multiple sklerose gesellschaft oberösterreich

JOHANNES KEPLER UNIVERSITÄT LINZ | Kepler Universitäts Klinikum

Aktuelles zur MS Behandlung 2025

Einfach erklärt für Betroffene

OA Dr. Gerhard TRAXLER
Universitätsklinik für Neurologie

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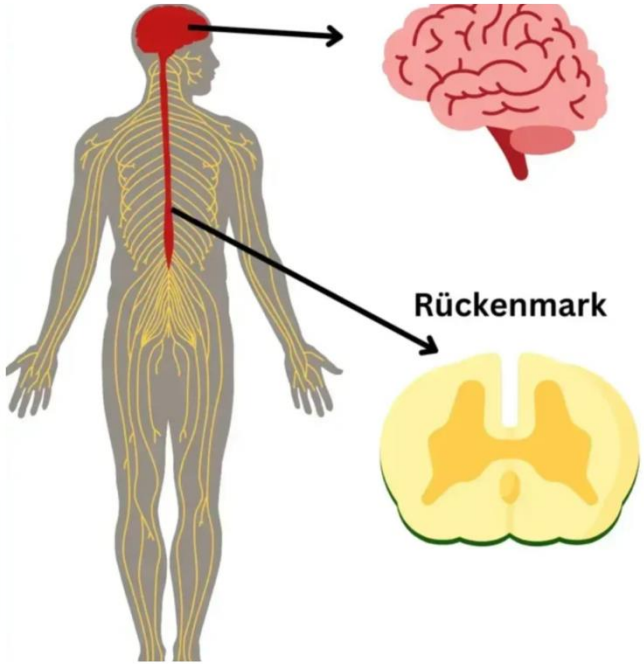


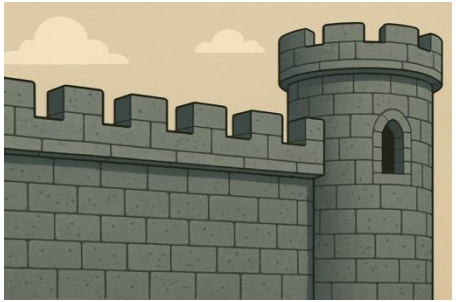
MS betrifft „nur“

Gehirn und Rückenmark

*https://www.nachhilfe-team.net/lernen-leicht-gemacht/wp-content/uploads/2024/03/Anatomie-ZNS-2-1-e1710418418694-600x650.webp

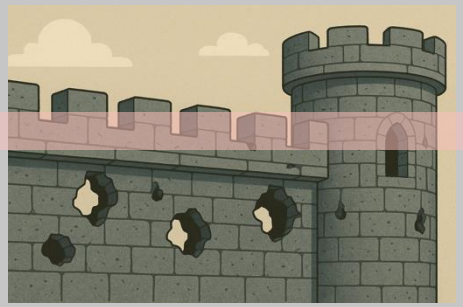
Immunologie

Peripherie



Blut-Hirnschranke

zentrales Nervensystem

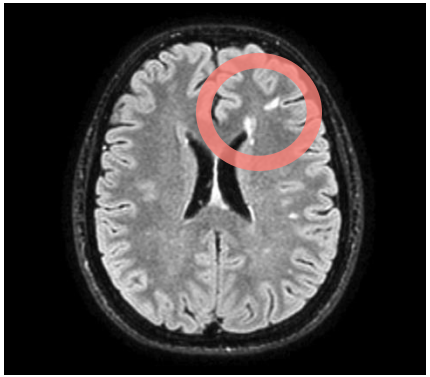


„Krankheitsaktivität“

erstellt mit ChatGPT

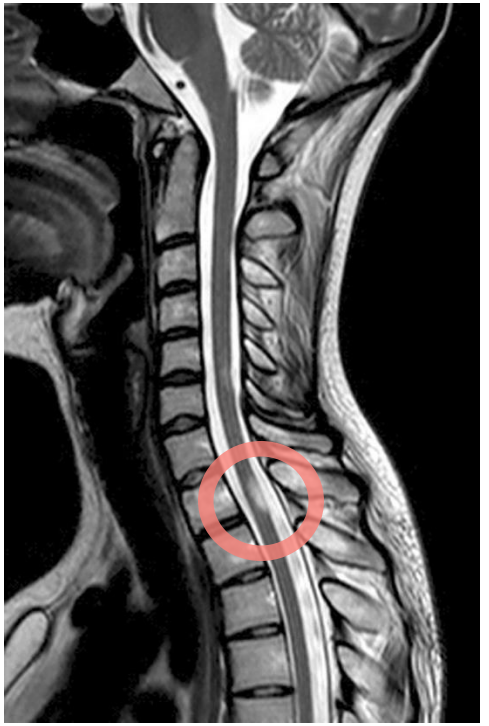
Bildgebung

periventrikulär + juxtacortikal



infratentoriell

Rückenmark



Phase 1

Phase 2

Inflammation

Degeneration

Inflammation

= Entzündung

- Schübe
- „Attacke von außen“ über BHS
- neue Läsionen (+ KM Aufnahme)
- Regenerationspotential
- nimmt im Laufe ab
- vorhandene Therapieoptionen

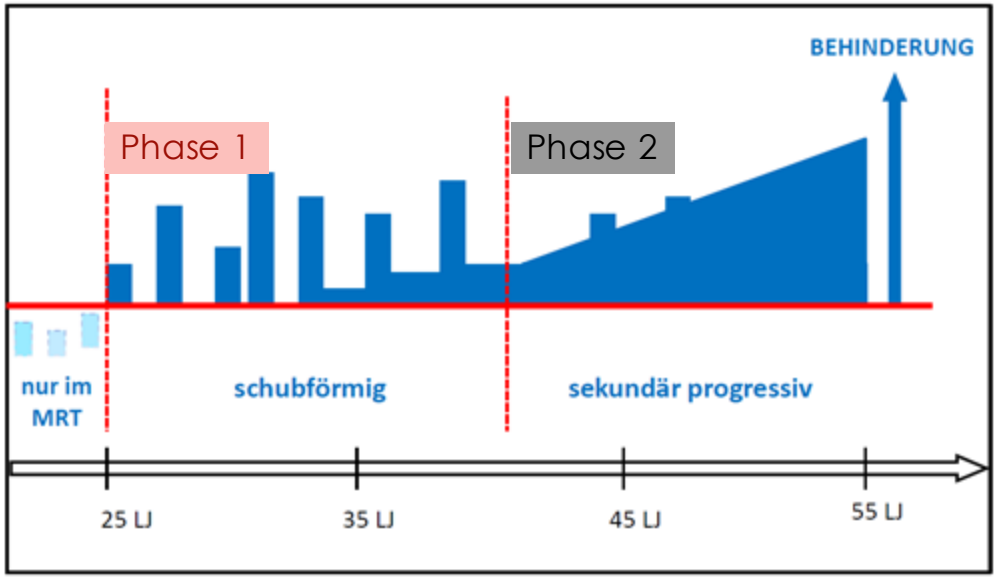
Degeneration

= Abbau/Verschleiß

- kontinuierliche Behinderung
- „Attacke von innen“ im ZNS
- expanding lesions (- KM Aufnahme)
- fehlendes Regenerationspotential
- nimmt im Laufe zu
- weitgehend fehlende Therapieoptionen

