Update Neurologie – Halle Münsterland | 06.12.2025

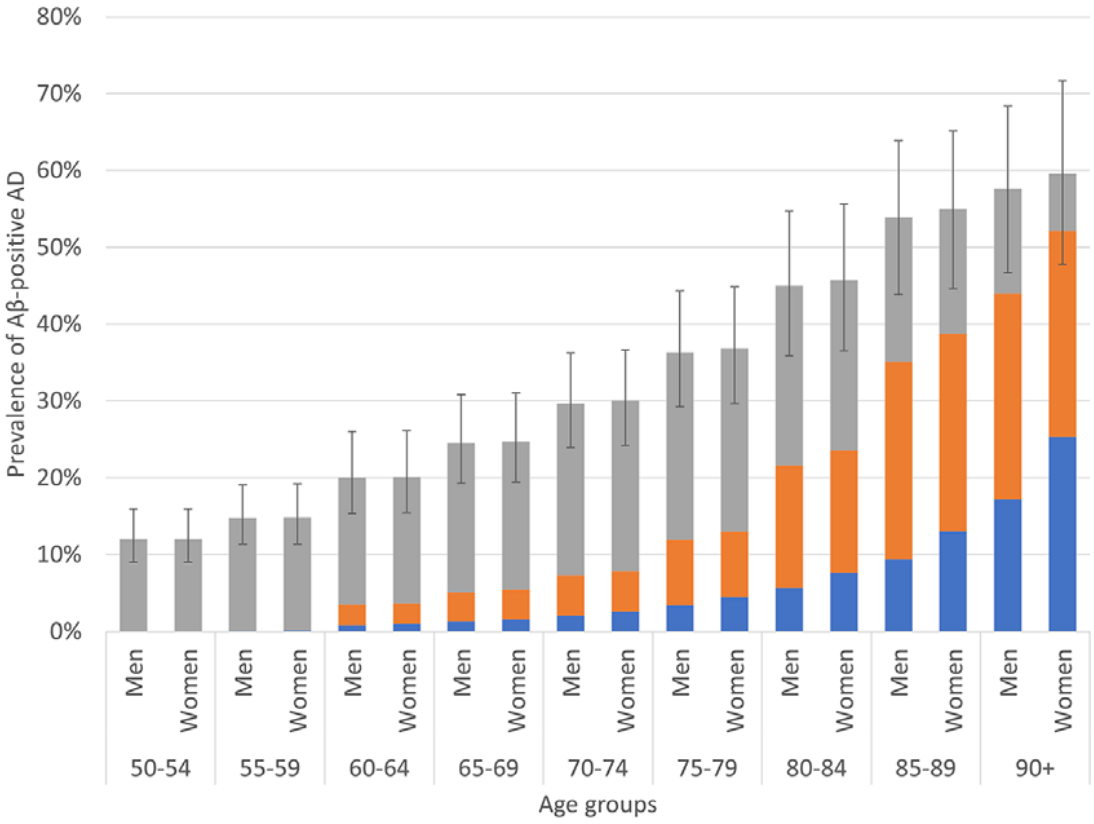
Alzheimer-Krankheit: Update 2025

Priv.-Doz. Dr. Dr. med. Matthias Pawlowski

Klinik für Neurologie
Universitätsklinikum Münster

KFO 342

Alzheimer-Krankheit | Prävalenz der Kontinuum-Erkrankung

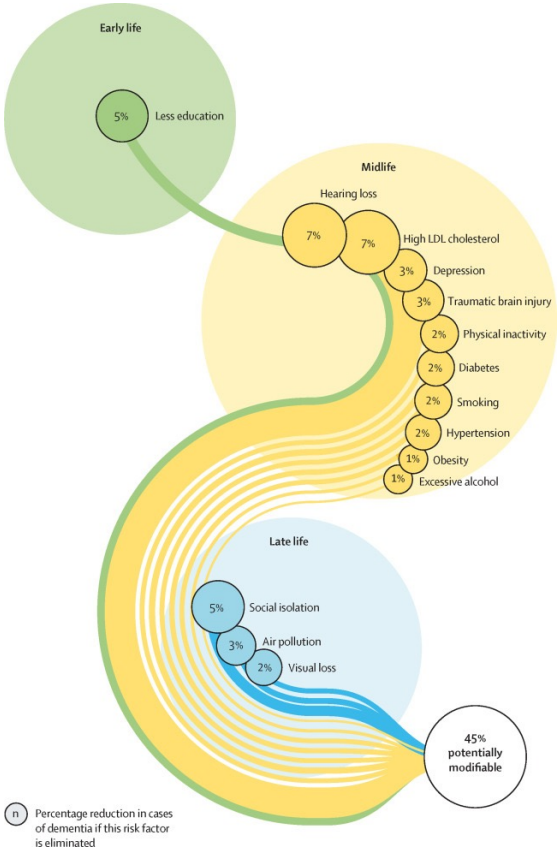


Globale AD-Kontinuum-Prävalenz:
416 Millionen

- Alzheimer-Demenz: 32 Millionen
- Alzheimer-Prodromalstadien: 69 Millionen
- Alzheimer-präklinisch: 315 Millionen

