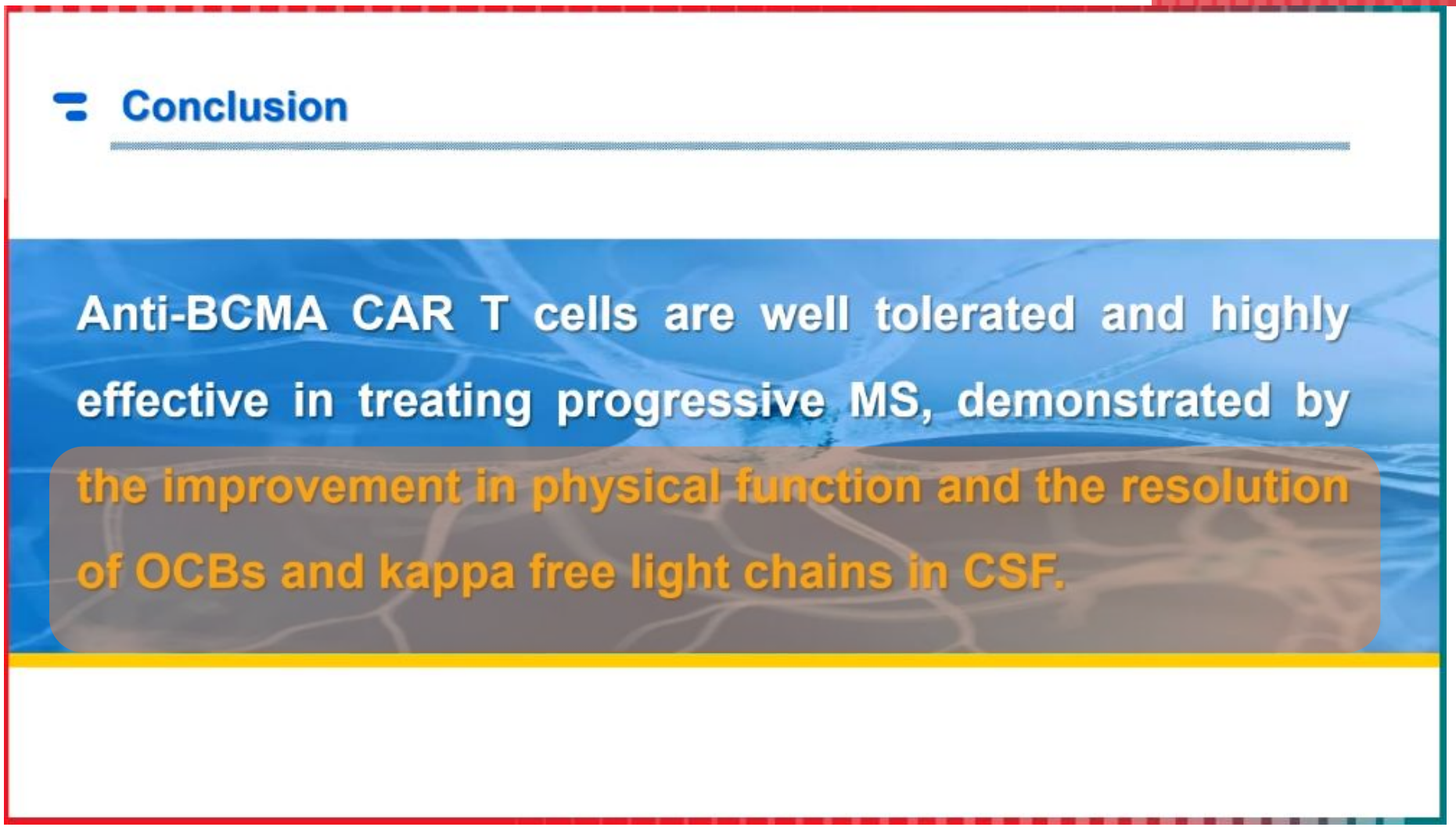

BTK Inhibitors

EXPERT OPINION ON EMERGING DRUGS
2020, VOL. 25, NO. 4, 377–381
https://doi.org/10.1080/14728214.2020.1822817

Taylor & Francis
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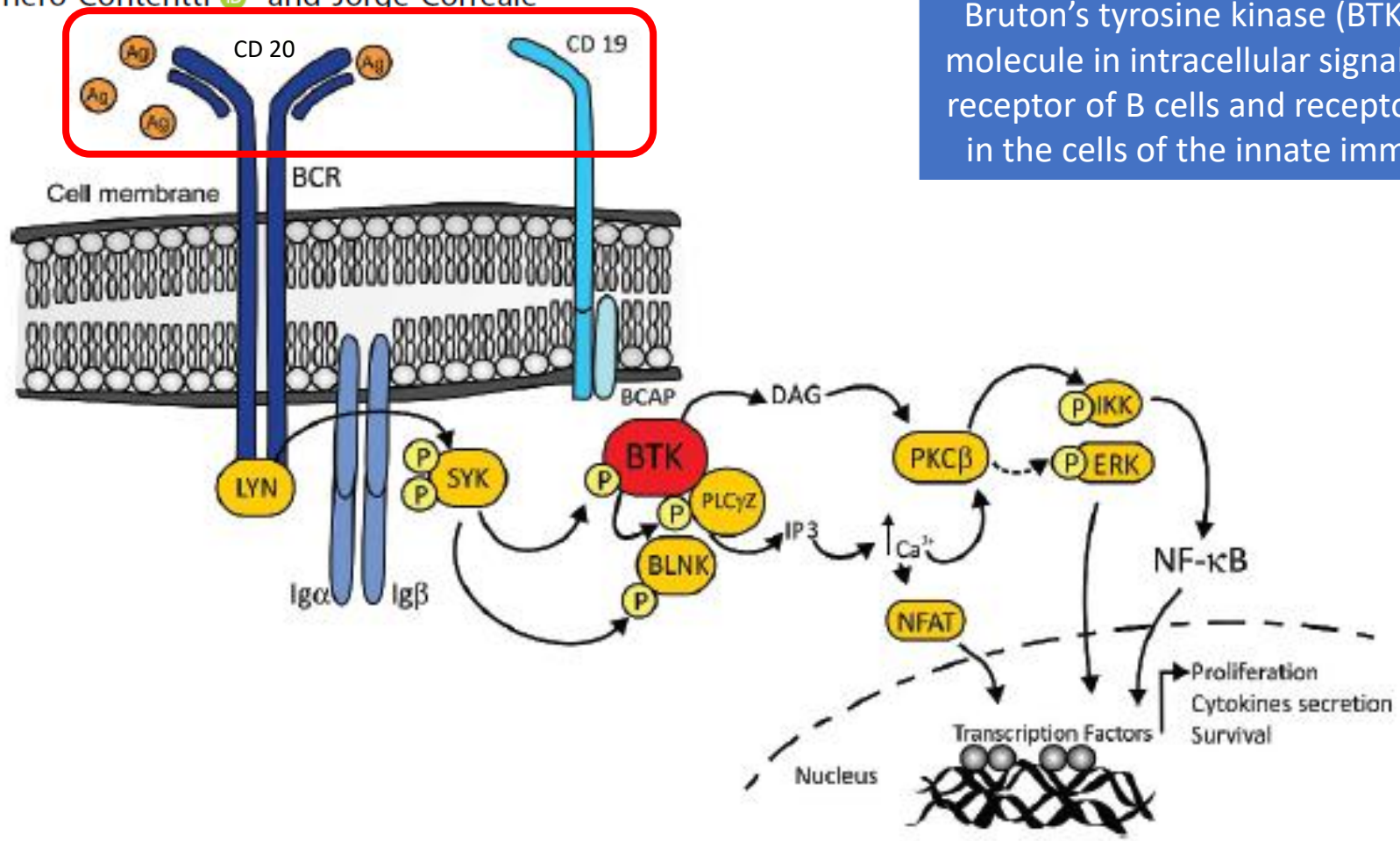
EDITORIAL

Check for updates

Bruton's tyrosine kinase inhibitors: a promising emerging treatment option for multiple sclerosis

Edgar Carnero Contentti [a] and Jorge Correale [b]

Bruton's tyrosine kinase (BTK) is a critical molecule in intracellular signalling from the receptor of B cells and receptors expressed in the cells of the innate immune system

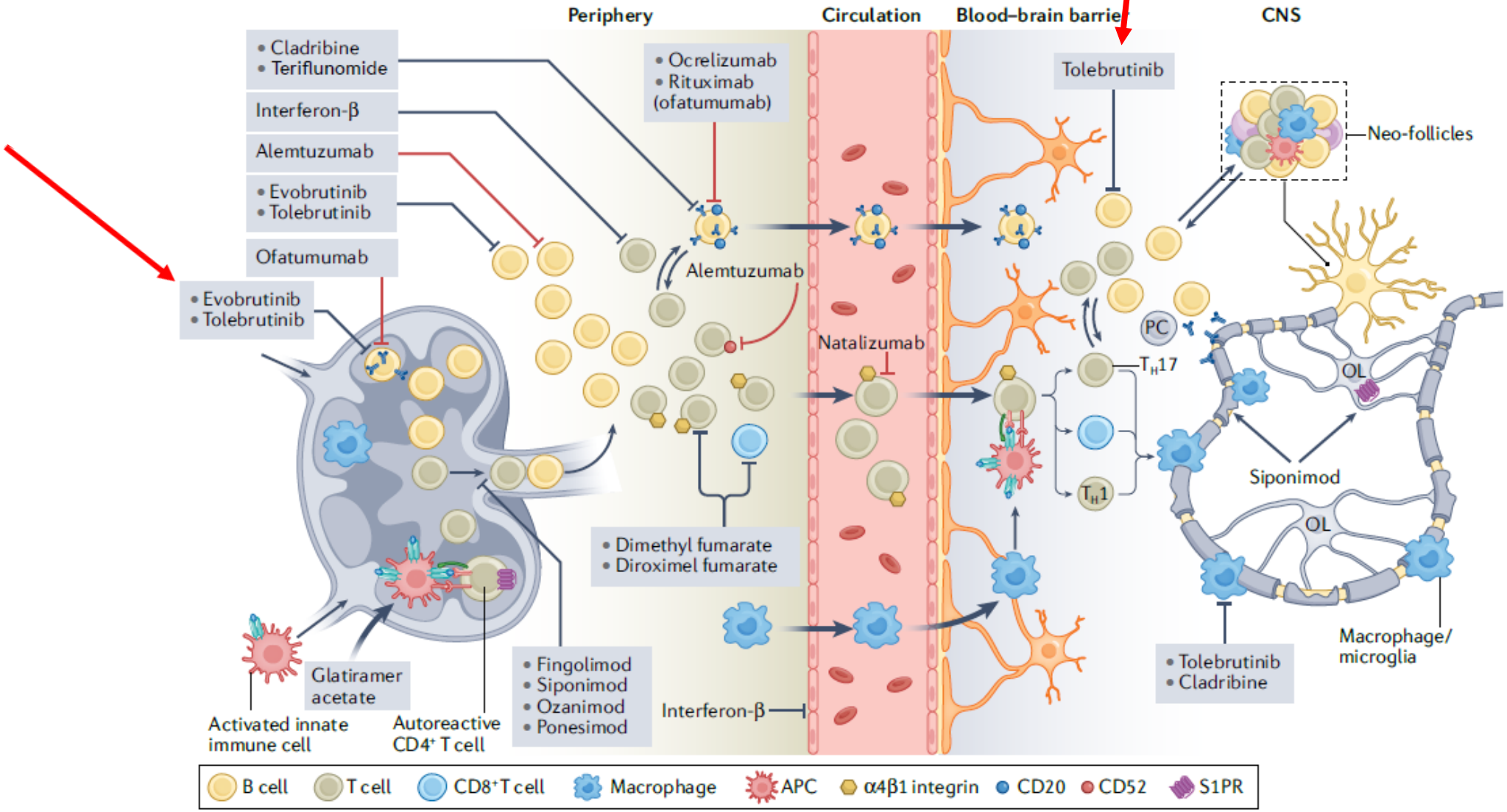


Thinking outside the box: non-canonical targets in multiple sclerosis

Laura Bierhansl[1], Hans-Peter Hartung[2,3,4], Orhan Aktas[2], Tobias Ruck[2], Michael Roden[5,6,7] and Sven G. Meuth[2]✉