schubförmige ➡ sekundär progressive MS

Phase 1

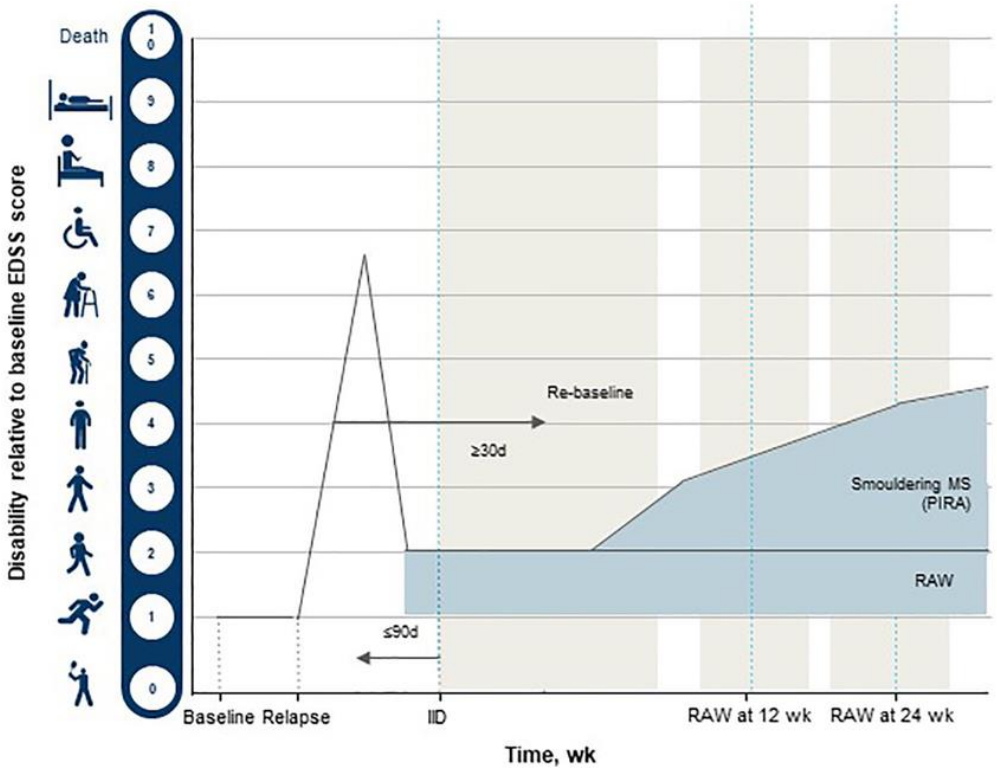


Phase 2

https://www.oemsg.at/wp-content/uploads/2017/10/primaer_progressive_verlauf.png

Immunologie

Verlaufsform



PIRA: Progression independent of relapse activity

RAW: relapse associated worsening

*1 Giovannoni G et al. Smouldering multiple sclerosis: the 'real MS'. Ther Adv Neurol Disord. 2022 Jan 25;15:17562864211066751

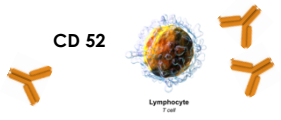
Mode of action

gezielte Zelllyse

Alemtuzumab

Lyse von Immunzellen
u.a. reife T- und B-Lymphozyten

CD 52

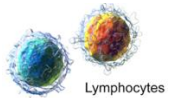


Ocrelizumab
Ofatumumab
Ublituximab
(Rituximab)

Lyse reifer B-Zellen

CD 20

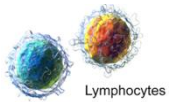
rasche Reduktion von T- und B-Lymphozyten (ruhende Zellen)



reduzierte Proliferation

Cladribin

Verringert die Verfügbarkeit von Desoxyadenosin (teilende Zellen)



Teriflunomid ⊣ Verringert die Verfügbarkeit von Pyrimidin für eine schnelle Zellteilung

pleiotrope Effekte

Interferone → Aktivierung von über 100 Genen der „Interferon Response“ → Veränderung der Th1/Th2-Balance

Glatirameracetat

Dimethylfumarat
Diroximelfumarat → Aktivierung von über 700 Genen der „nrf2 Response und HCAR2“

