key points 2025

Was gibt es neues zur MS

- key points 2025 -

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Universitätsklinikum Münster

KFO 342

Conflicts of Interest

Prof. Dr. Luisa Klotz erhielt Honorare als Referentin, Beraterin, Kongressreisen-Unterstützung und finanzielle Unterstützung für Forschung von Alexion, Amgen, Argenx, Bayer, Biogen, Bristol Myers Squibb, Grifols, Hexal, Horizon, Janssen, Merck Serono, Novartis, Roche, Sandoz, Sanofi, Santhera, Teva und Viatris.

key points 2025

UKM Universitätsklinikum Münster

Inhalt

Neues zur Diagnose

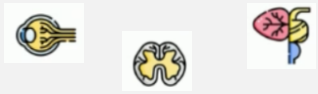
Neues zur Progression

Neues zur Immuntherapie

1 - Diagnostik

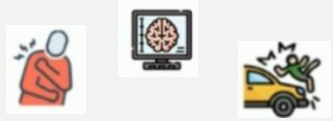
Diagnostik

Typische Symptome
Akut oder progressiv



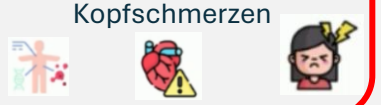
1 DIS	DIT + CSF	2 Add
2-3 DIS	DIT + CSF + 6CVS + 1PRL	1 Add
4-5 DIS	DIT + CSF + 6CVS + 1PRL	No Add

Atypische Symptome
Zufallsbefunde



2-3 DIS	DIT + CSF	1 Add
4-5 DIS	DIT + CSF + 6CVS	No Add

Individuell
>50 Jahre
Komorbidität
Kopfschmerzen



1 DIS	DIT + CSF + SC	2 Add
2-3 DIS	DIT + CSF + SC + 6CVS + 1PRL + 3PV	1 Add
4-5 DIS	DIT + CSF + SC + 6CVS + 1PRL + 3PV	No Add

Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria

Xavier Montalban, Christine Lebrun-Frénay, Jiwon Oh, Georgina Arrambide, Marcello Moccia, Maria Pia Amato, Lilyana Amezcua, Brenda Banwell, Amit Bar-Or, Frederik Barkhof, Helmut Butzkueven, Olga Ciccarelli, Jeremy Chataway, Jeffrey A Cohen, Giancarlo Comi, Jorge Correale, Florian Deisenhammer, Massimo Filippi, Julie Fiol, Mark S Freedman, Kazuo Fujihara, Cristina Granziera, Ari J Green, Hans-Peter Hartung, Kerstin Hellwig, Ludwig Kappos, Dorlan Kimbrough, Joep Killestein, Fred Lublin, Romain Marignier, Ruth Ann Marrie, Aaron Miller, Susana Otero-Romero, Daniel Ontaneda, Sudarshini Ramanathan, Daniel Reich, Maria A Rocca, Àlex Rovira, Shiv Saidha, Amber Salter, Jaume Sastre-Garriga, Deanna Saylor, Andrew J Solomon, Maria Pia Sormani, Bruno Stankoff, Mar Tintore, Helen Tremlett, Anneke Van der Walt, Shanthi Viswanathan, Heinz Wiendl, Brigitte Wildemann, Bassem Yamout, Paola Zaratin, Peter A Calabresi, Timothy Coetzee, Alan J Thompson

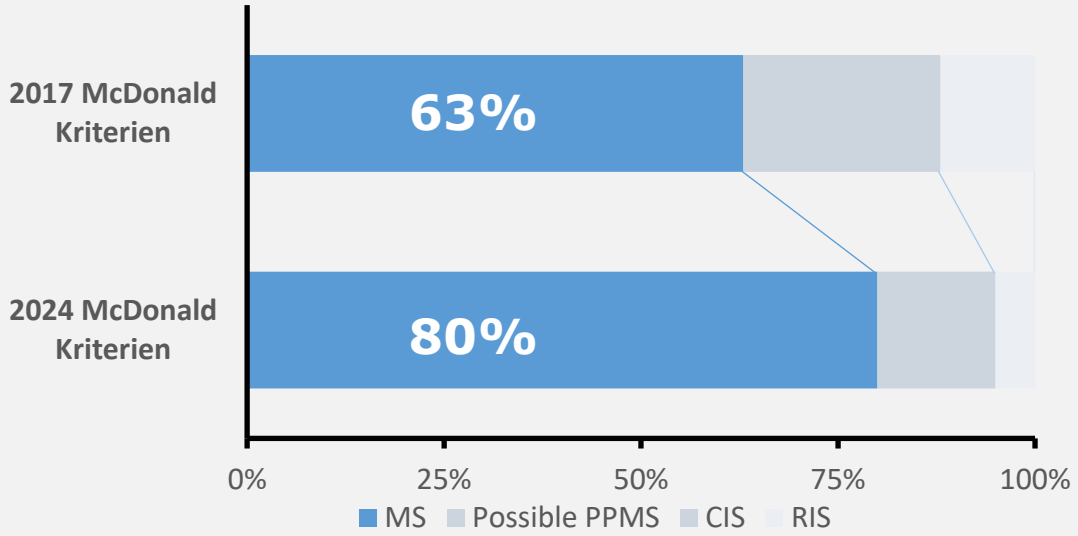
Lancet Neurol 2025; 24: 850–65 Advances in the understanding of multiple sclerosis and the development of biomarkers of pathophysiology prompted

C. Lebrun-Frenay, ECTRIMS 2025

1 - Diagnostik

Diagnostik

Anwendung der 2024 McDonald Kriterien



Höherer Anteil an Diagnosen (80% vs 63%)

Performance der 2024 Kriterien

	Sensitivität	Spezifität	Genauigkeit
Alle Patienten (n=275)	95% (91.5 - 97.9%)	58.2% (46.6 – 69.2%)	84.7% (79.9 – 88.8%)
Kinder <18 Jahre (n=27)	100% (76.8 – 100%)	92.3% (64.0 – 99.8%)	96.3% (81.0 – 99.9%)
Erwachsene >50Jahre (n=57)	100% (90.5 – 100%)	55.0% (31.5 – 76.9%)	84.2% (72.1 – 92.5%)