NATURE REVIEWS | DRUG DISCOVERY VOLUME 21 | AUGUST 2022 | 579

Bruton's tyrosine kinase inhibitors, which are very small molecules, address not only the adaptive but also the innate immune system and can reach the CNS easily



HERCULES (NCT04411641) was a double-blind randomized phase 3 clinical study evaluating the efficacy and safety of tolebrutinib in participants with nrSPMS, defined at baseline as:

- having a SPMS diagnosis with an expanded disability status scale (EDSS) between 3.0 and 6.5,
- no clinical relapses for the previous 24 months and
- documented evidence of disability accumulation in the previous 12 months.

Participants were randomized (2:1) to receive either an oral daily dose of tolebrutinib or a matching placebo for up to approximately 48 months.

Completed

Nonrelapsing Secondary Progressive Multiple Sclerosis (NRSPMS) Study of Bruton's Tyrosine Kinase (BTK) Inhibitor Tolebrutinib (SAR442168) (HERCULES) (HERCULES)

The primary endpoint was 6-month CDP defined as the increase of ≥1.0 point from the baseline EDSS score when the baseline score is ≤5.0, or the increase of ≥0.5 point when the baseline EDSS score was >5.0.

ClinicalTrials.gov ID

Sponsor Sanofi

Information provided

Last Update Posted 2025-02-03

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

This article was published on April 8, 2025, at NEJM.org.

DOI: 10.1056/NEJMoa2415988

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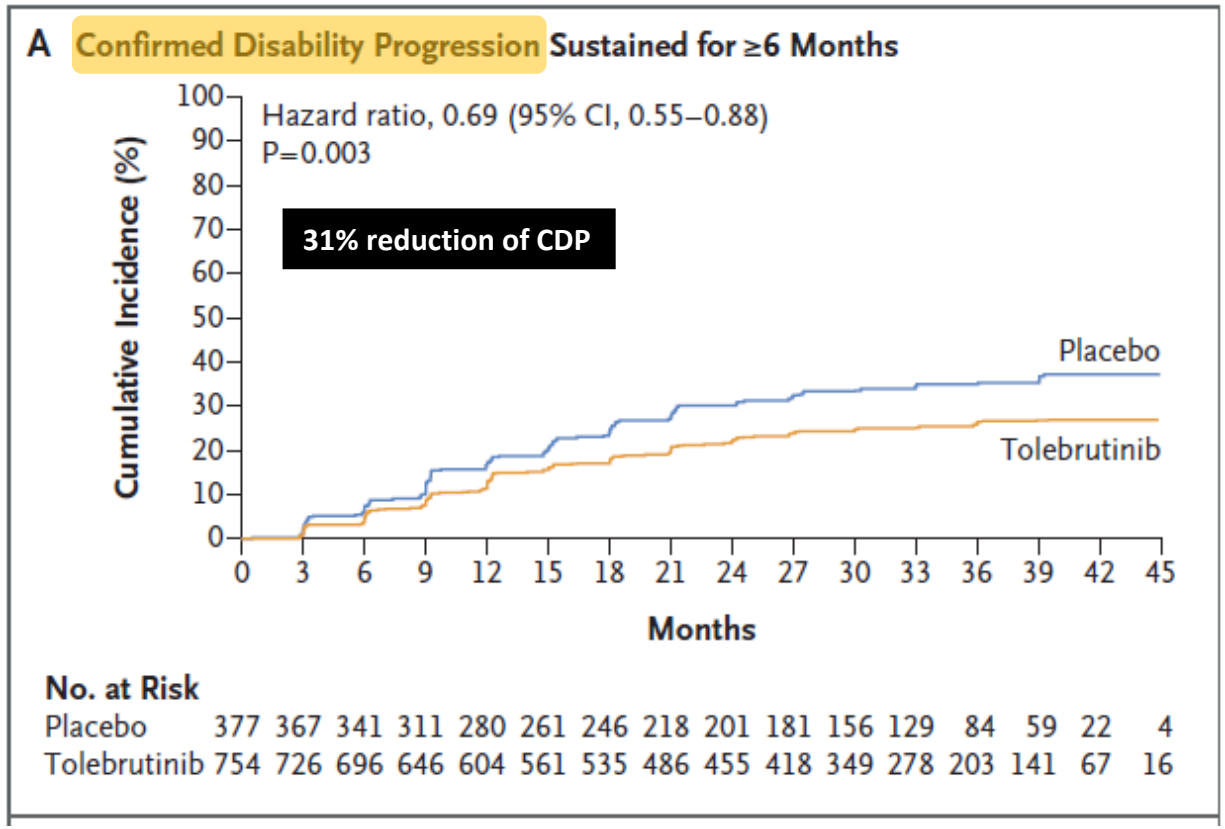
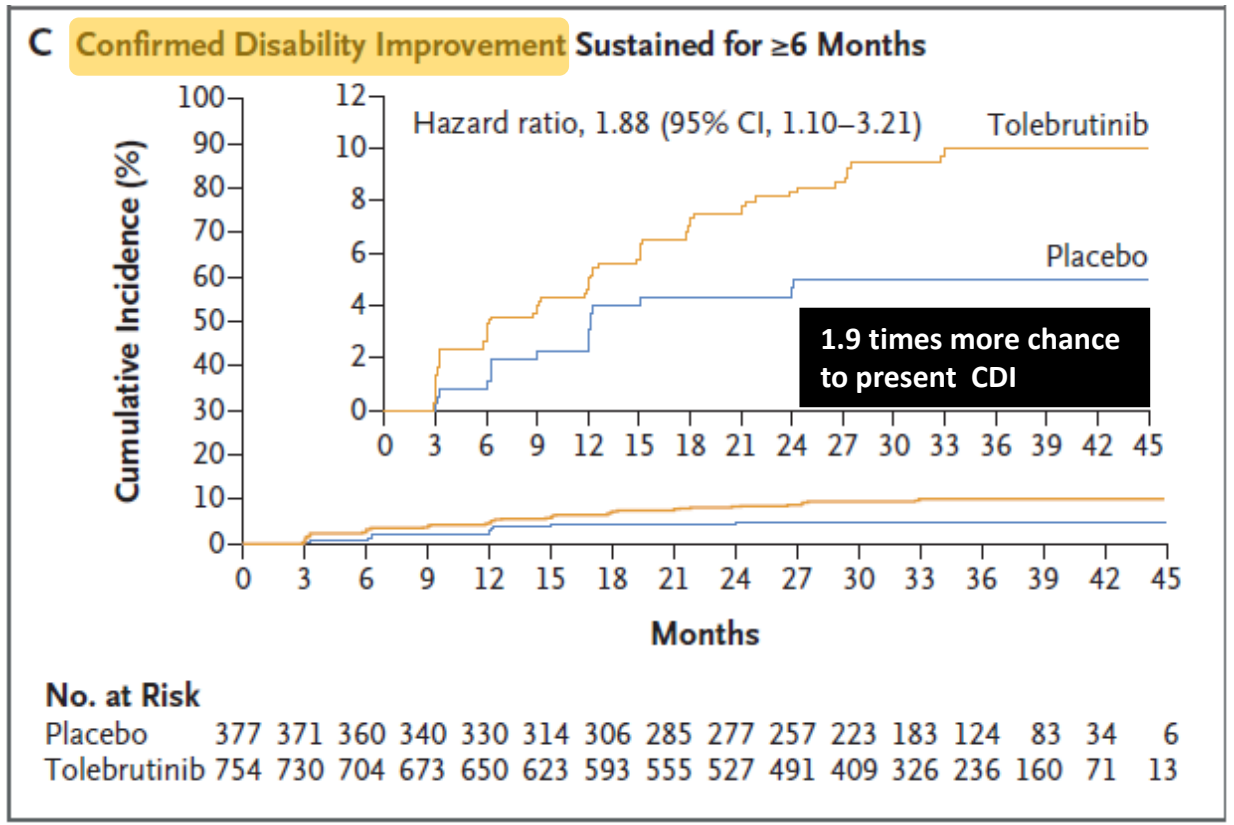
Tolebrutinib in Nonrelapsing Secondary Progressive Multiple Sclerosis





In participants with non-relapsing secondary progressive multiple sclerosis, the risk of disability progression was lower among those who received treatment with tolebrutinib than among those who received placebo.

Scientific Session 13: Emergent therapies in MS and related conditions

Track Therapy

Room Lecture Hall Auditorium

Date Friday, 26 September 2025, 08:30 - 10:00 CEST

BTK inhibitors
Heinz Wiendl (Germany)

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Tolebrutinib

FDA review

Press Release sanofi

Update on the US regulatory review of tolebrutinib in non-relapsing, secondary progressive multiple sclerosis

Paris, September 22, 2025. The US Food and Drug Administration (FDA) has extended by three months the target action date of its review of the new drug application (NDA) of tolebrutinib, an oral and brain-penetrant investigational Bruton's tyrosine kinase (BTK) inhibitor to treat non-relapsing, secondary progressive multiple sclerosis (nrSPMS) and to slow disability accumulation independent of relapse activity in adult patients.