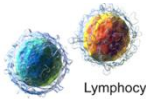
antimigratorisch

Fingolimod
Ponesimod
Ozanimod
Siponimod

S1P1

Natalizumab

α4-Integrin

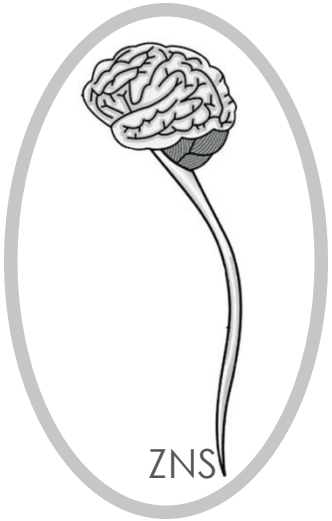


Bluthirnschranke

PNS

ZNS

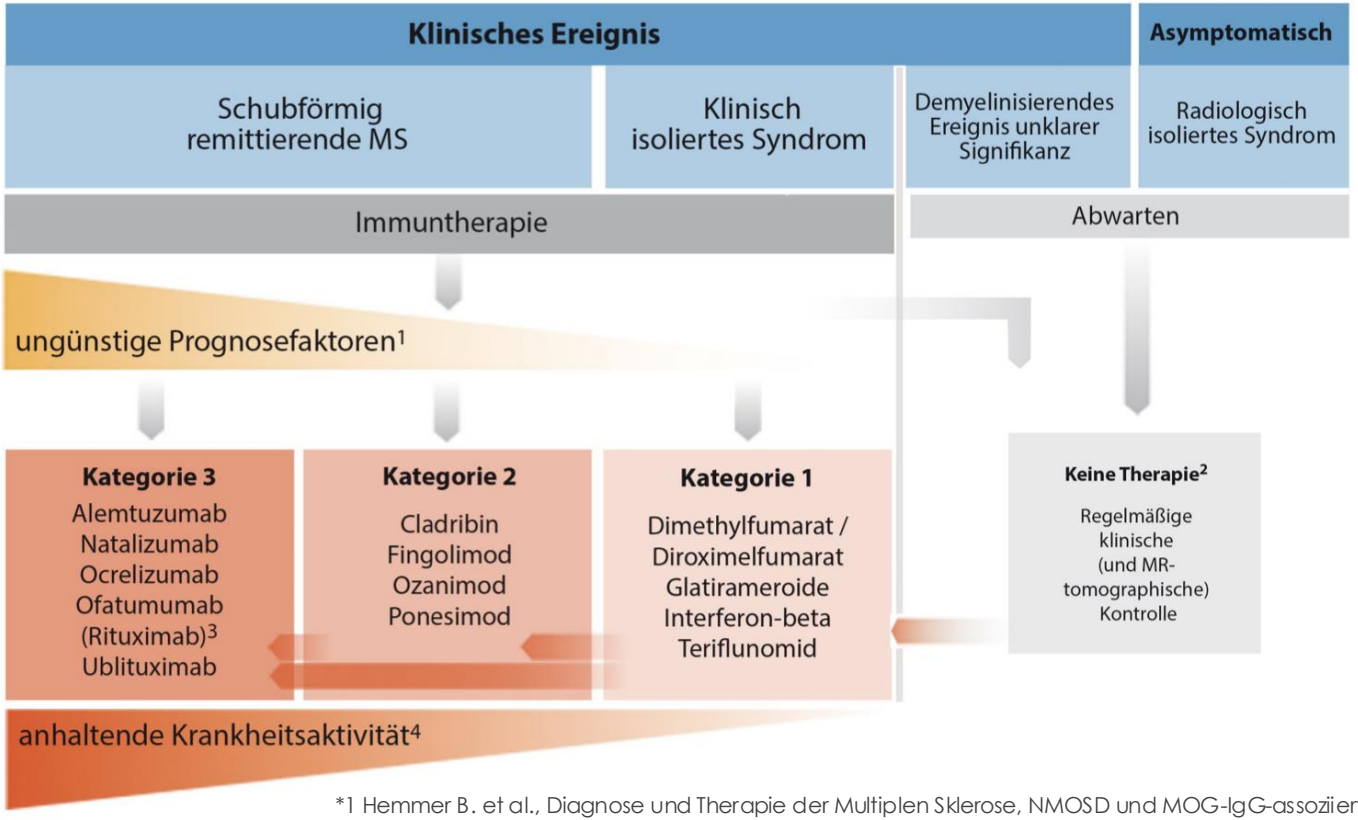
Therapie



- alle bekannten **Wirkmechanismen** zugelassener Präparate wirken (hauptsächlich) **außerhalb des ZNS**
- **Schub = Attacke von außen** in das ZNS
- Versuch „Peripherie“ positiv zu beeinflussen um im ZNS günstige Wirkung zu erzielen
- Therapien ohne relevante Wirkung auf **Degeneration = Attacke von innen**

https://upload.wikimedia.org/wikipedia/commons/thumb/0/0f/Central_nervous_system.svg/1024px-Central_nervous_system.svg.png

Therapie

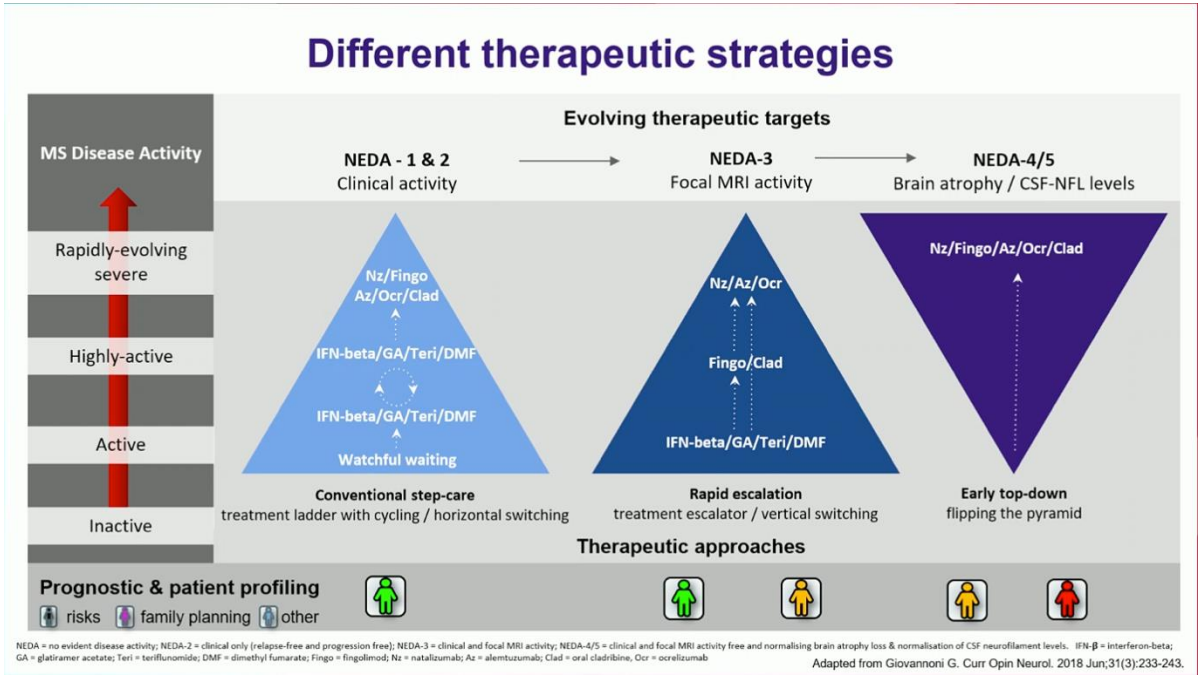


*1

*1 Hemmer B. et al., Diagnose und Therapie der Multiplen Sklerose, NMOSD und MOG-IgG-assoziierten Erkrankungen, S2k-Leitlinie, 2024

Therapie

by Giovannonni @ Hot Topic 1: High efficacy therapies/ECTRIMS 2022



ESC – Eskalation-/Stufenschema

vs.