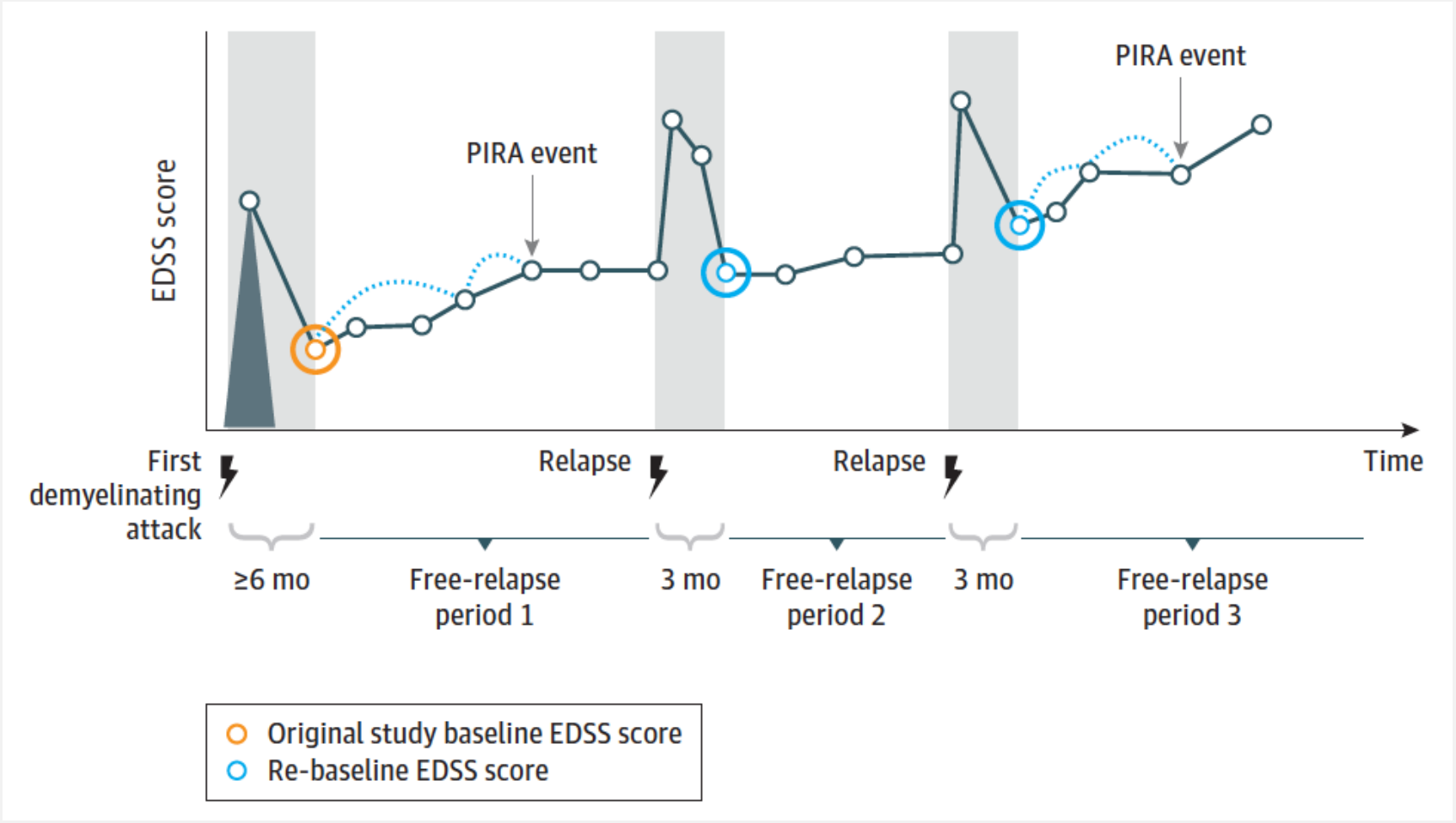
Goldstandard = Diagnose einer MS gemäß den **McDonald-Kriterien 2017** beim letzten Follow-up.

Aber: geringere Spezifität!

W.Brownlee, ECTRIMS 2025

2 - PIRA

Was ist PIRA überhaupt?

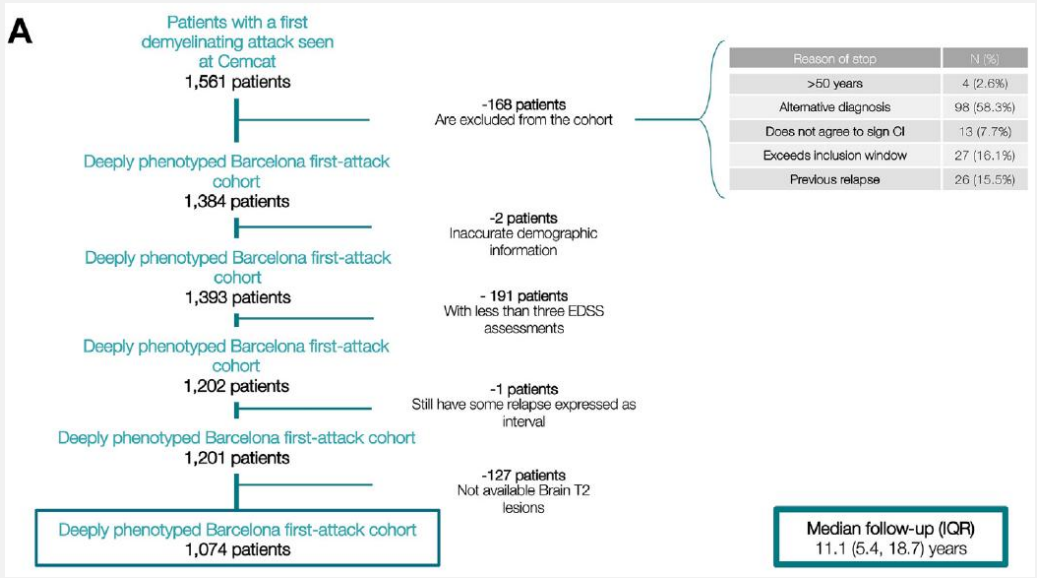


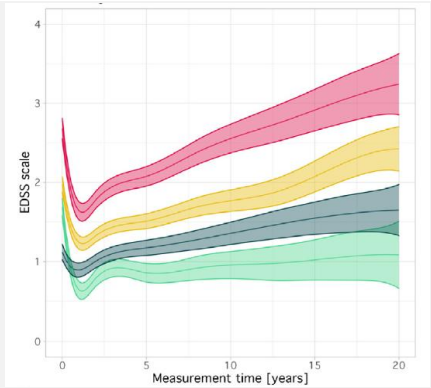
Tur et al., JAMA Neurol 2023

2- PIRA – prognostische Faktoren

Was sind die Haupt Treiber von PIRA?