- Tolebrutinib achieved breakthrough therapy designation by the FDA for nrSPMS treatment
- Submission of additional analyses from HERCULES and GEMINI trials was deemed a major amendment
- New FDA review target 28th December 2025

EMA: 1st 2026 Trimester

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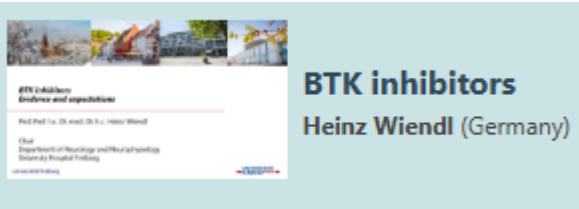

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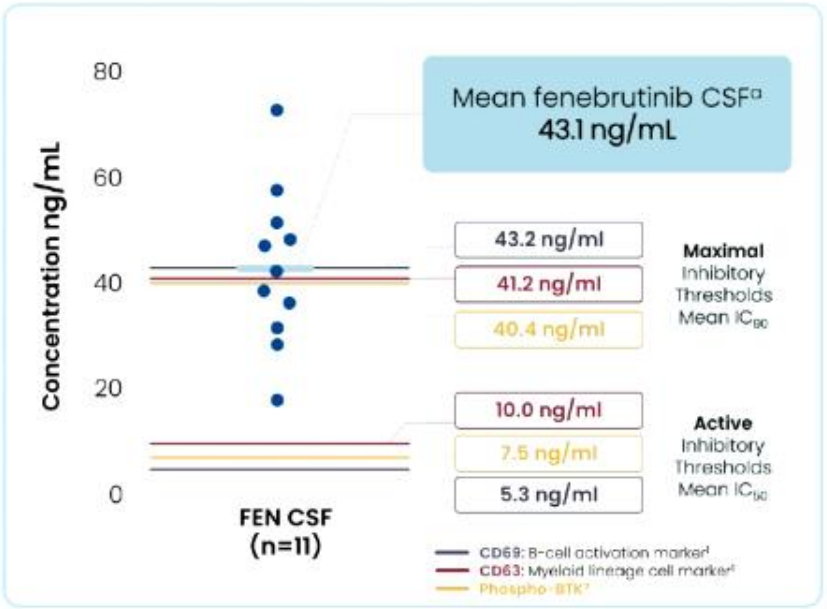
Fenebrutinib CSF concentrations



All patients had values within the active range (above IC_{50}), and the CSF-to-plasma ratio indicated CNS penetration

Fenebrutinib concentration (ng/mL)[b,c]	Median (min–max)
n	4
CSF	50.2 (36.5–72.8)
Total plasma	691 (630–1760)
CSF: plasma ratio (%)	6.1 (4.1–8.3)

Bar-Or et al., *AAN* 2024

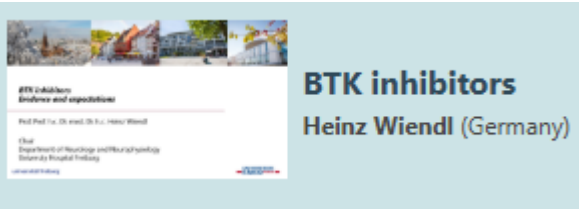
UNIVERSITÄTS KLINIKUM FREIBURG

Scientific Session 13: Emergent therapies in MS and related conditions

Track Therapy

Room Lecture Hall Auditorium

Date Friday, 26 September 2025, 08:30 - 10:00 CEST



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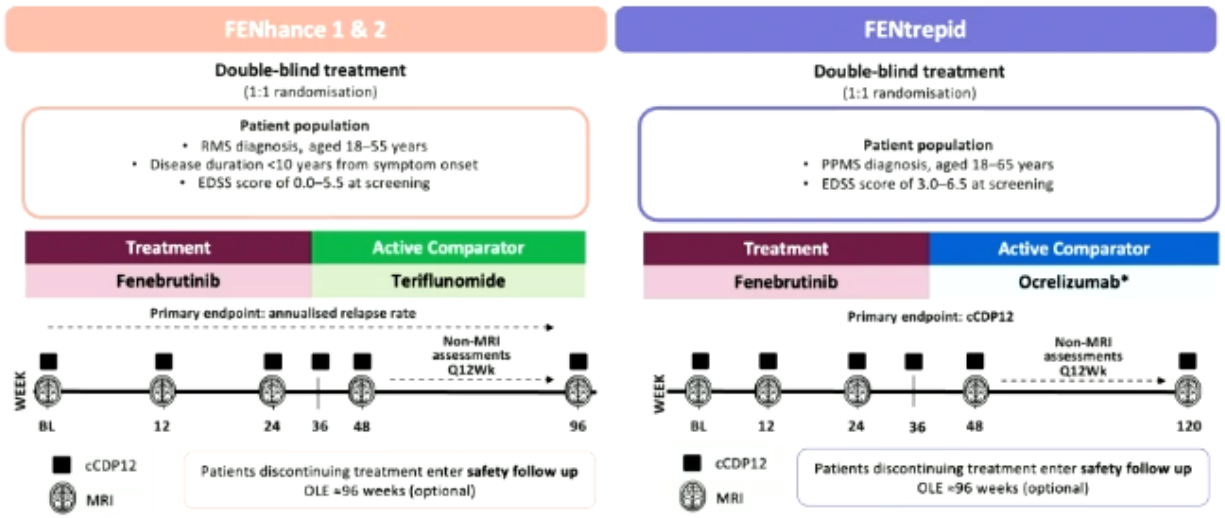
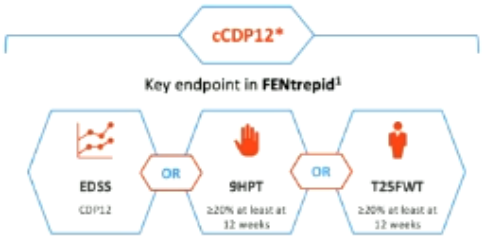
Fenebrutinib – perspectives

Study	Phase	Indication	Comparator	NCT
FENhance I & II	III	RMS/aSPMS	Teriflunomide	NCT04586010 NCT04586023
FENtrepid	III	PPMS	Ocrelizumab	NCT04544449





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FREXALIMAB

Scientific Session 13: Emergent therapies in MS and related conditions

Track Therapy

Room Lecture Hall Auditorium

Date Friday, 26 September 2025, 08:30 - 10:00 CEST

PRESENTATION ID O111

Safety and Efficacy of Frexalimab in Participants With Relapsing Multiple Sclerosis: 2.5-Year Results From the Phase 2 Open-label Extension

Gavin Giovannoni (United Kingdom)

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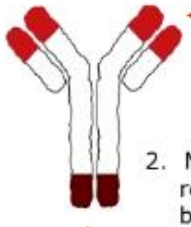
Frexalimab: Proposed Mechanism of Action

Frexalimab, a **second-generation anti-CD40L humanized IgG1 mAb**, is derived from a first-generation Ab, with 2 major modifications:



1. Affinity maturation of the variable region
2. Mutations in the Fc region to prevent binding to FcγRIIa, which is broadly expressed on platelets, monocytes, and macrophages

Adaptive immune cells

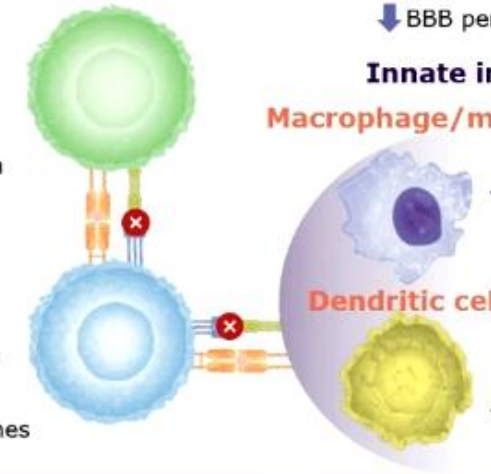
B Cells
- ↓ Activation
- ↓ Proliferation
- ↓ Antigen presentation
- ↓ Antibody production

T Cells
- ↓ Activation
- ↓ Th cell differentiation (Th1, Th17)
- ↓ Inflammatory cytokines

Endothelial cells
- ↓ BBB permeability

Innate immune cells

Macrophage/microglia



- ↓ Activation
- ↓ Inflammatory cytokines
- ↓ Antigen presentation

Key
- Frexalimab (anti-CD40L)
- TCR
- Peptide-MHCII complex
- CD40L
- CD40

- The CD40/CD40L costimulatory pathway regulates **adaptive and innate** immune responses and is implicated in the pathogenesis of MS[1–3]
- Frexalimab blocks this pathway and modifies **T and B cell activation** and innate immune cell function (**macrophage/microglia and dendritic cell**), without depleting lymphocytes[4,5]

Ab, antibody; BBB, blood-brain barrier; CD40, cluster of differentiation 40; CD40L, CD40 ligand; FcγRIIa, fragment crystallizable gamma receptor IIa; IgG, immunoglobulin G; mAb, monoclonal Ab; MHC, major histocompatibility complex; MS, multiple sclerosis; TCR, T-cell receptor; Th, T helper; W, week.

1. Gerritse K, et al. *Proc Natl Acad Sci USA*. 1996;93:2499–2504; 2. Howard LM, et al. *J Clin Invest*. 1999;103:281–290; 3. t'Hart BA, et al. *J Neuroimmunol*. 2005;163:31–39; 4. Vermersch P, et al. *N Engl J Med*. 2024;390(7):589–600; 5. Vermersch P, et al. *Curr Treat Options Neurol*. 2025;27(7):1–11.

Scientific Session 13: Emergent therapies in MS and related conditions

Track Therapy

Room Lecture Hall Auditorium

Date Friday, 26 September 2025, 08:30 - 10:00 CEST

PRESENTATION ID O111

Safety and Efficacy of Frexalimab in Participants With Relapsing Multiple Sclerosis: 2.5-Year Results From the Phase 2 Open-label Extension

Gavin Giovannoni (United Kingdom)

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Frexalimab Met Primary Endpoint in Phase 2 Trial

In the 12-week DBP of a Phase 2 trial in participants with relapsing MS (NCT04879628), frexalimab showed **favorable safety and efficacy**[1]

89% reduction (p=0.0004) in **new Gd+ T1 lesions** (primary endpoint) in frexalimab$_{1200mg/IV}$ Q4W arm vs pooled placebo at W12[1]

Sustained reduction in number of lesions was noted **over 2 years** in the OLE with frexalimab treatment[2]

Objective: To report safety and efficacy of frexalimab at W120 (2.5 years) in the OLE of phase 2 trial in participants with relapsing MS

DBP, double-blind period; Gd+, gadolinium enhancing; IV, intravenous; MS, multiple sclerosis; OLE, open-label extension; Q4W, every 4 weeks; W, week.

1. Vermersch P, et al. *N Engl J Med*. 2024;390(7):589–600; 2. Vermersch P, et al. *Neurology*. 2025;1785(104):7_Supplement_1. doi: 10.1212/WNL.0000000000208742.