HEET – high efficacy early treatment

„hit hard and early“

Induktionstherapie

„flipping the pyramid“

Therapie

Early highly effective versus escalation treatment approaches in relapsing multiple sclerosis

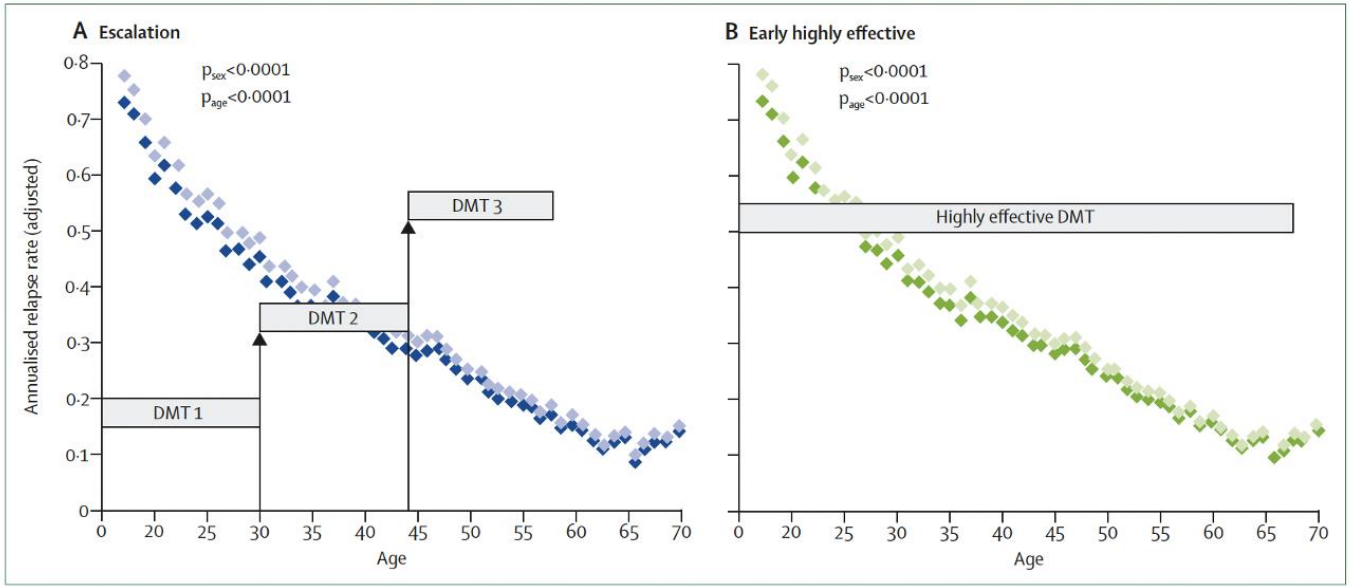


Figure: **Relapse incidence and escalation versus early highly effective treatment approaches in patients with relapsing multiple sclerosis**

„HEET“ zu bevorzugen! Richtige Pat. mittels RF identifizieren!

Ontaneda D et al., Early highly effective versus escalation treatment approaches in relapsing multiple sclerosis. Lancet Neurol. 2019 Oct;18(10):973-980.

Risikofaktoren für hochaktive Verlaufsform

Reaching an evidence-based prognosis for personalized treatment of multiple sclerosis

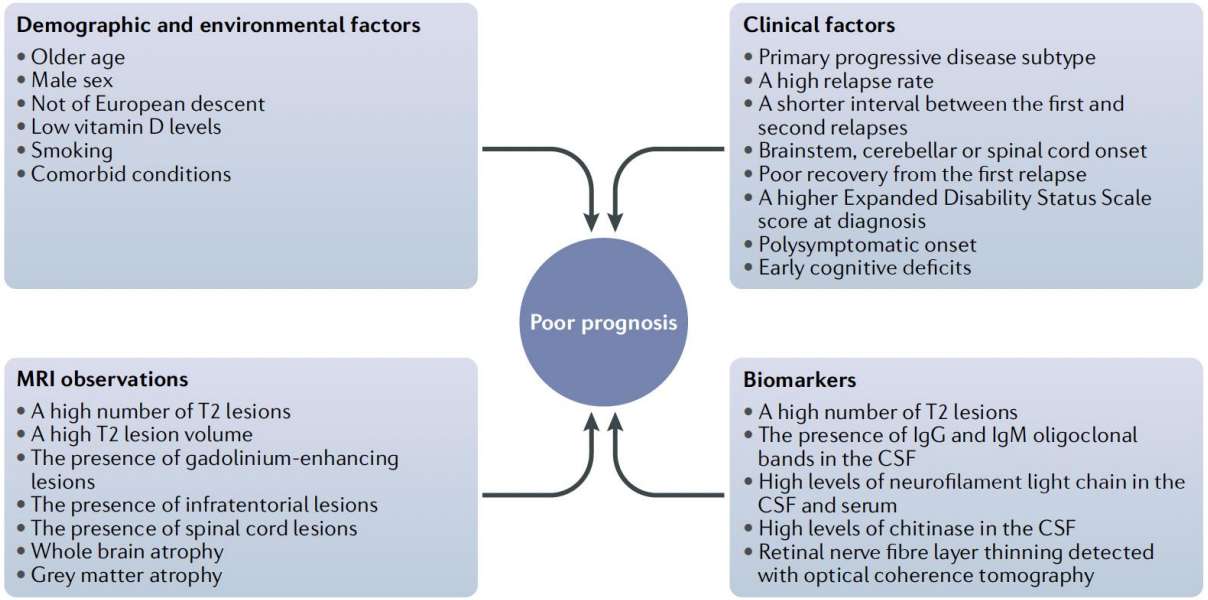


Fig. 1 | **Predictors of a poor prognosis in multiple sclerosis.** The demographic and environmental factors, clinical factors, MRI observations and biomarkers that have been associated with a poor prognosis in multiple sclerosis are listed. CSF, cerebrospinal fluid; IgG, immunoglobulin G; IgM, immunoglobulin M.

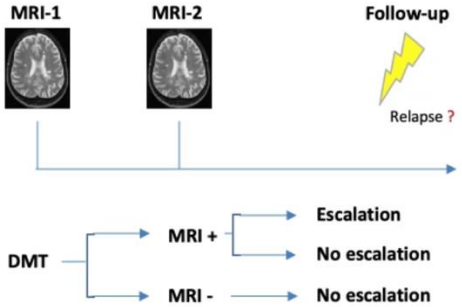
Rotstein D et al., Reaching an evidence-based prognosis for personalized treatment of multiple sclerosis. Nat Rev Neurol. 2019 May;15(5):287-300.

Therapie

Treatment escalation in multiple sclerosis based on isolated MRI activity – how much is too much?