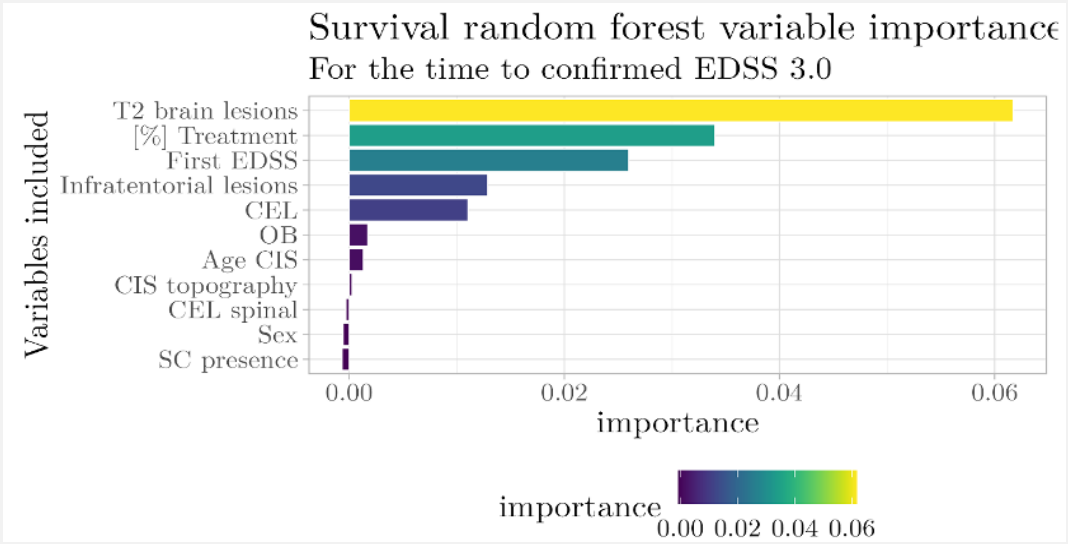
Barcelona CIS Kohorte





EDSS Trajektorie über 20 Jahre

Prädiktive Faktoren



Tur et al., The Lancet Regional Health - Europe 2025

3 - KI getriebene Klassifikation der Progression

Standard Parameter verwendet; 8.000 Pat.; 118.000 Visiten, 35.000 MRI scans

	Key dimensions of MS			
Original variables	**Physical disability**	**Brain damage**	**Relapse**	**Asymptomatic activity**
Clinical				
EDSS	0.58	0.34	-0.04	-0.11
T25FWT (s)	0.66	0.09	0.00	0.00
9HTP (s)	0.57	0.20	-0.01	0.02
PASAT (correct responses)	-0.29	-0.35	0.00	-0.08
Relapse	-0.01	0.00	0.36	0.07
MRI				
T2 lesion volume (ml)	0.22	0.54	0.04	0.33
Brain volume (l)	-0.19	-0.53	0.01	0.01
Number of Gd^+ T1 lesion	-0.05	0.07	0.16	0.56

EDSS, Extended Disability Status Scale; MRI, Magnetic Resonance Imaging; PASAT, Paced Auditory Serial Addition Test; T25FW, Timed 25-Foot Walk; 9HPT, Nine-Hole Peg Test.

Ganjaghi et al., Nature Med 2025

3 - KI getriebene Klassifikation der Progression

Discovery Kohorte NO.MS

	Key dimensions of MS			
Original variables	**Physical disability**	**Brain damage**	**Relapse**	**Asymptomatic activity**
Clinical				
EDSS	0.58	0.34	-0.04	-0.11
T25FWT (s)	0.66	0.09	0.00	0.00
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T2 lesion volume (ml)	0.22	0.54	0.04	0.33
Brain volume (l)	-0.19	-0.53	0.01	0.01
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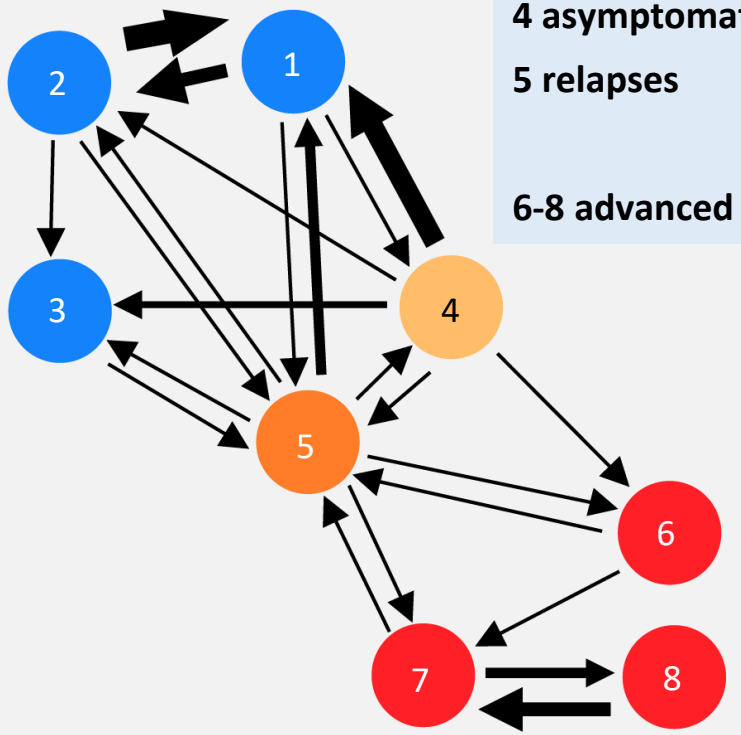


1-3: early / mild / evolving states

4 asymptomatic MRI activity (i.e. Gd+)

5 relapses

6-8 advanced states

EDSS, Extended Disability Status Scale; MRI, Magnetic Resonance Imaging; PASAT, Paced Auditory Serial Addition Test; T25FW, Timed 25-Foot Walk; 9HPT, Nine-Hole Peg Test.

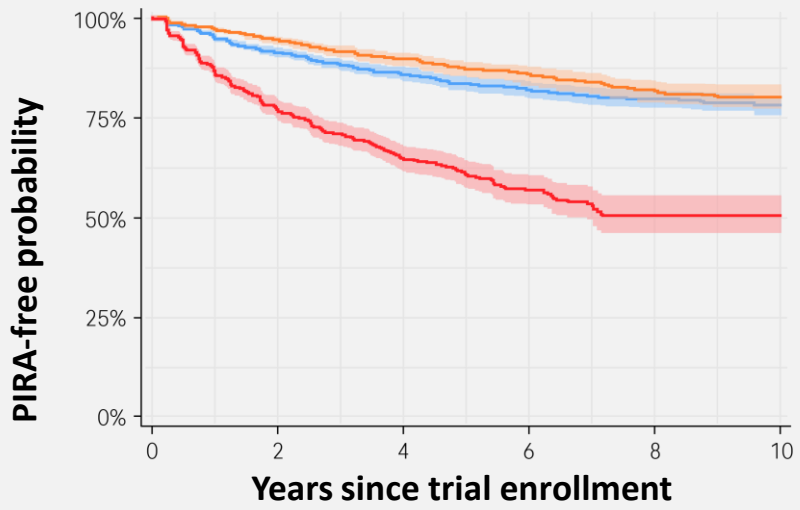
Ganjaghi et al., Nature Med 2025

3 - KI getriebene Klassifikation der Progression

1-3: early/ mild/ evolving states; 4: asymptomic MRI activity; 5. relapses; 6-8 advanced MS states