Scientific Session 13: Emergent therapies in MS and related conditions

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Conclusions

Frexalimab treatment resulted in a sustained **reduction of disease activity** over 2.5 years (W120), demonstrated by a low number of Gd+ T1 lesions and new/enlarging T2 lesions

Clinical endpoints remained stable over 2.5 years:

- Low frequency of relapses
- 88% participants relapse-free
- Stable EDSS scores

Frexalimab was **well-tolerated** through 2.5 years, with no new safety signals and **stable lymphocyte counts**

Phase 3 trials, FREXALT CLINICAL TRIAL (NCT06141473) and FREVIVA CLINICAL TRIAL (NCT06141486), are **actively recruiting** and will assess the efficacy and safety of frexalimab in people with RMS and nrSPMS, respectively

Frexalimab continues to show favorable safety and sustained reduction in disease activity in people with RMS through 2.5 years, supporting its further development in Phase 3 trials as a potential high-efficacy, non-lymphocyte-depleting therapy

EDSS, Expanded Disability Status Scale; Gd+, gadolinium enhancing; IV, intravenous; MRI, magnetic resonance imaging; nrSPMS, non-relapsing secondary progressive multiple sclerosis; OLE, open-label extension; RMS, relapsing multiple sclerosis; W, week.

ΑΛΛΕΣ ΠΡΟΣΠΑΘΕΙΕΣ

The role of the complement system in Multiple Sclerosis: A review

Front. Immunol. 13:970486.
doi: 10.3389/fimmu.2022.970486

Nil Saez-Calveras[1] and Olaf Stuve[1,2]*

Effects of complement inhibition in MS animal models.

Inhibition	Animal model	Effect
C1q -/-	MOG_{35-55} induced EAE mice	Density of Iba1+ cells, microglia with reactive gliosis morphologies, expression of DAM marker CLEC7A lower in C1q -/- mice. No effect on disease phenotype [138]
ANX-M1.21 (C1q blocking antibody)	MOG_{35-55} induced EAE mice	Decreased Iba1+ and Iba1+/FTL+ microglia [138]
CVF (depletes C3)	Myelin + CFA immunized Lewis rats	CVF given at day 9 delayed onset of EAN by 2-3 days, when given at days 9-12 delayed onset by 4-5 days [132]
	BPN myelin immunized rats	Lower clinical scores, less demyelination. Fewer ED1-positive macrophages, CD11bc-positive cells [133]
C3-/-	MOG_{35-55} induced EAE mice	In both C3 -/- and factor B -/- mice, little infiltration of the parenchyma by macrophages and T cells, protection from demyelination [135]
		Mice equally susceptible to EAE. No differences in production of proinflammatory cytokines (IL-2, IL-4, IL-12, TNF-a, and IFN-γ) [136]
CR2-Crry	MOG_{35-55} induced EAE mice	Synaptic preservation in LGN where CR2-Crry AAV injected. Reduced synaptic terminal engulfment within microglial lysosomes. Visual acuity preservation. No effect on demyelination, axonal loss, gliosis, myelin engulfment [57]
		Administration prior to and during onset of EAE attenuates both MOG-induced and transferred EAE in CR2-Crry and CR2-factor H treated mice [99]
C3aR -/- C3a CNS expression	MOG_{35-55} induced EAE mice	C3aR -/- attenuated chronic EAE, modestly reduced macrophage and T cell infiltrates in the SC. Selective C3a-GFAP expression exacerbated chronic EAE, mortality, increased macrophage and T cell infiltrates [172]
Dual C3aR -/- C5aR -/-	MOG_{35-55} induced EAE mice	Delayed onset of disease but no attenuation of disease severity. Greater infiltration of CD4+ T cells [173]
C5aR -/-	MOG_{35-55} induced EAE mice	Mice fully susceptible to MOG-induced EAE, no difference in disease onset or severity. Similar macrophage and T cell infiltrates. Equal proinflammatory gene expression [171]
C5 -/-	Guinea pig myelin + incomplete Freund's adjuvant immunized mice	*Acute EAE:* Delay in inflammatory cell infiltrates and tissue damage *Chronic EAE:* Axonal depletion and severe gliosis in C5 -/-. Extensive remyelination in C5-sufficient mice [146]
	Myelin-induced EAE mice	Increased TUNEL + apoptotic cells in C5 -/- mice during clinical recovery (lymphocytes, monocytes, OLG) [147]
PMX205 (C5aR1 inhibitor)	Biozzi AB/H mice (syngeneic Biozzi AB/H spinal cord homogenate + CFA)	Amelioration of progressive neurological disability (not complete rescue). Reduction of NLPR3 inflammasome, upregulation of PPAR [143]
AcF-[OPdChaWR] (C5aR inhibitor)	*EAE:* gpBMP + CFA immunized rats *ADEAE:* Additional injection of Z12 (anti-myelin) mAb	Neutrophil response to C5a blocked. No effect on clinical disease or pathology [170]

Major difficulty: poor penetration of closed BBB- Techniques to overcome this obstacle

This session is sponsored by: **F. Hoffmann-La Roche**

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Looking ahead: What's next on the horizon for MS beyond anti-CD20 therapies?

Jiwon Oh (Canada)

Satellite Symposium 2: How anti-CD20 therapies have shaped our understanding of MS and sparked future innovations

Track	Satellite Symposia
Room	Lecture Hall 7
Date	Wednesday, 24 September 2025, 13:15 - 14:15 CEST

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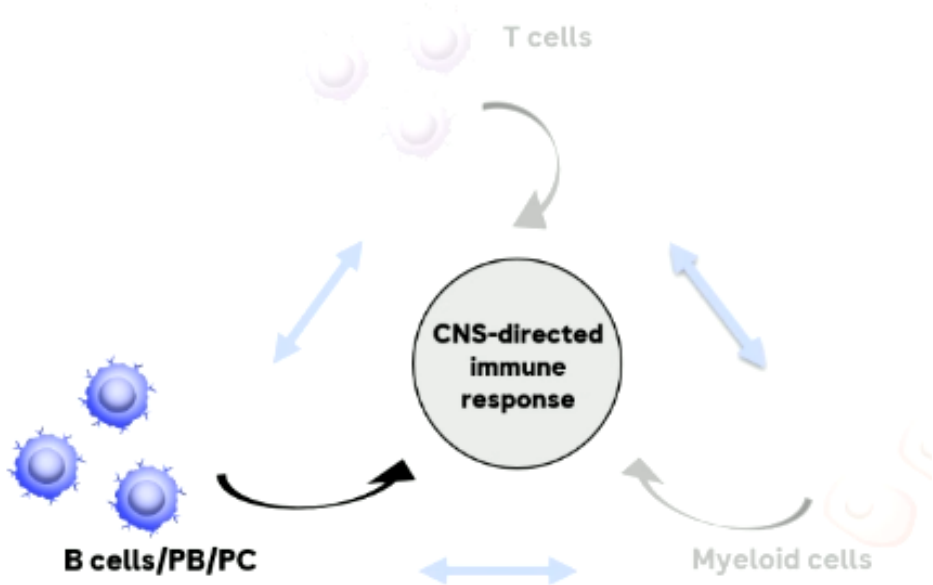
Optimise therapies to target B cell-T cell interactions:

Brainshuttle™ technology

Brainshuttle™ technology

An anti-transferrin receptor 1 (TfR1)-antigen-binding antibody fragment that binds to monoclonal antibodies to help them cross the blood-brain barrier[1-3]

Rationale:[1-3]
Improve CNS penetration of monoclonal antibodies to target compartmentalised inflammation



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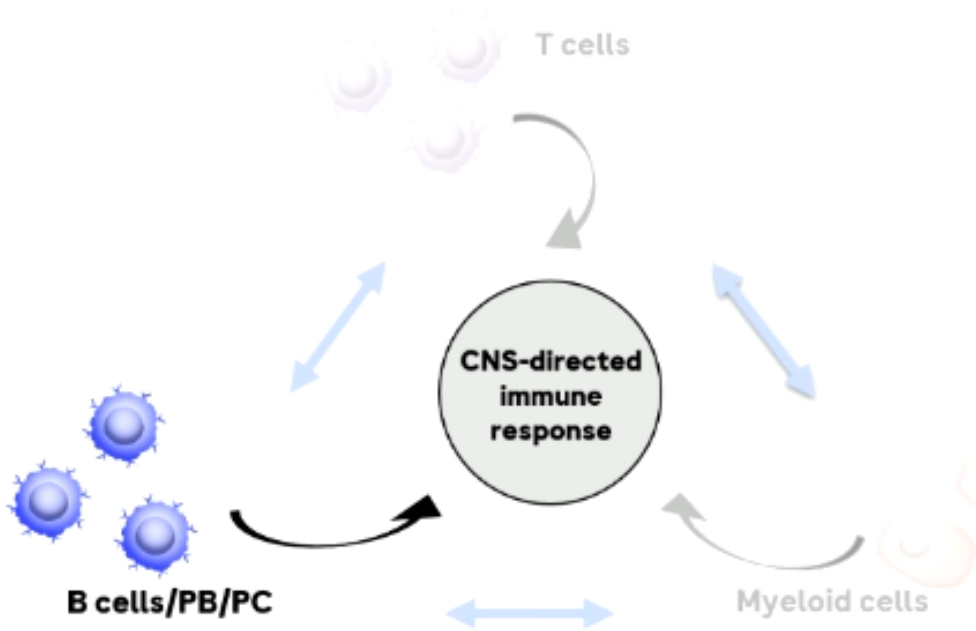
Explore preventative and reparative mechanisms:

Prevention strategies (e.g. EBV vaccinations)

EBV vaccinations

Vaccines to reduce the risk of EBV infection, which may be linked to MS pathology[1-4]

Rationale:[1-4]
Increased levels of EBV antibodies have been observed to precede MS diagnosis; therefore, reducing the risk of EBV infection is hypothesised to help prevent MS onset



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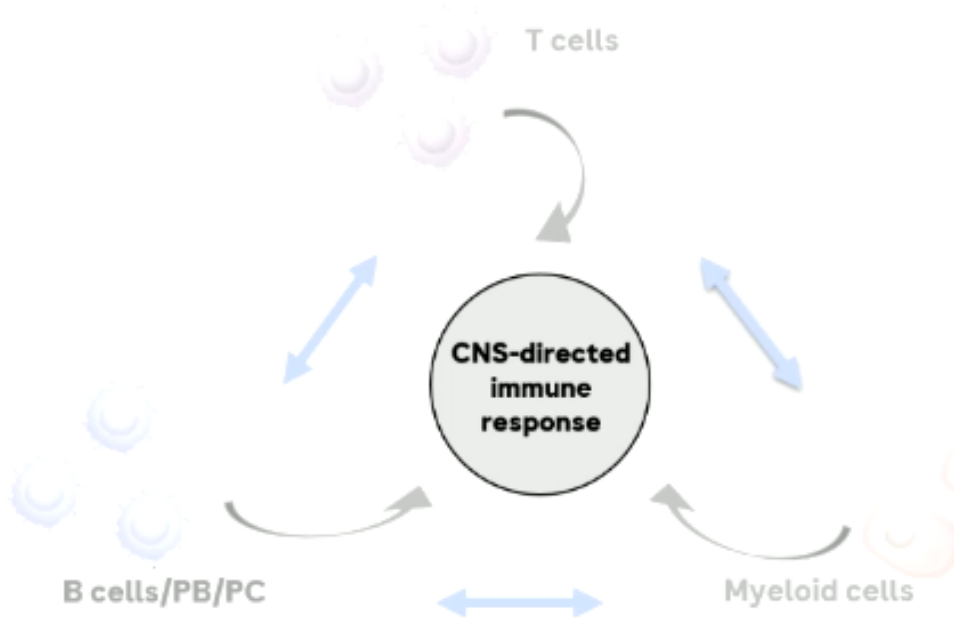
Track	Satellite Symposia
Room	Lecture Hall 7
Date	Wednesday, 24 September 2025, 13:15 - 14:15 CEST

Explore preventative and reparative mechanisms:
CNS repair strategies

CNS repair strategies

Targeting various mechanisms involved in reducing neuroinflammation and/or fostering an environment favorable to regeneration and repair (e.g. monoacylglycerol lipase, thyroid hormones, M1 receptor, histamine)[1-7]

Rationale:[1-3]
Prevention of disease progression or restoration of neuronal function by targeting neuroinflammation and neural repair, including remyelination



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Looking ahead: What's next on the horizon for MS beyond anti-CD20 therapies?