Gabriel Bsteh[1,2], Marie Louise Aicher[3*], Janette Walde[4], Nik Krajnc[1,2], Lukas Haider[2,5], Gerhard Traxler[6], Christiane Gradl[7], Anke Salmen[3], Katharina Riedl[1,2], Philipp Leyendecker[8], Paulina Poskaite[8], Patrick Altmann[1,2], Michael Auer[9], Klaus Berek[9], Franziska Di Pauli[9], Barbara Kornek[1,2], Fritz Leutmezer[1,2], Paulus Rommer[1,2], Gudrun Zulehner[1,2], Tobias Zrzavy[1,2], Florian Deisenhammer[9], Andrew Chan[3], Thomas Berger[1,2], Robert Hoepner[3], Helly Noemi Hammer[3*] and Harald Hegen[9*]

- 131 RRMS patiens
- five MS centres in Austria and Switzerland



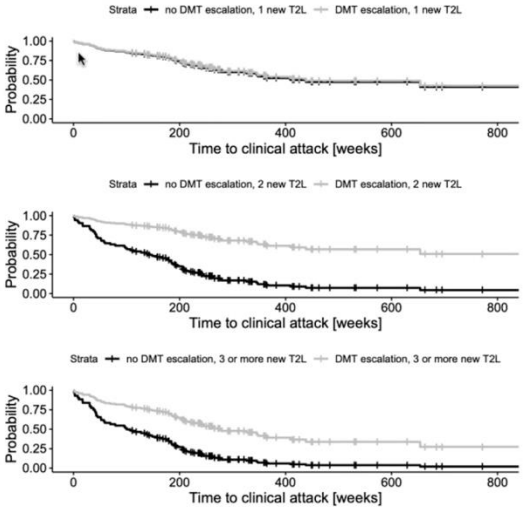


Table 3: Relapse free probability at year 4 depending on MRI activity and treatment strategy score

		No DMT escalation	DMT escalation	
New T2L on brain MRI at Year 1	1	87%	87%	DMF
	2	60%	90%	
	≥3	54%	81%	
New T2L on brain MRI at Year 1	1	69%	70%	IFNb/ GLAT/ TER
	2	27%	76%	
	≥3	20%	58%	

Legend:

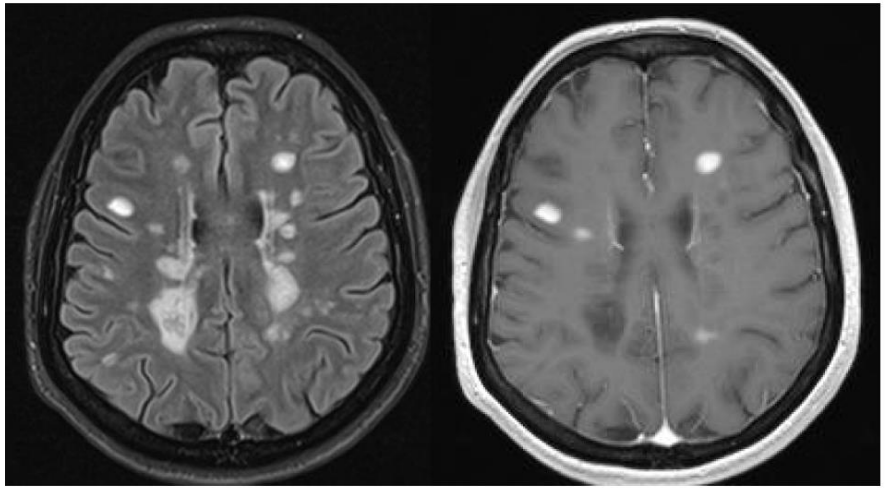
Abbreviations: GLAT, glatiramer acetate; DMF, dimethyl fumarate; DMT, disease-modifying treatment; IFNb, interferon-beta; TER, teriflunomide

RRR 65-80% bei Therapieeskalation ≥2 neuen Läsionen

Bsteh G et al. Neurology – under review

Bildgebung

T2-weighted



Post-contrast
T1-weighted

KM-Aufnahme
- Dauer 2-6 Wochen
- Homogen bis ringförmig
- Randständig bei Reaktivierung von Läsionen
- Im Rückenmark seltener

* Rovira A et al. Magnetic resonance monitoring of lesion evolution in multiple sclerosis. Ther Adv Neurol Disord. 2013 Sep;6(5):298-310.

Therapieerneuerungen

Tysabri subkutan

Ocrevus subkutan

Briumvi intravenös

https://images.coopvitality.ch/product-images/ocrevus-subkutan-inj-loes-920-mg-23ml-durchstf-main-0037E2.jpg
https://images.ctfassets.net/evoe4hvfuo1p/14TU50Ib7YcpYZWu2kpgIP/ca43217c2d37065ac5df4f311abd7d31/dosage4_1.svg
https://static.neuraxpharm.com/wp-content/uploads/sites/6/2023/12/19123027/np2321a-aufbereitung-packshot-paerchen-luckyu-02-rz-scaled.jpg

Generika:

- **Gleicher Wirkstoff → gleiche Wirkung im Körper**

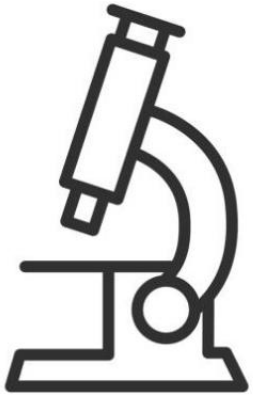
- **Gleiche Stärke, Darreichungsform und Qualität**
  → Tablette, Kapsel, Lösung etc. entsprechen dem Original.
- **Bioäquivalenz**
  → Wirkstoff geht in derselben Menge und Geschwindigkeit ins Blut

- **Unterschiede** können **nur in den Hilfsstoffen** (Füllstoffe, Farbstoffe, Bindemittel) **oder im Design/Verpackung** bestehen

btki-Inhibitoren

Bruton-Tyrosin-Kinasen Inhibitoren

Phase III Studien



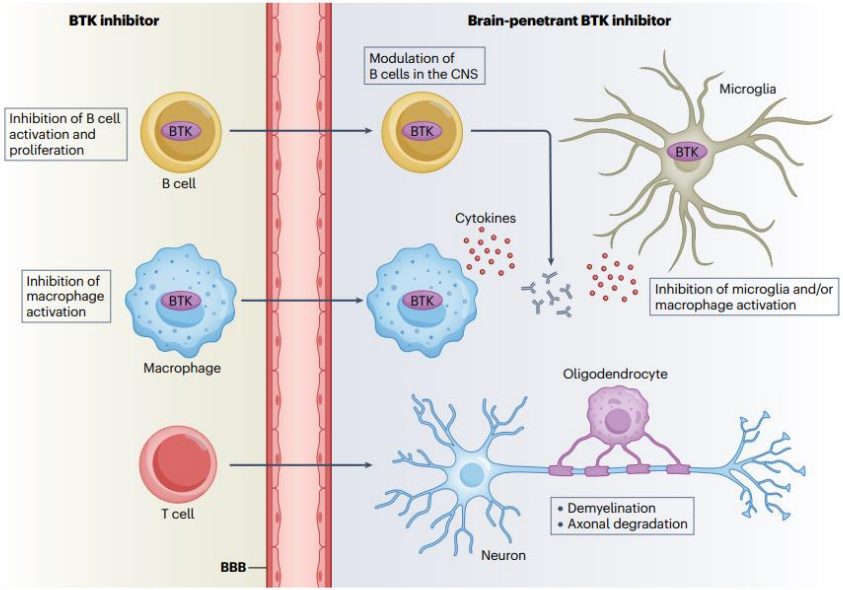


Fig. 2 | Putative mechanism of action of Bruton tyrosine kinase inhibitors in multiple sclerosis. Bruton tyrosine kinase (BTK) inhibitors directly modulate the functions of B cells and myeloid cells (including macrophages and microglia) and therefore target both adaptive and innate mechanisms that contribute to the immunopathology of multiple sclerosis on both sides of the blood–brain barrier (BBB)[43]. Although BTK inhibitors do not modulate T cell function directly, they can interfere with deleterious B cell–T cell interactions (not shown)[163]. CNS, central nervous system.