PIRA Risiko

a



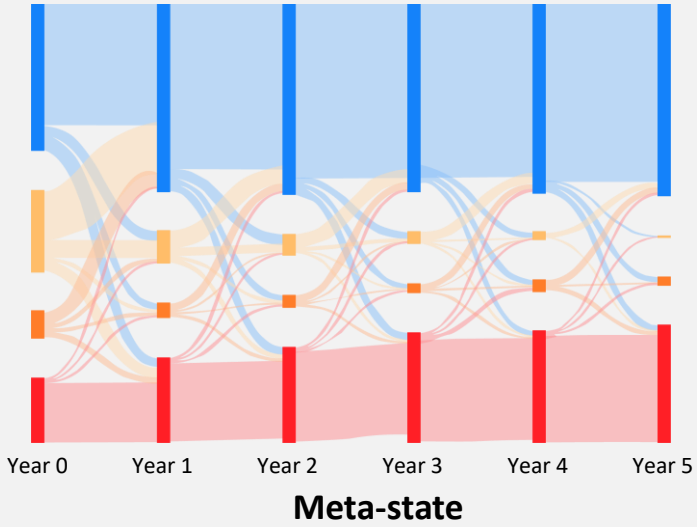
EME

Advanced MS

Relapse or asymptomatic radiological disease activity

Wechsel zwischen states

b



EME

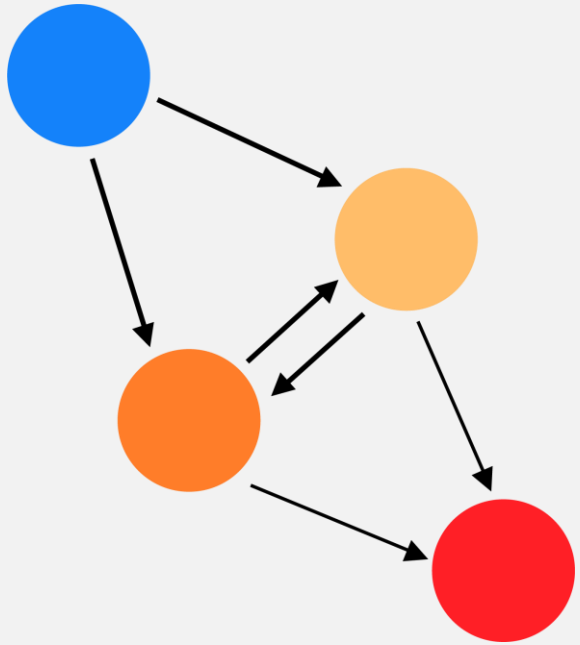
Relapse

Asymptomatic radiologigal disease activity

Advanced MS

Effekt einer Immuntherapie

c

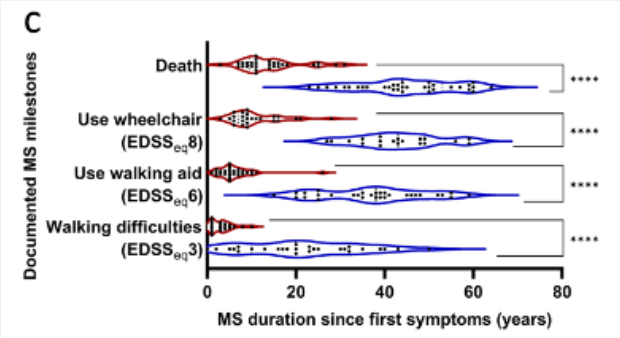


DMT, disease modifying therapy; EME early/mild/evolving states

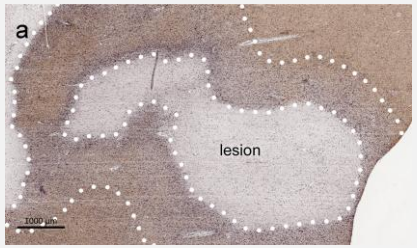
Ganjaghi et al., Nature Med 2025

4 - Neuer MS Läsionstyp assoziiert mit Krankheitsprogression

Kooperation mit Netherland brain bank: Stratifikation anhand der Progression

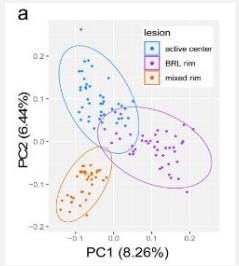


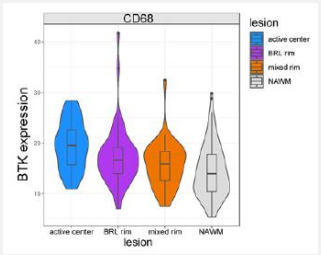
Identifikation eines neuen MS Läsionstyps



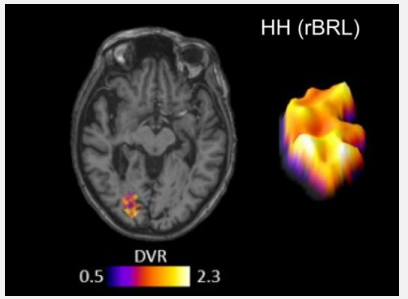
Broad rim lesion

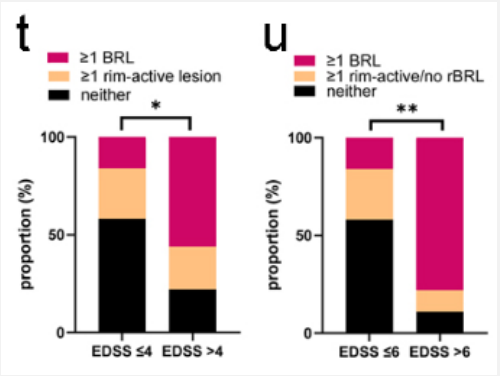
Spezifische Signatur der myeloiden Zellen



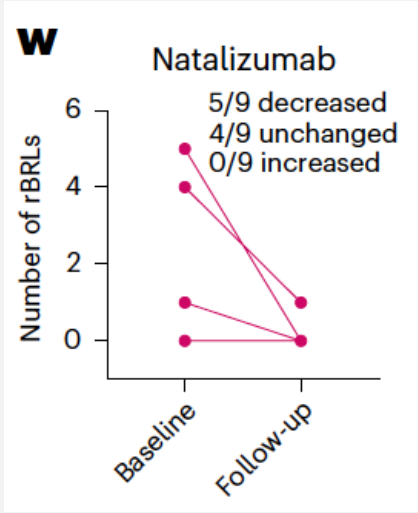


Kooperation mit L. Airas: TSPO PET Kohorte





Läsionen mit rascher Progression assoziiert



Periphere Immunzellen tragen zum Erhalt der Läsionen bei!