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Room	Lecture Hall 7
Date	Wednesday, 24 September 2025, 13:15 - 14:15 CEST

Protective and reparative therapies in MS are currently in early stages of clinical development

Emerging protective and reparative therapies

Treatment	Phase	MoA	Estimated readout
MAGLi (RG6182)[1]	I	MAGL inhibitor	-
LL-341070[2]	Pre-clinical	Thyromimetic	-
PIPE-307[3]	II	M1 receptor antagonist	Q3 2025
Clemastine[4]	I/II	Antihistamine	Q2 2025

Description/ Summary:

MAGL inhibitor (RG6182) has a unique and multimodal mechanism of action to target compartmentalized inflammation in the central nervous system. MAGLi has disease modifying potential to tackle the accumulation of persistent neurological disability in Multiple Sclerosis. **Neuroprotection**

Managed By:

Pharma Research and Early Development (pRED)

PIPE-307 is an investigational, first-in-class oral therapy in development for relapsing-remitting multiple sclerosis (RRMS) by promoting the production of myelin in the brain. **Remyelination**

A combination of **metformin and clemastine,** an antihistamine, helps repair myelin- 2025. (previous studies with clemastine alone- worsening disability!). **Remyelination**

LL-341070 increases the number of oligodendrocytes, boosts myelin production or repair, and improves nerve cell function. - **Remyelination**

frontiers | Frontiers in Cellular Neuroscience

TYPE Review
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DOI 10.3389/fncel.2023.1197492

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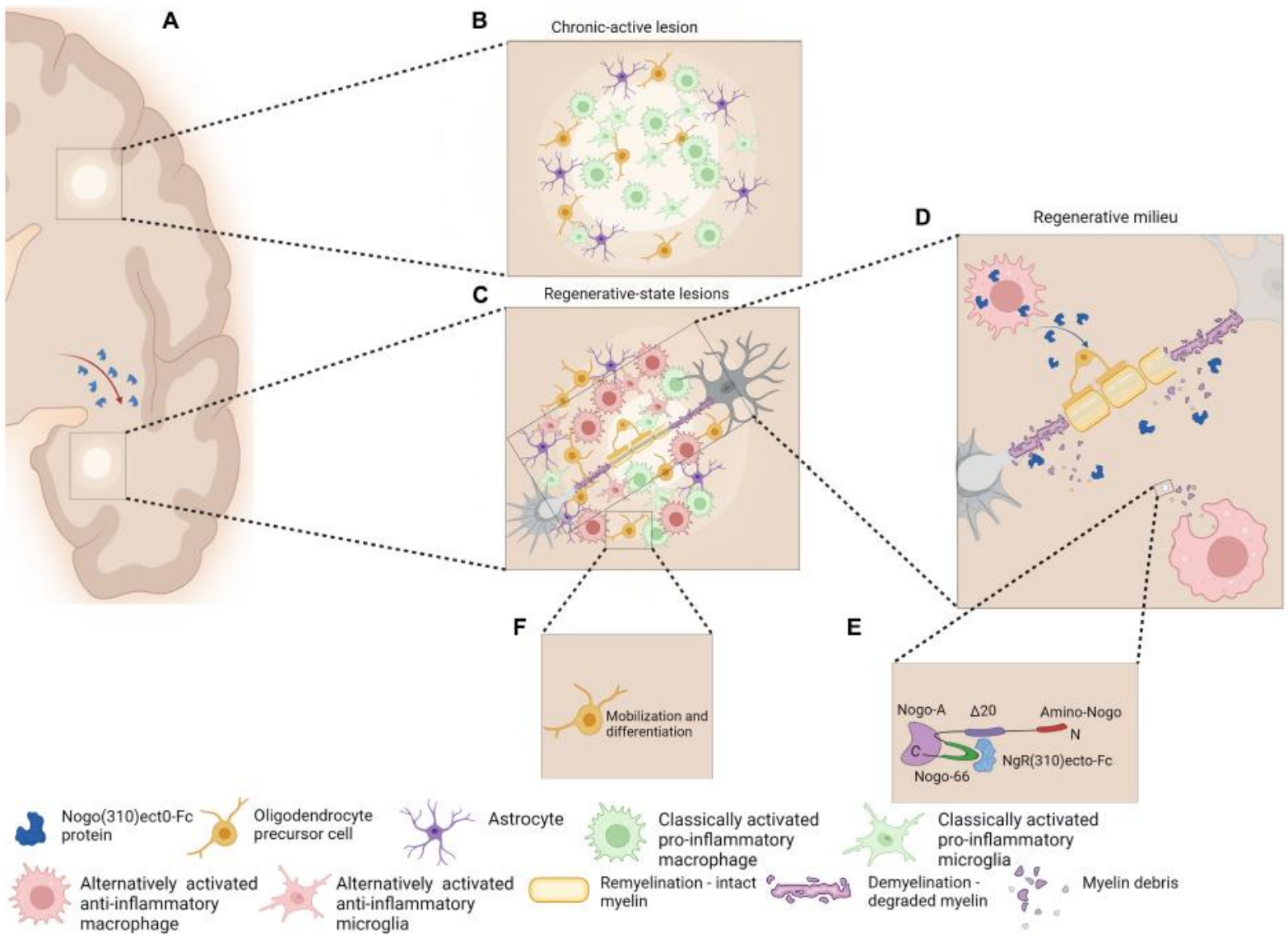
How does Nogo receptor influence demyelination and remyelination in the context of multiple sclerosis?

Zahra Rashidbenam[1], Ezgi Ozturk[1], Maurice Pagnin[1], Paschalis Theotokis[2], Nikolaos Grigoriadis[2] and Steven Petratos[1]*

Chronic active lesions in MS white matter are characterized by the presence of classically activated pro-inflammatory phenotype microglia/macrophage, with the occurrence of partial remyelination, which is observed as shadow plaques (B). Regenerative milieu through MS plaques may be possible as a result of a novel cellular delivery of **NgR(310)ecto-Fc protein** to the site of inflammatory lesions. The modification of the diseased tissue milieu may shift the phenotype of microglia/macrophages from a classically active pro-inflammatory to an alternatively activated anti-inflammatory phenotype (C). Anti-inflammatory microglia/macrophages may increase phagocytosis of NgR(310)ecto-Fc-bound myelin debris to expedite neural repair (D,E). The events favour differentiation and mobilization of OPCs to the site of lesions and the **enhancement of remyelination** (F).



ΜΕΤΑΜΟΣΧΕΥΣΗ ΜΕΣΕΓΧΥΜΑΤΙΚΩΝ ΒΛΑΣΤΟΚΥΤΤΑΡΩΝ- Secretome

International Journal of Molecular Sciences

Int. J. Mol. Sci. 2024, 25, 1365.

MDPI

Review

The Therapeutic Mechanisms of Mesenchymal Stem Cells in MS—A Review Focusing on Neuroprotective Properties

Sonia Gavasso [1,2,*], Torbjørn Kråkenes [1,2], Håkon Olsen [1,2], Elisabeth Claire Evjenth [1,2], Marie Ytterdal [1,2], Jonas Bull Haugsøen [1,2] and Christopher Elnan Kvistad [1,2]

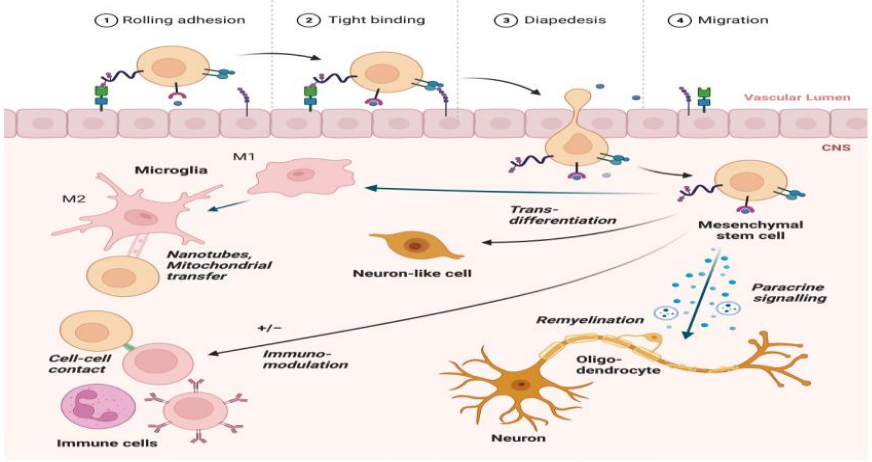


Figure 1. Potential regenerating mechanisms of MSCs in MS.

Paracrine Function

- MSCs are highly secretory. ***Neurotrophic growth factors*** increase neuronal proliferation, survival (MSCs neuroprotective capacity), and endogenous neurogenesis.
- The paracrine functions of the MSCs are mediated through secreted molecules (cytokines, chemokines, growth factors, *extracellular vesicles*), collectively named the ***Secretome***. The secretome effectively inhibits T-cell proliferation and reduces the production of pro-inflammatory cytokines. Macrophages are shifted from a pro-inflammatory phenotype to a pro-regenerative phenotype. Finally, it enhances oligodendrogenesis and neurogenesis.

Remyelination

- The secreted factors of MSCs can activate oligodendrogenesis in postmitotic neural progenitor cells by boosting oligodendroglial differentiation and maturation leading to ***Remyelination***.