Liquorgängigkeit: Wirksamkeit auf Degeneration?

Krämer J et al. Bruton tyrosine kinase inhibitors for multiple sclerosis. Nat Rev Neurol. 2023 May;19(5):289-304

Studien

btki-Inhibitoren

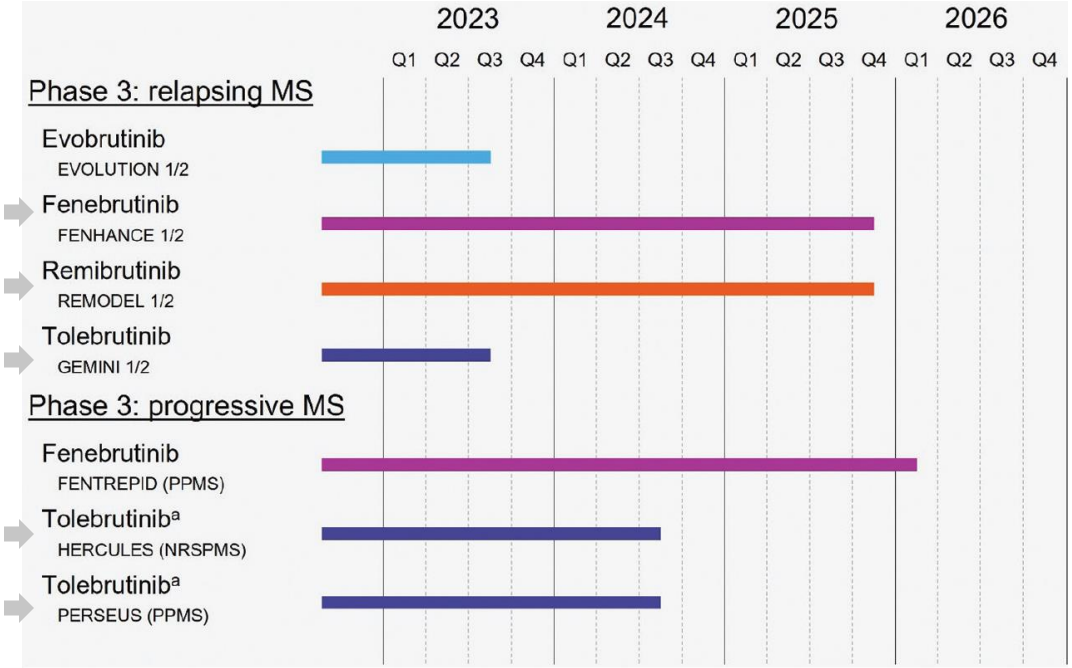


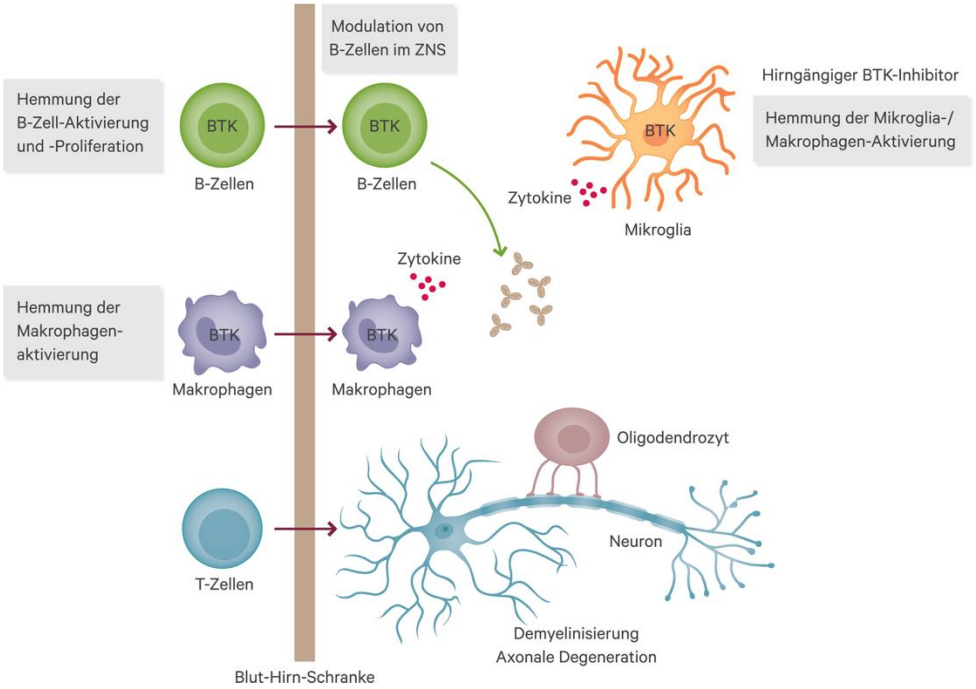
TABLE 2. STATUS OF CLINICAL INVESTIGATIONS OF BTK INHIBITORS IN MS

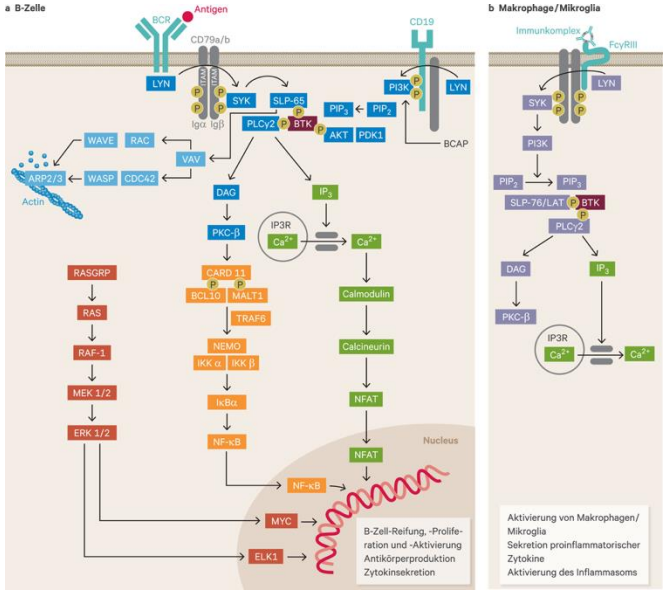
BTK inhibitor	Phase of study	MS subtype	Dosing
Evobrutinib	3	RMS	75 mg BID
Fenebrutinib	2, 3	RMS, PPMS	200 mg BID
Orelabrutinib	2	RMS	(dose-ranging) QD to BID
Remibrutinib	3	RMS	100 mg BID
Tolebrutinib	3	RMS, NRSPMS, PPMS	60 mg QD