Klotz et al., *Nature Med* 2025

5 - Einfluss einer Immuntherapie auf RAW und PIRA

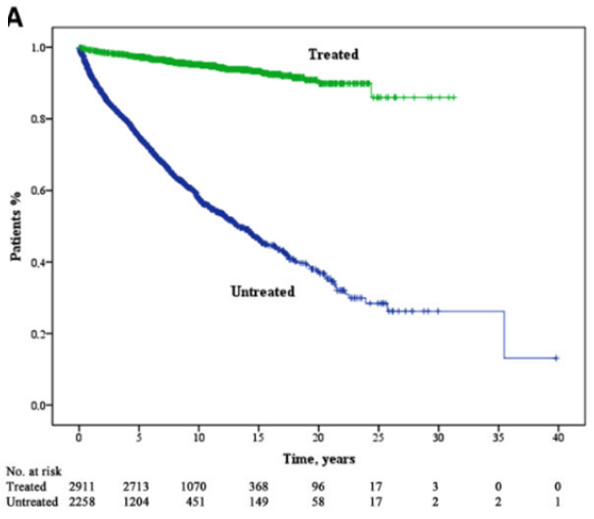
Italienisches MS Register; 5169 Patienten, CIS und frühe MS

BRAIN
ORIGINAL ARTICLE
2022

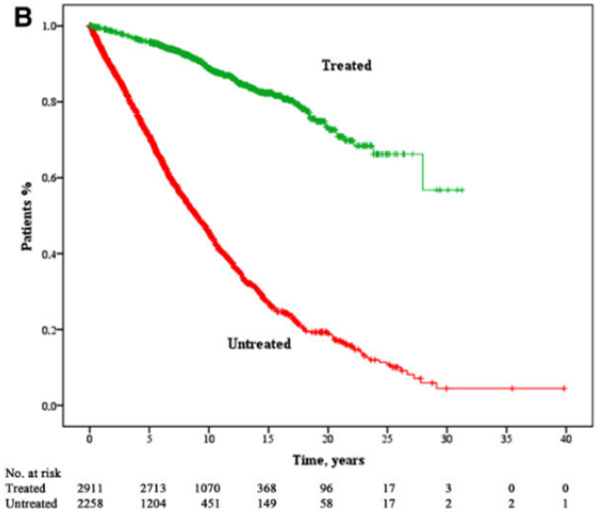
Progression is independent of relapse activity in early multiple sclerosis: a real-life cohort study

Emilio Portaccio,[1,2] Angelo Bellinvia,[1] Mattia Fonderico,[1] Luisa Pastò,[1] Lorenzo Razzolini,[1] Rocco Totaro,[3] Daniele Spitaleri,[4] Alessandra Lugaresi,[5,6] Eleonora Cocco,[7] Marco Onofrj,[8] Franco Di Palma,[9] Francesco Patti,[10] Davide Maimone,[11] Paola Valentino,[12] Paolo Confalonieri,[13] Alessandra Protti,[14] Patrizia Sola,[15] Giacomo Lus,[16] Giorgia Teresa Maniscalco,[17] Vincenzo Brescia Morra,[18] Giuseppe Salemi,[19] Franco Granella,[20] Ilaria Pesci,[21] Roberto Bergamaschi,[22] Umberto Aguglia,[23] Marika Vianello,[24] Marta Simone,[25] Vito Lepore,[26] Pietro Iaffaldano,[27] Massimo Filippi,[28,29] Maria Trojano[27] and Maria Pia Amato[1,2] on behalf of the Italian Multiple Sclerosis Register Centers Group