Immunomodulation of the Adaptive Immune System in MS

- MSCs offer a potential avenue for immunomodulation in MS fostering regenerative processes. This is done through ***induction of regulatory T and B cells*** as well as ***regulation and suppression of T cell activation***

International Journal of *Molecular Sciences*

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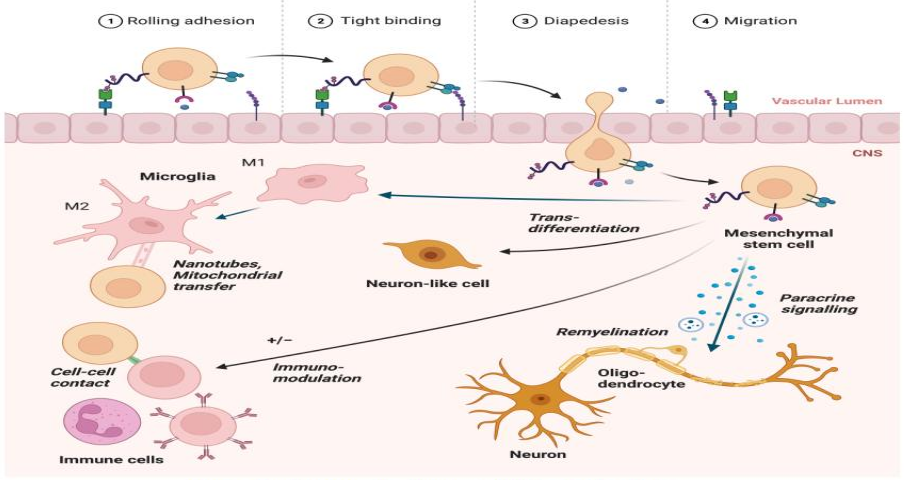


Figure 1. Potential regenerating mechanisms of MSCs in MS.

Immunomodulation of Microglia in MS

- MSCs significantly ***inhibit the expression of pro-inflammatory mediators in M1*** microglia promoting in that way the release of anti-inflammatory factors and helps for ***neural cells regeneration*** through the secretion of neurotrophic factors

Migration

- MSCs have the impressing ability to ***migrate toward areas of damage*** or inflammation within the CNS. The initial step involves MSCs tethering and rolling on the endothelial cell surface, mediated by interactions between endothelial cell selectins and MSC-expressed ligands. MSCs are directed toward the injury site by chemotactic signals.

A significant hurdle is the pulmonary first-pass effect, where most intravenously administered MSCs become entrapped in the lungs!

Alleviation of Ferroptosis

In MS, iron accumulation progressively increases from RRMS to progressive MS. A hallmark of slowly expanding lesions that are more common in progressive MS is a rim of activated iron-containing microglia. Ferroptosis in microglia could be suppressed and symptoms alleviated by treating animals with MSC-derived exosomes containing the microRNA, miR-367-3p.

Clinical Neurology and Neurosurgery 223 (2022) 107475

Contents lists available at ScienceDirect

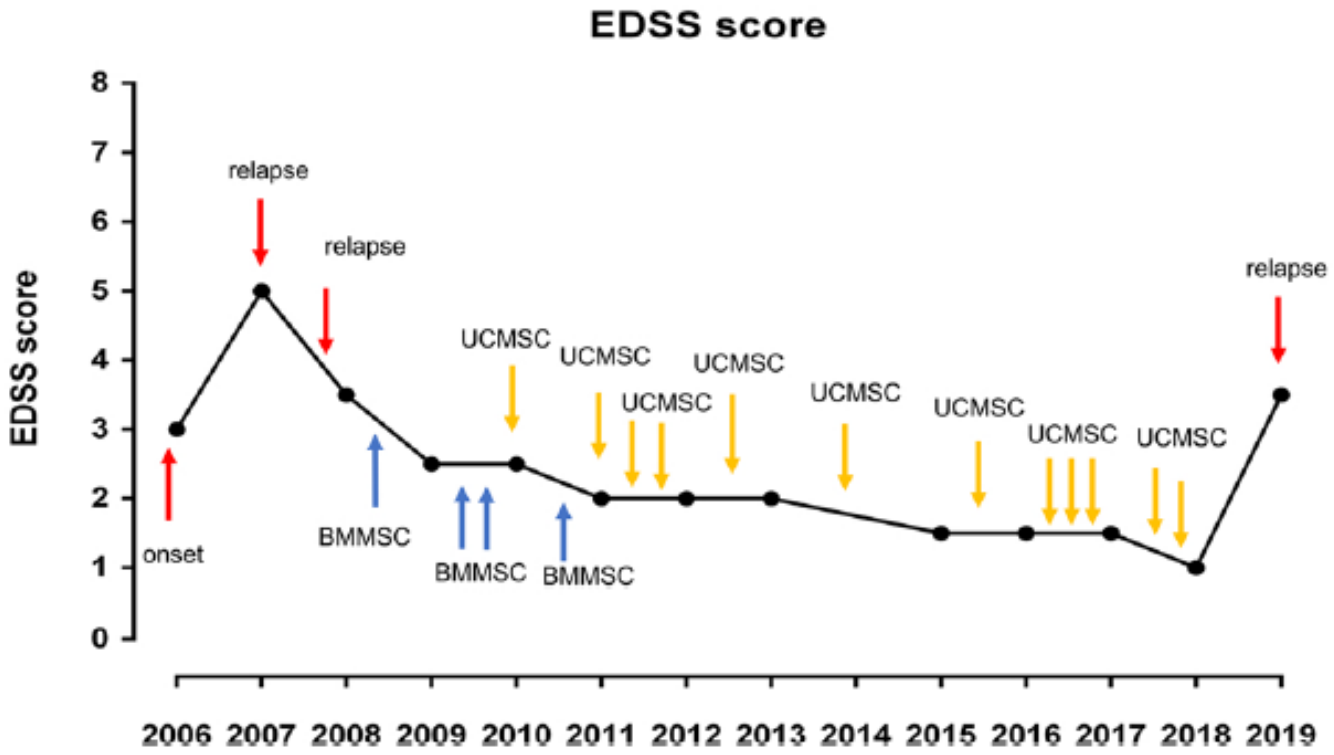
Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Case report

Multiple transplantation of mesenchymal stem cells in a patient with active progressive multiple sclerosis: Long term therapeutic outcomes

Shijie Liu [a,b,d,1], Xihong Mao [d,1], Zongliu Hou [a,b,c], Huan Wei [a,b,c], Hui Gao [a,b,c], Ying Liu [a,b,c], Yanhua Xie [a,b,c], Weiwei Tang [a,b,c], Shan He [a,b,c], Yiyi Zhao [a,b,c], Wenju Wang [a,b,c], Lin Li [a,b,c], Xiaodan Wang [a,b,c,*], Mingyao Meng [a,b,c,*]



Summary of MSCs treatment and EDSS score.

	Date	MSC source	Route	Dose	EDSS score
Pre-treatment	06/09/2006	–	–	–	3.0
	26/11/2008	BM-MSCs	iv	1.32×10^7	3.5
		BM-MSCs	it	6.3×10^5	
	19/02/2009	BM-MSCs	iv	6.0×10^7	2.5
		BM-MSCs	it	1.4×10^7	
	07/05/2009	BM-MSCs	iv	8.9×10^7	2.5
	04/08/2009	UC-MSCs	iv	1.2×10^8	2.0
	08/01/2010	BM-MSCs	it	1.47×10^5	2.0
	29/08/2010	UC-MSCs	iv	3.27×10^8	2.0
	22/04/2011	UC-MSCs	iv	1.4×10^8	2.0
	29/12/2011	UC-MSCs	iv	1.51×10^8	2.0
	04/09/2012	UC-MSCs	iv	8.65×10^7	2.0
	22/09/2013	UC-MSCs	iv	1.07×10^8	1.5
	15/01/2015	UC-MSCs	iv	1.66×10^8	1.5
	06/01/2016	UC-MSCs	iv	9.1×10^7	1.5
	21/04/2016	UC-MSCs	iv	5.09×10^7	1.5
	22/07/2016	UC-MSCs	iv	9.32×10^7	1.5
	28/03/2017	UC-MSCs	iv	1.03×10^8	1.5
	22/09/2017	UC-MSCs	iv	7.0×10^7	1.5
Post-treatment	01/12/2018	–	–	–	1.0
Post-treatment	011/8/2019	–	–	–	3.5

Journal of Clinical Medicine J. Clin. Med. 2023, 12, 6311. https://doi.org/10.3390/jcm12196311 MDPI

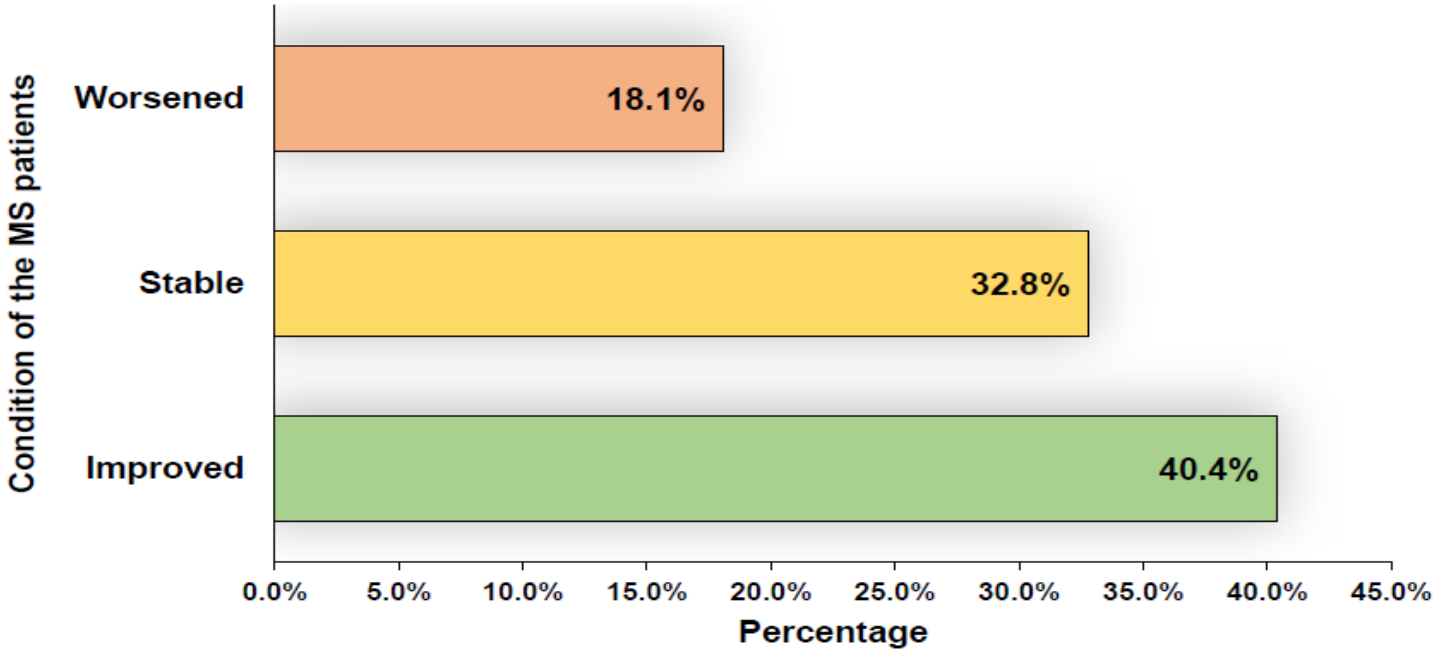
Systematic Review

Mesenchymal Stem Cell Therapy in Multiple Sclerosis: A Systematic Review and Meta-Analysis

Md Asiful Islam [1,*], Sayeda Sadia Alam [2], Shoumik Kundu [3], Saleh Ahmed [4], Shabiha Sultana [5], Azim Patar [6] and Tareq Hossan [2,7,*]

The primary aim of this systematic review and meta-analysis (SRMA) was to comprehensively assess the effectiveness and safety of MSC therapy in individuals diagnosed with MS.