Abbreviations: BID, twice daily; BTK, Bruton tyrosine kinase; NRSPMS, nonrelapsing secondary progressive multiple sclerosis; PPMS, primary progressive multiple sclerosis; QD, once daily; RMS, relapsing multiple sclerosis.

https://practicalneurology.com/articles/2023-mar/updates-in-bruton-tyrosine-kinase-inhibition-for-multiple-sclerosis/pdf

Btki – Brutinkinase Inhibitoren





mit ChatGPT erstellt

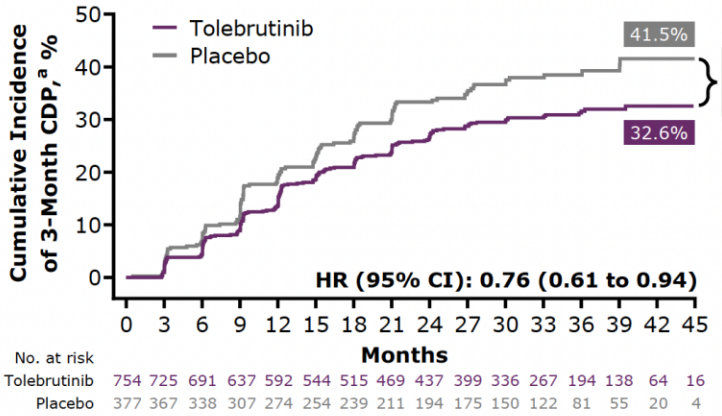
https://www.ppt-online.de/_Resources/Persistent/7/c/e/c/7cec2a6b748c5bb9c7ad1900b5c39a2c86b39c4e/kraemer_btk_ms_01_converted_eps-1162x1034.png

Therapieerneuerungen

Tolebrutinib Phase 3 HERCULES Trial in nrSPMS

ECTRIMS 2024
Presentation #O136

Secondary Endpoint: Time to 3-Month CDP



- Tolebrutinib demonstrated a significant effect on time to 3-month CDP

[a]3-month CDP is defined as an increase of ≥1.0 point from baseline EDSS score when baseline score is ≤5.0 or an increase of ≥0.5 points whe
score is >5.0, confirmed over ≥3 months. [b]P-value is from Cox proportional hazards model.
CDP=confirmed disability progression; CI=confidence interval; EDSS=Expanded Disability Status Scale; HR=hazard ratio.

Verhinderung Entzündung = Verhinderung Degeneration

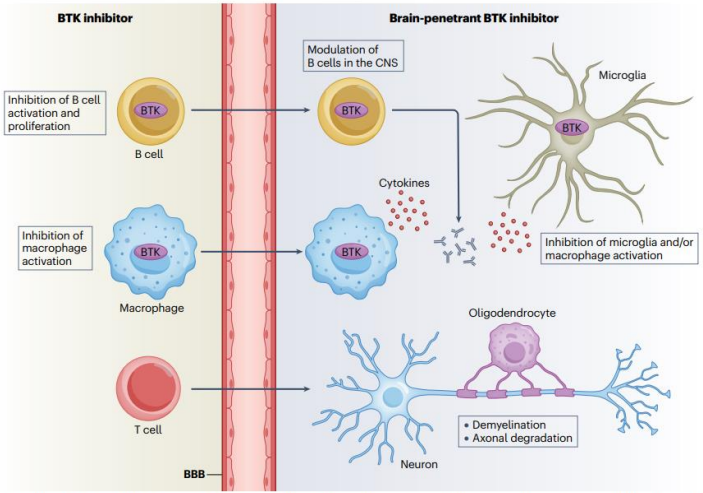
"echte" Verhinderung Degeneration vs versteckte subklinische Entzündungsunterdrückung?

EMA- Zulassung:
frühestens Anfang **2026** (Q1)

laufende Studientätigkeit

Remibrutinib (Btki)

Phase III Studien



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Voraussetzungen:

RMS

≤65a

EDSS ≤5.5

laufend

Voraussetzungen:

naSPMS + Worsening

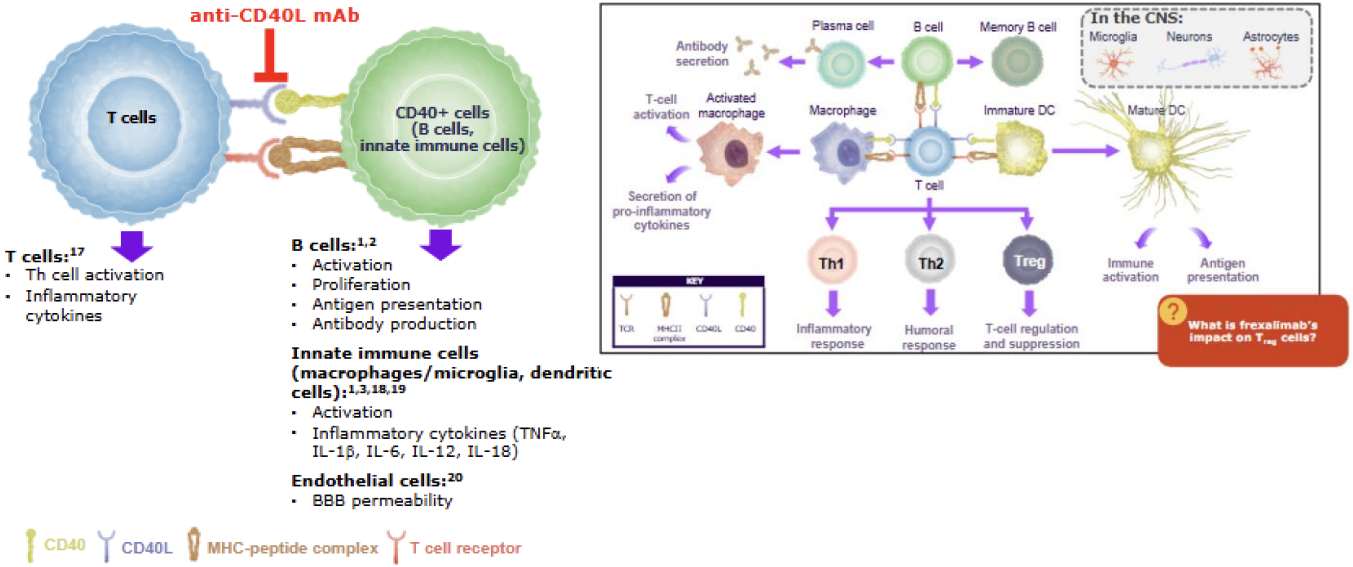
≤65a

EDSS 3.0 - ≤6.0

Beginn demnächst

Frexalimab (Anti-CD40-Therapie)