RAW



PIRA

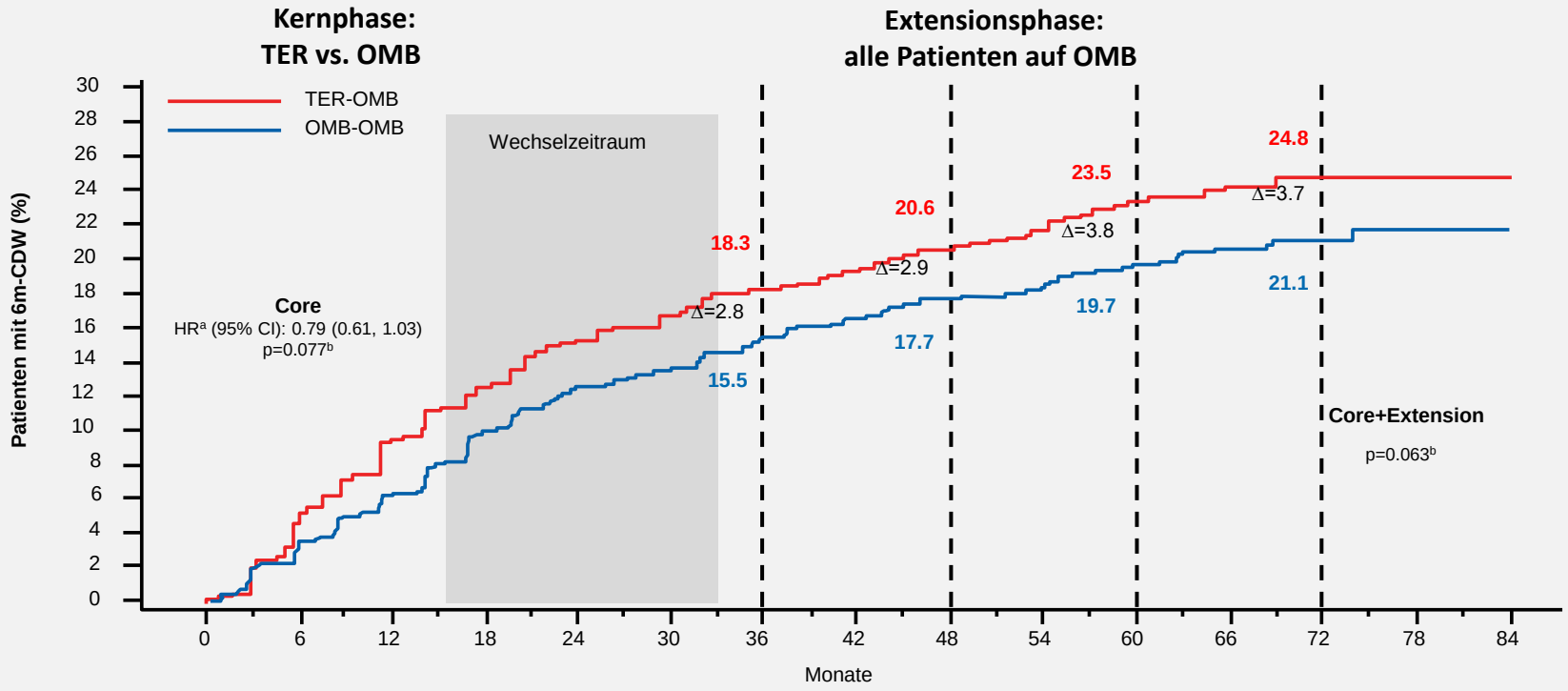


Immuntherapie senkt Risiko für RAW und PIRA

Portaccio et al., Brain 2022

5 - Post-hoc Analyse zum Effekt von Ofatumumab auf PIRA

Anteil von Patienten mit bestätigter Behinderungsprogression

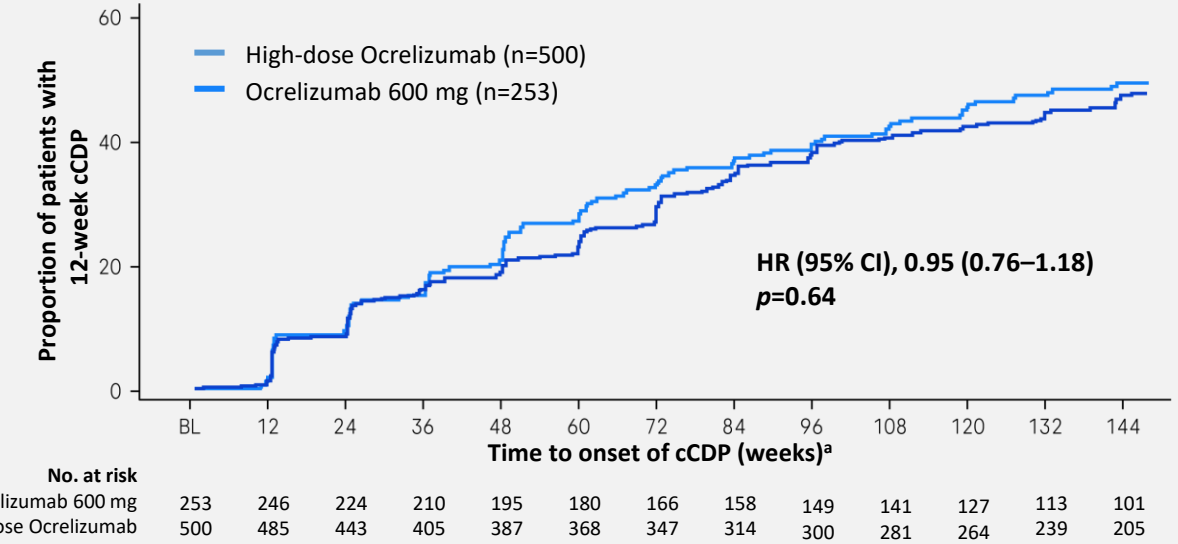


Effekt einer B Zell Depletion mit Ofatumumab auf schubunabhängige Progression

nach: Hauser et al., Neurol Ther 2025

6 - Hochdosis B Zell Depletion bietet keinen Vorteil für den klinischen Effekt: GAVOTTE Studie

Zeit bis zum ersten 6m CDW Event



No. at risk													
Ocrelizumab 600 mg	253	246	224	210	195	180	166	158	149	141	127	113	101
High-dose Ocrelizumab	500	485	443	405	387	368	347	314	300	281	264	239	205

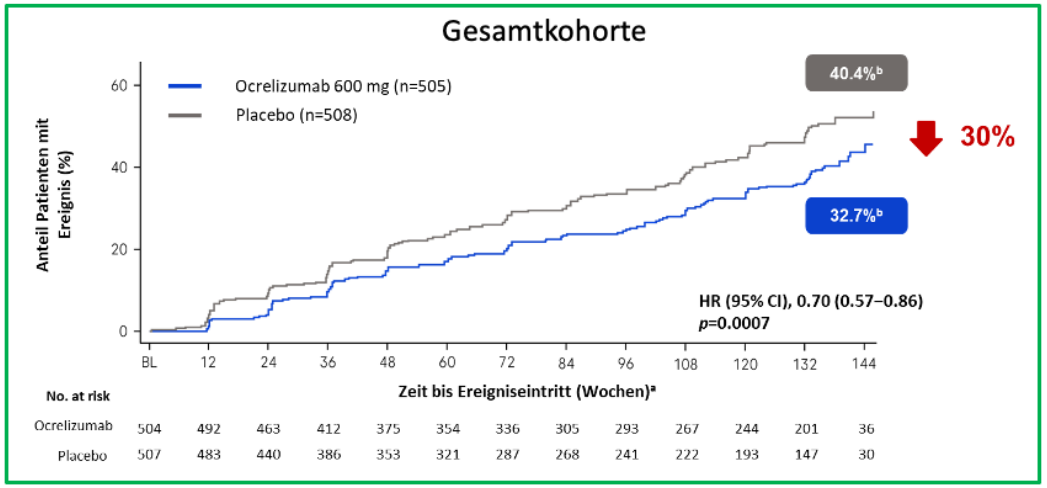
	High-dose Ocrelizumab patients with events, %	Ocrelizumab 600 mg patients with events, %	HR (95% CI)	*p* value
12-week cCDP[a]	**47.0**	**49.0**	0.95 (0.76–1.18)	0.64
EDSS	26.0	29.6	0.86 (0.65–1.15)	0.32
T25FW	38.7	41.8	0.93 (0.73–1.18)	0.55
9HPT	13.8	14.3	0.96 (0.64–1.44)	0.85