Eligibility Criteria: We only included studies in this SRMA that reported the efficacy and safety of MSC therapy in human patients with MS based on the changes in the Expanded Disability Status Scale (EDSS) score from the baseline to the follow-up period.



Harris et al. Stem Cell Research & Therapy (2024) 15:151
https://doi.org/10.1186/s13287-024-03765-6

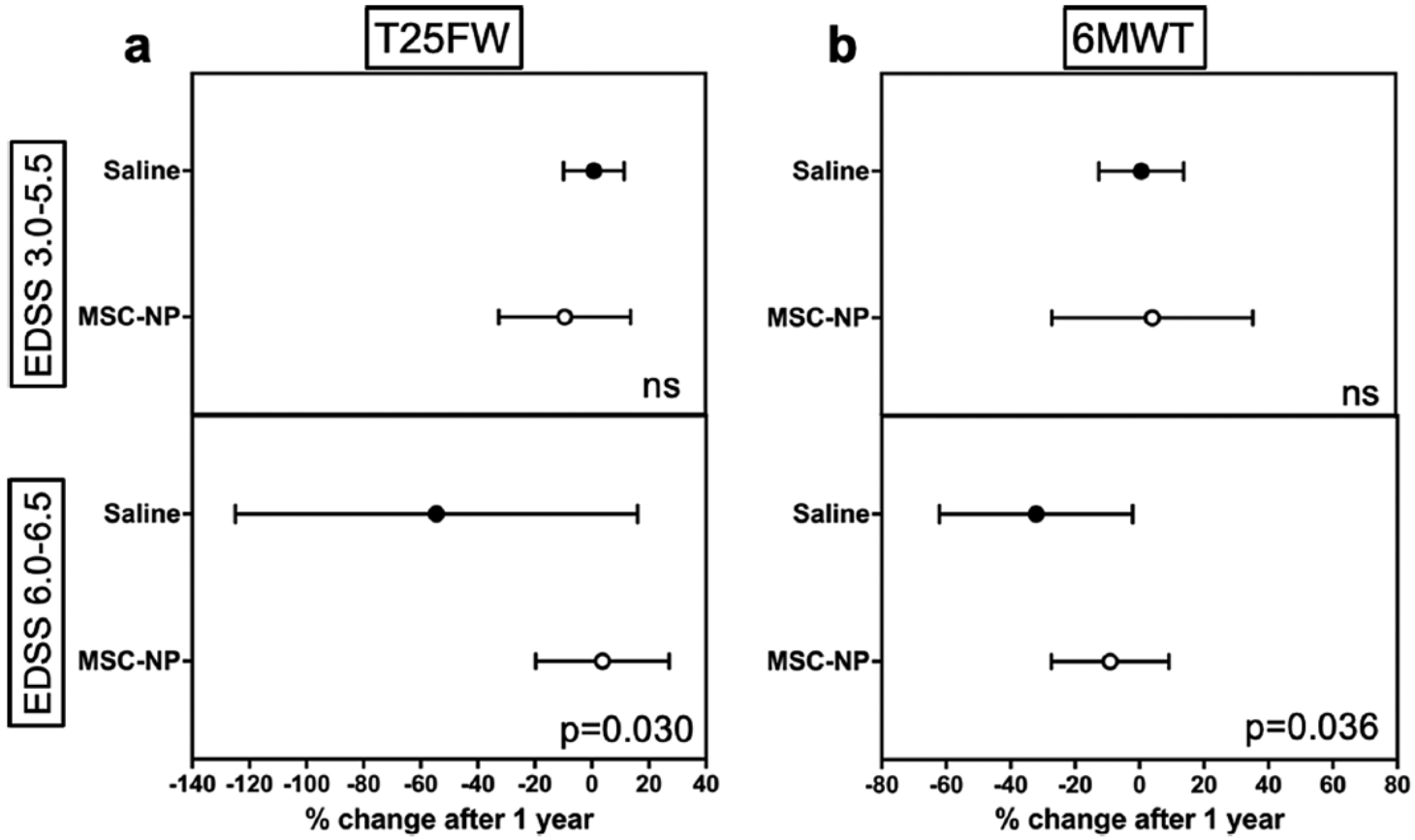
RESEARCH Open Access

Efficacy of intrathecal mesenchymal stem cell-neural progenitor therapy in progressive MS: results from a phase II, randomized, placebo-controlled clinical trial

Subjects were stratified according to baseline Expanded Disability Scale (EDSS) (3.0-6.5) and disease subtype (secondary or primary progressive MS) and randomized into either treatment or placebo group to receive six IT injections of autologous MSC-NPs or saline every two months.

Table 1 Subject demographics

	MSC-NP group N = 27	Saline group N = 27
Female sex, n (%)	18 (67%)	20 (74%)
MS Subtype/EDSS block, n (%)		
SPMS/3.0–4.0	5 (19%)	6 (22%)
SPMS/4.5–5.5	5 (19%)	4 (15%)
SPMS/6.0	5 (19%)	5 (19%)
SPMS/6.5	5 (19%)	6 (22%)
PPMS/3.0–4.0	3 (11%)	3 (11%)
PPMS/4.5–5.5	1 (4%)	1 (4%)
PPMS/6.0	2 (7%)	1 (4%)
PPMS/6.5	1 (4%)	1 (4%)
Age at treatment start (years),		
Mean (SD)	51 (7)	49 (9)
Median (IQR)	53 (44, 56)	49 (40, 57)
Disease duration (years),		
Mean (SD)	12 (5)	11 (6)



The study population consisted of ambulatory, **non-relapsing** SPMS and PPMS patients who **did not have MRI evidence of active disease.**

International Journal of Molecular Sciences

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Discussion 1

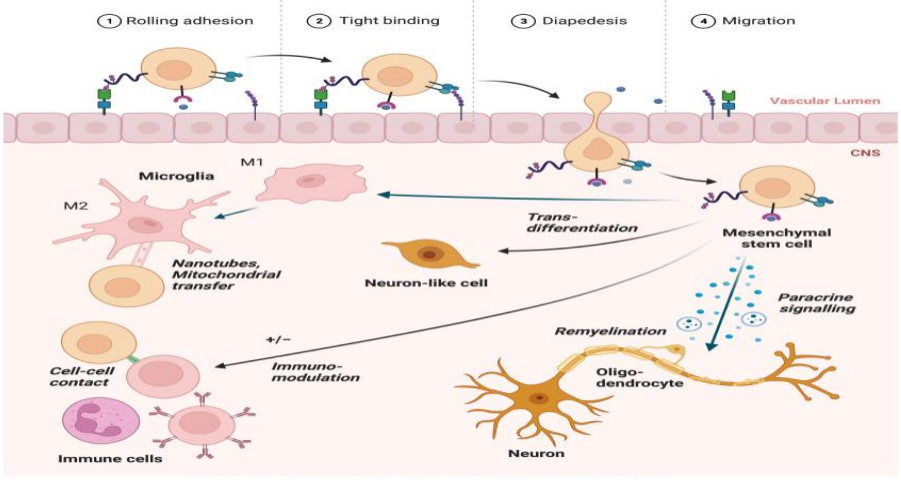

Figure 1. Potential regenerating mechanisms of MSCs in MS.

- Although MSCs have shown ***beneficial results in in vitro and in vivo models*** of demyelination and axonal injury, this does not necessarily mean the same applies to the human CNS.
- Several clinical trials have been performed testing MSCs transplantation in MS. **Although most studies have shown safety and clinical improvement in a subset of patients, the studies differ in inclusion criteria, endpoints, MSC administration, type of MSCs, method of culturing, and study design, which makes the results hard to combine or compare**. Trials showing the most promising results have a small number of participants and lack a control group!

Why do we have this discrepancy?

- First, as ***MS is a disease only occurring in humans***, there is no completely satisfactory in vivo MS model.
- Secondly, ***MSCs represent a heterogeneous population*** with minor variations from person to person, which may affect therapeutic efficacy. BM-derived MSCs from MS patients have also shown a reduced proliferative capacity and accelerated cellular aging compared to BM-MSCs from healthy persons. Similarly, cryopreservation can also impact the MSCs, which can lead to altered clinical effects. Most clinical trials have used cryopreserved MSCs.
- Third, in many rodent studies showing beneficial results, the ***number of administered MSCs*** has proportionally been far higher than in clinical trials. One million MSCs per mouse have been injected intravenously or intraperitoneally. As mice weigh 20 g, the equivalent dose for a 70 kg human would be 3.5 billion MSCs! It may not be surprising that a trial with an intravenous dose of 1–2 million MSCs/kg body weight in humans has failed to show the same positive effects!

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Discussion 2

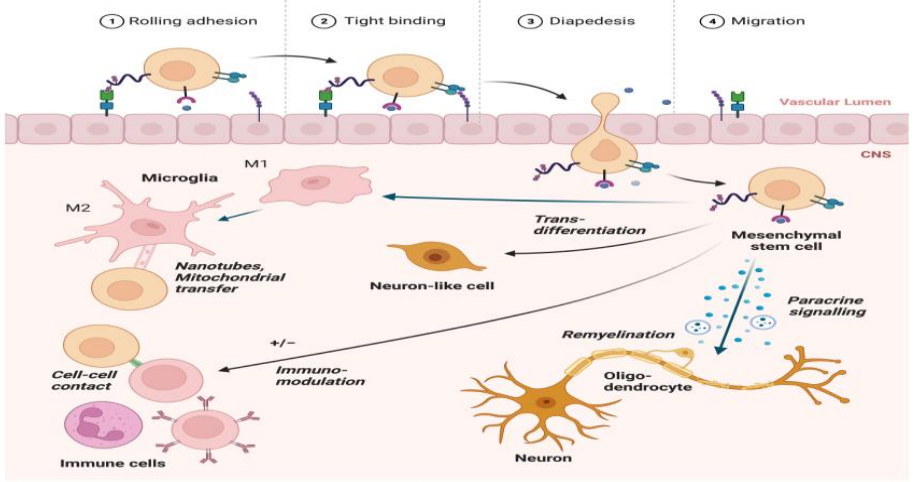


Figure 1. Potential regenerating mechanisms of MSCs in MS.