Phase III Studien



Voraussetzungen:

RMS

≤55a

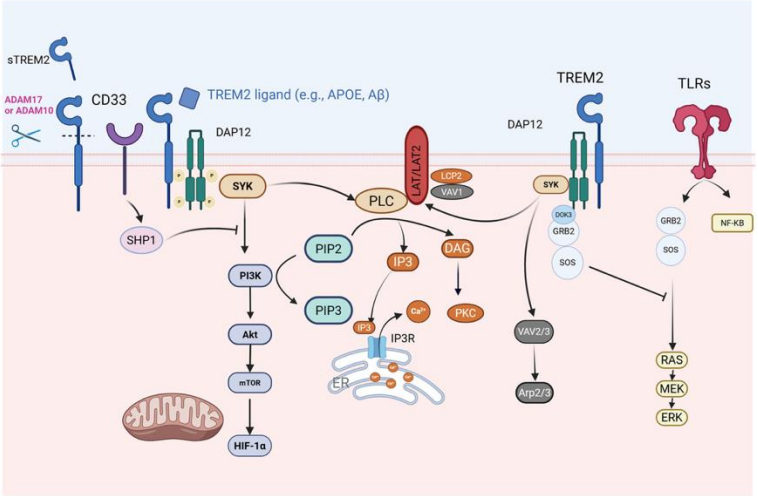
EDSS ≤5.5

rekrutierend

laufende Studientätigkeit

VHB937 (TREM2)

Phase II Studien



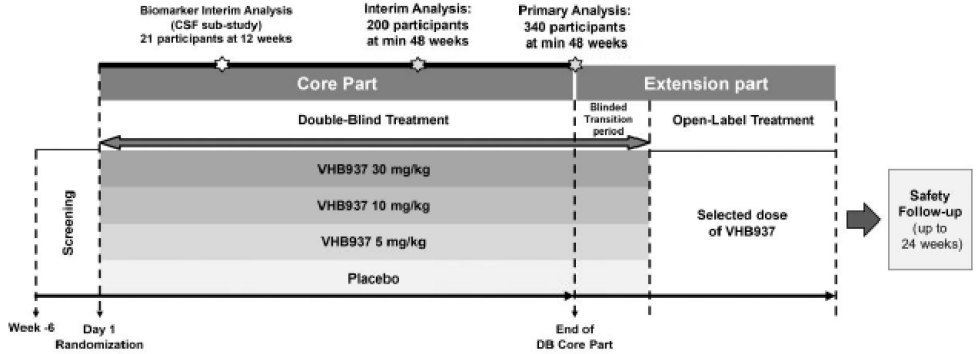
Voraussetzungen:

PPMS + naSPMS

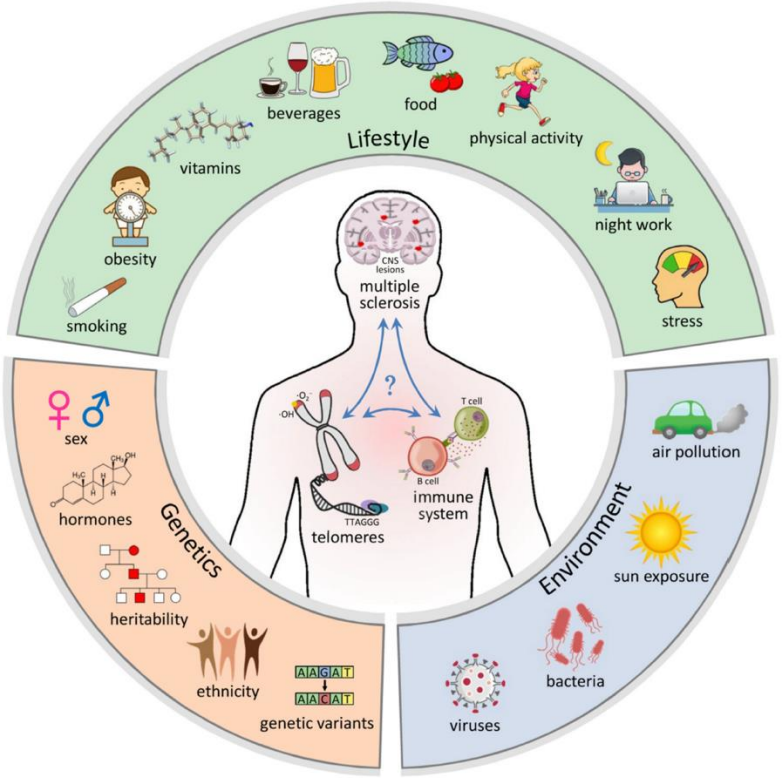
≤60a

EDSS ≤6.0

Start Q1 2026



Therapie



*1

Lifestyle ~ 50% Einfluss

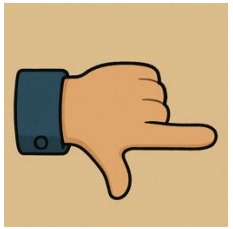
jedoch zumeist **kein krankheitsspezifscher Effekt!**

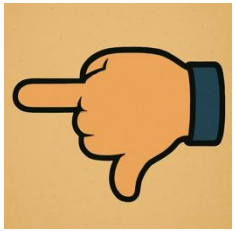
*1 Hecker et al., Biomolecules. 2021 Oct 13;11(10):1510

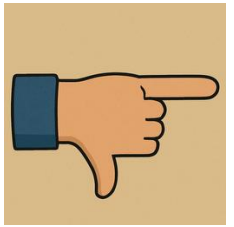
Conclusio

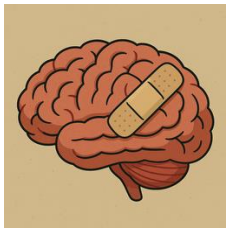
Inflammation

Degeneration

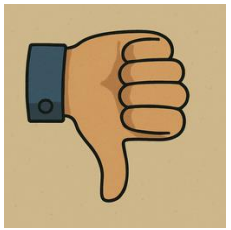








Remyelinisierung



Vielen Dank!

bei Fragen/Anmerkungen e-mail an:

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