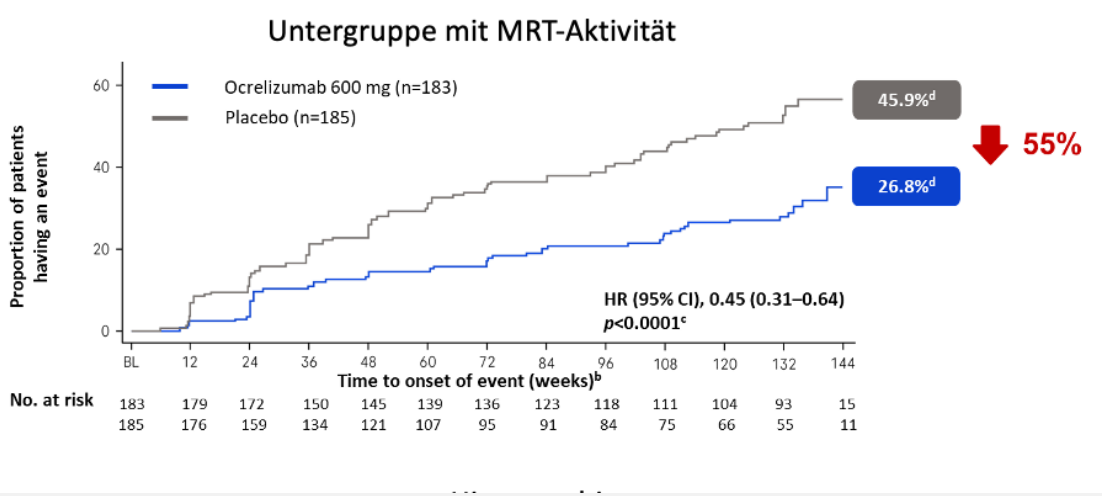
- Clinical cutoff date: 30 June, 2025; 9HPT, 9-Hole Peg Test; BL, baseline; cCDP, composite confirmed disability progression; EDSS, Expanded Disability Status Scale; HR, hazard ratio; T25FW, Timed 25-Foot Walk Test.
- [a]CDP is also termed confirmed disability progression; composite CDP requires at least one of the following: (1) an increase in EDSS score of ≥1.0 points from a baseline score of ≤5.5 points, or a ≥0.5-point increase from a baseline score of >5.5 points; (2) a 20% increase from baseline in time to complete the 9HPT; (3) a 20% increase from baseline in the T25FW.

Mod. Hauser S et al. ECTRIMS Congress 2025, Scientific Session 17: Late Breaking Abstracts, Abstract No. O129

7 – Ocrelizumab bei älteren Patienten mit stärkerer Behinderung: O-Hand Studie

Konsistente Reduktion der Behinderungsprogression

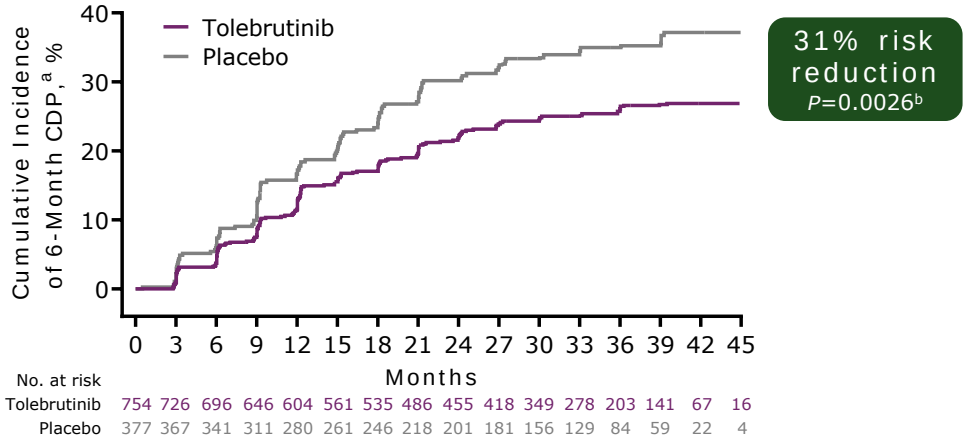


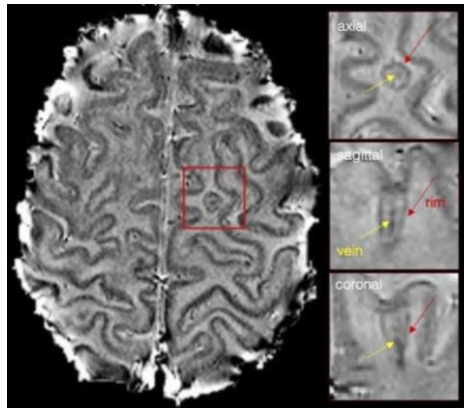


Mod. Giovannoni G et al. ECTRIMS Congress 2025, Scientific Session 17: Late Breaking Abstracts, Abstract No. O128

8 – Tolebrutinib: Effektstärke abhängig von PRLs zur Baseline

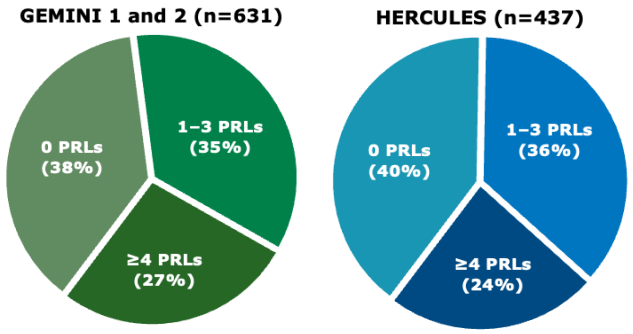
Tolebrutinib in RMS und SPMS – Abhängigkeit von PRLs



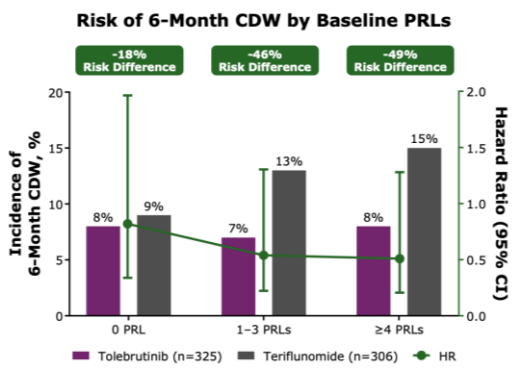


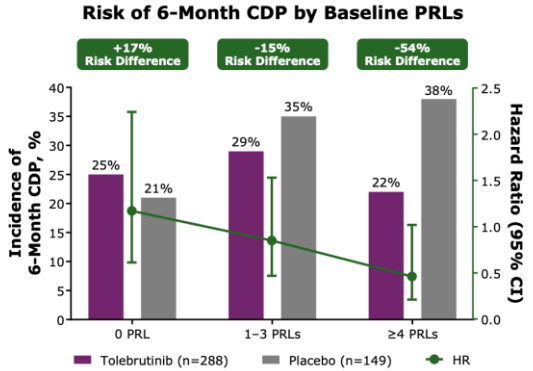
PRL BEISPIEL

Periläsionaler Randsaum
Eisenbeladene Mikroglia



Anteil Patienten mit PRLs zur Baseline





Oh Y, oral presentation ECTRIMS 2024, Fox R, oral presentation ECTRIMS 2024; Oh Y, oral presentation ACTRIMS 2025; ECTRIMS 2025, Poster P796