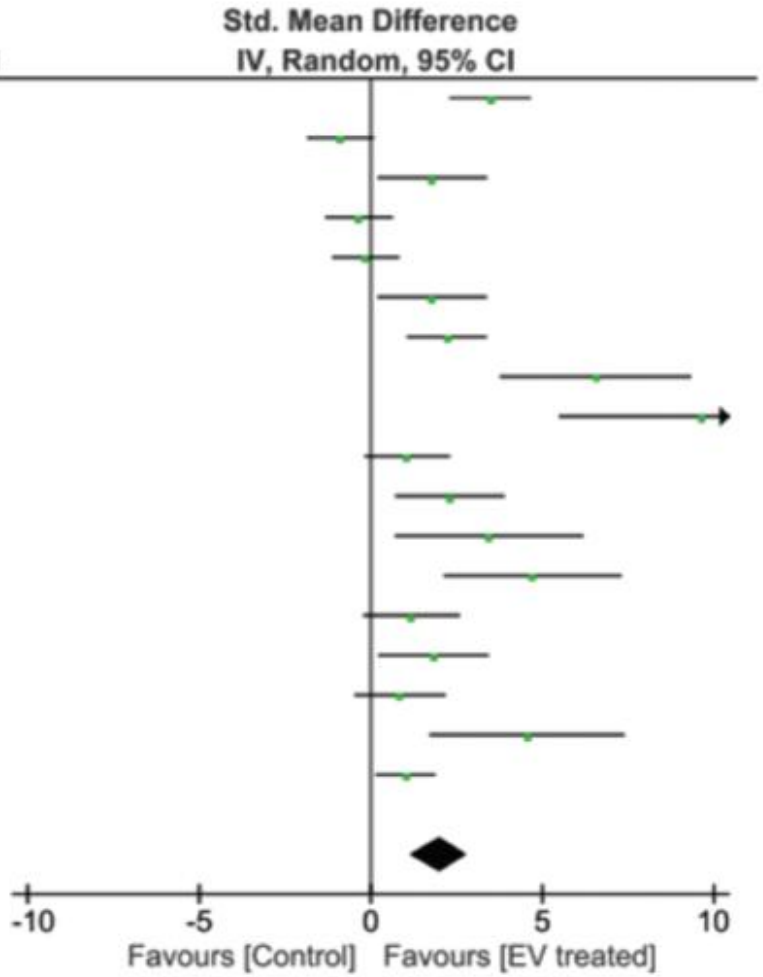
- Small numbers of MSCs can migrate into the CNS following systemic administration since most ***MSCs become trapped in the lungs*** shortly after injection. Trials assessing intrathecally delivered MSCs have generally shown more promising results than those applying the intravenous route.
- Recently, the results of the first placebo-controlled trial using ***intrathecal administration*** were published and showed that more patients treated with MSCs exhibited no evidence of disease activity and improved disability scores compared to the sham-treated group.
- ***Despite these promising results, more data from randomized trials are needed, especially in patients with progressive MS without active disease***, for which there is no treatment available to prevent neural degeneration.
- We cannot answer simple questions, like what happens to the cells once they are infused into the patient. How long do they survive and exert their function? If the MSCs are not integrated within the CNS tissue, which most pre-clinical studies suggest, the effect will likely be transient. Consequently, the transplantation must be repeated, decreasing its therapeutic value as the production of MSCs for clinical use is expensive and resource-demanding. Recent trials have also shown that inflammatory reactions in the form of arachnoiditis can appear as a complication after intrathecal transplantation.
- ***Because MSCs are highly secretory***, the repeated administration of a cell-free secretome may be an alternative, as studies have indicated in pre-clinical models. A cell-free product may also be injected in less invasive ways, ***such as intranasal***.

Stem Cells Translational Medicine, 2024, **13**, 436–447
https://doi.org/10.1093/stcltm/szae011
Advance access publication 20 March 2024
Concise Review

Stem Cell Derived Extracellular Vesicle Therapy for Multiple Sclerosis, A Systematic Review and Meta-Analysis of Preclinical Studies

	control			EV treated				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Farinazzo 2018 (a)	42.8	6.4	15	21.8	5.3	15	6.4%	3.48 [2.29, 4.66]
Farnazzo 2018 (b)	40.81	4.73	9	46.07	6.43	9	6.7%	-0.89 [-1.87, 0.09]
Fathollahi 2020	25.69	7.84	5	11.68	6.21	5	5.8%	1.79 [0.19, 3.39]
Giunti 2021 (a)	31.39	7.52	8	33.98	6.5	8	6.7%	-0.35 [-1.34, 0.64]
Giunti 2021 (b)	37.56	13.15	8	39.41	9.56	8	6.7%	-0.15 [-1.13, 0.83]
Jafarnia 2020	53.65	9.52	5	34.04	10.32	5	5.8%	1.78 [0.19, 3.38]
Koohsari 2021	57.48	10.82	10	33.6	9.82	10	6.4%	2.21 [1.05, 3.38]
Li 2018	11.01	0.7	8	6.88	0.47	8	4.0%	6.55 [3.76, 9.34]
Rajan 2017 (a)	11.97	1.01	10	3.2	0.3	5	2.6%	9.63 [5.48, 13.79]
Riazifar 2019 (a)	34.45	6	6	28.14	4.91	6	6.3%	1.06 [-0.18, 2.31]
Riazifar 2019 (b)	34.45	6	6	22.43	3.22	6	5.8%	2.30 [0.71, 3.90]
Riazifar 2019 (c)	43.11	1.21	4	35.75	2.33	4	4.1%	3.45 [0.70, 6.19]
Riazifar 2019 (d)	43.11	1.21	4	31	2.72	8	4.3%	4.72 [2.12, 7.31]
Shamili 2019 (a)	77.25	0.78	5	72.12	5.47	5	6.1%	1.19 [-0.22, 2.59]
Shamili 2019 (b)	77.25	0.78	5	49.63	19.34	5	5.8%	1.82 [0.21, 3.43]
Shamili 2019 (c)	77.25	0.78	5	64.25	19.52	5	6.2%	0.85 [-0.48, 2.18]
Shamili 2019 (d)	77.25	0.78	5	60.63	4.6	5	3.9%	4.55 [1.70, 7.40]
Zhang 2022 (a)	58.78	16.03	12	41.83	16.48	11	6.8%	1.01 [0.13, 1.88]
Total (95% CI)			**130**			**128**	**100.0%**	**2.00 [1.18, 2.83]**

Heterogeneity: Tau² = 2.42; Chi² = 100.02, df = 17 (P < 0.00001); I² = 83%
Test for overall effect: Z = 4.75 (P < 0.00001)



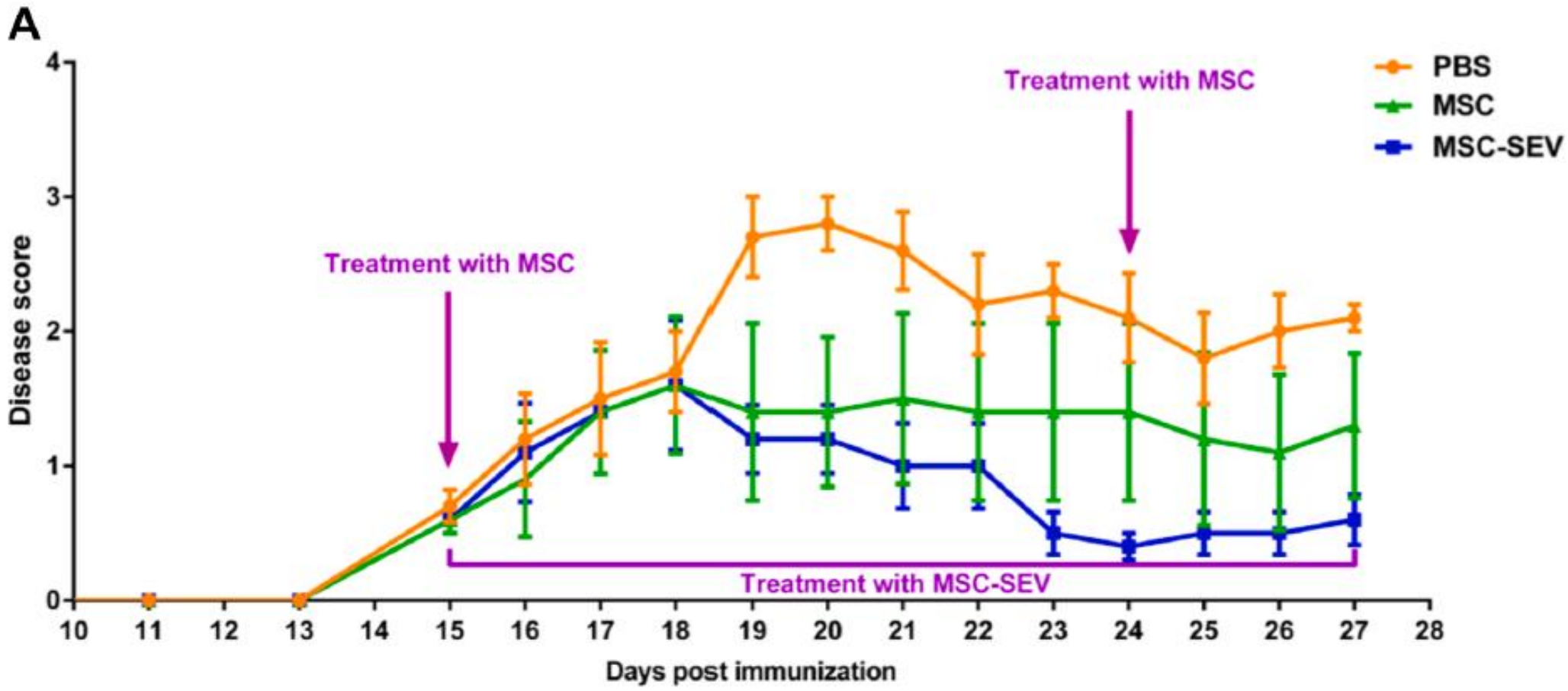
International Immunopharmacology 90 (2021) 107207

Contents lists available at ScienceDirect

International Immunopharmacology

journal homepage: www.elsevier.com/locate/intimp

Intranasal administration of small extracellular vesicles derived from mesenchymal stem cells ameliorated the experimental autoimmune encephalomyelitis



International Immunopharmacology
Volume 146, 27 January 2025, 113853

Intranasal delivery of mesenchymal stem cell-derived exosomes ameliorates experimental autoimmune encephalomyelitis

- BMSCs- Exos were isolated and characterized. An EAE model was then established, and these exosomes were administered intranasally to the mice.

- Intranasal delivery of BMSCs-Exos ameliorates the severity of EAE disease, reducing inflammatory infiltration in the CNS and demyelination in the spinal cord.

- Our study suggests that **intranasal administration of BMSCs-Exos significantly reduces inflammatory infiltration and demyelination in the CNS of EAE mice**. Furthermore, this treatment does not influence the differentiation of T cells in the spleen.

ΣΑΣ ΕΥΧΑΡΙΣΤΩ ΠΟΛΥ ΓΙΑ ΤΗΝ ΥΠΟΜΟΝΗ ΣΑΣ

Πολλαπλή Σκλήρυνση: Επικαιροποιημένη Ενημέρωση

Κυριακή 5 Οκτωβρίου 2025 στις 12.30μ.μ,

Δημοσιογραφική Εστία, Λευκωσία

Ομιλητής: ***Δρ. Μάριος Παντζαρής,***

Νευρολόγος, Ινστιτούτο Νευρολογίας και Γενετικής Κύπρου