9 – Fenebrutinib Pressemeldung

Insgesamt 3 Studien, 2x RMS, 1x PPMS, Pressemeldung zu 2 der Studien

FENhance 2, RMS: met primary endpoint, significant relapse reduction over teriflunomide

(evobrutinib und tolebrutinib haben diesen Endpunkt nicht erreicht)

Daten zum Ausmaß der Reduktion der Behinderungsprogression liegen nicht vor

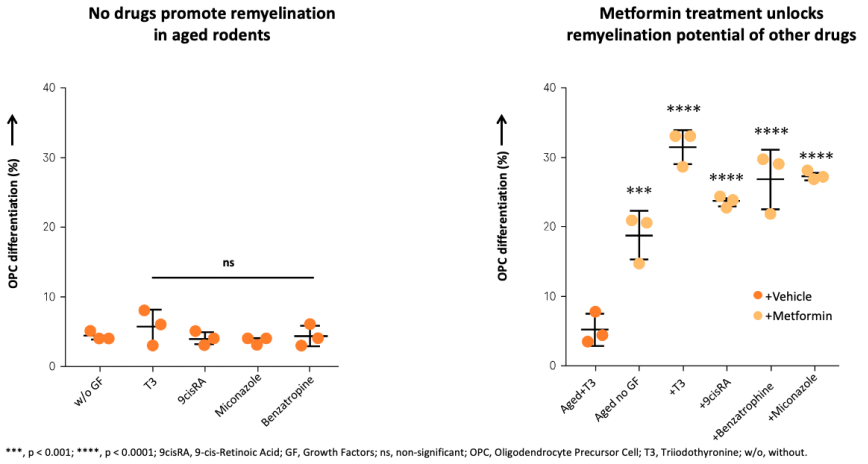
FENtrepid, PPMS: fenebrutinib non inferior to ocrelizumab in reducing disability progression,

(composite endpoint, numerical benefit for fenebrutinib)

Presss release, ad hoc announcement pursuant to Art. 53 LR, 10.11.2025

10 – Remyelinisierung: Kombination Metformin + Clemastin

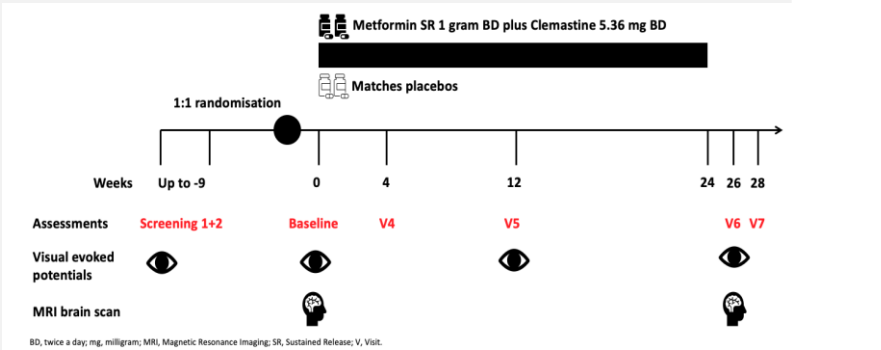
CCMR-Two Studie in der RRMS (Phase 2)



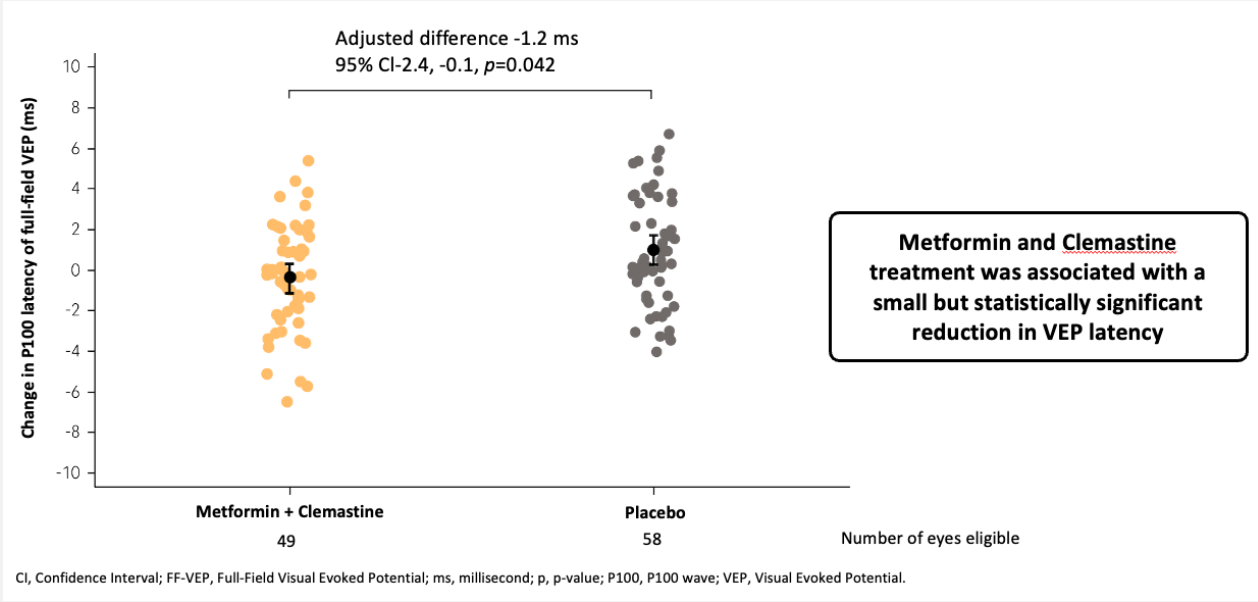
***, p < 0.001; ****, p < 0.0001; 9cisRA, 9-cis-Retinoic Acid; GF, Growth Factors; ns, non-significant; OPC, Oligodendrocyte Precursor Cell; T3, Triiodothyronine; w/o, without.

Rationale: verstärkender Effekt von Metformin auf die remyelinisierende Potenz von anderen Substanzen

VEP als klinisches readout



BD, twice a day; mg, milligram; MRI, Magnetic Resonance Imaging; SR, Sustained Release; V, Visit.



CI, Confidence Interval; FF-VEP, Full-Field Visual Evoked Potential; ms, millisecond; p, p-value; P100, P100 wave; VEP, Visual Evoked Potential.

Cunniffe NG et al. Scientific Session 17: Late breaking abstracts, O133



Vielen Dank für Ihre Aufmerksamkeit!

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