Gustavsson et al. Alzheimers Dement. 2023 Feb;19(2):658-670

Demenz-Prävention | Modifizierbare Risikofaktoren



1. Wenig Bildung

2. Hörstörungen
3. Sehstörungen

4. Rauchen
5. Arterielle Hypertonie
6. Diabetes mellitus
7. Adipositas
8. Erhöhtes LDL-Cholesterin

9. Alkohol (≥21 UK units)
10. Schädel-Hirn-Trauma
11. Luftverschmutzung

12. Depressionen

13. Soziale Isolation
14. Körperliche Inaktivität

xx. – yy. Schlaf, Ernährung, Infektionen, …

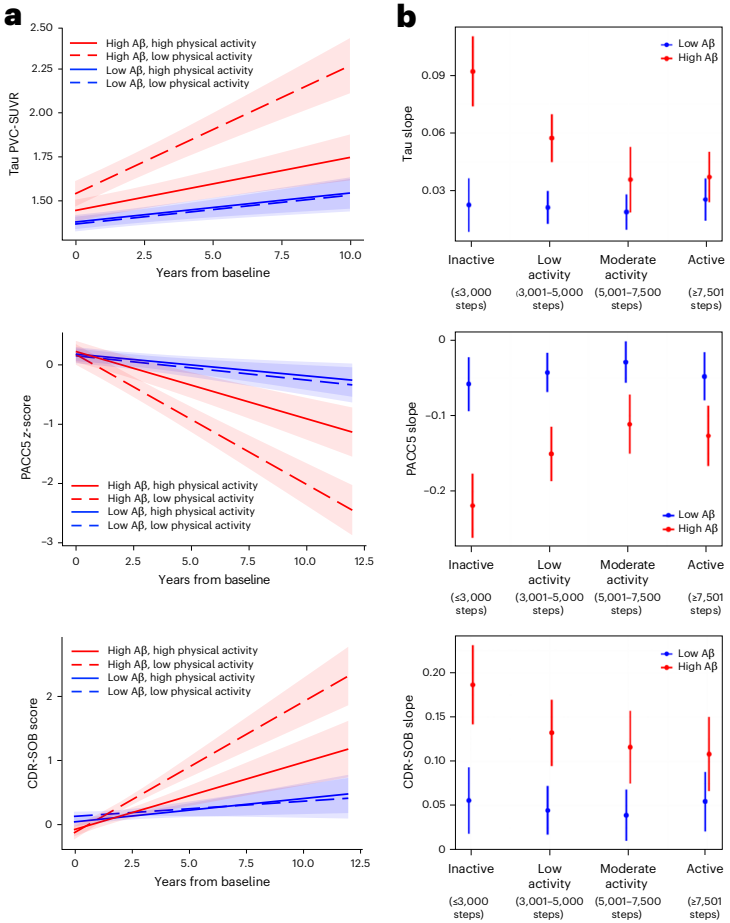
The Lancet Commissions

Dementia prevention, intervention, and care: 2024 report of the *Lancet* standing Commission

Gill Livingston, Jonathan Huntley, Kathy Y Liu, Sergi G Costafreda, Geir Selbæk, Suvarna Alladi, David Ames, Sube Banerjee, Alistair Burns, Carol Brayne, Nick C Fox, Cleusa P Ferri, Laura N Gitlin, Robert Howard, Helen C Kales, Mika Kivimäki, Eric B Larson, Noeline Nakasujja, Kenneth Rockwood, Quincy Samus, Kokoro Shirai, Archana Singh-Manoux, Lon S Schneider, Sebastian Walsh, Yao Yao, Andrew Sommerlad, Naaheed Mukadam**

Livingston et al. Lancet. 2024 Aug 10;404(10452):572-628

Körperliche Aktivität



nature medicine

Article

https://doi.org/10.1038/s41591-025-03955-6

Physical activity as a modifiable risk factor in preclinical Alzheimer's disease

Received: 4 December 2024

Accepted: 12 August 2025

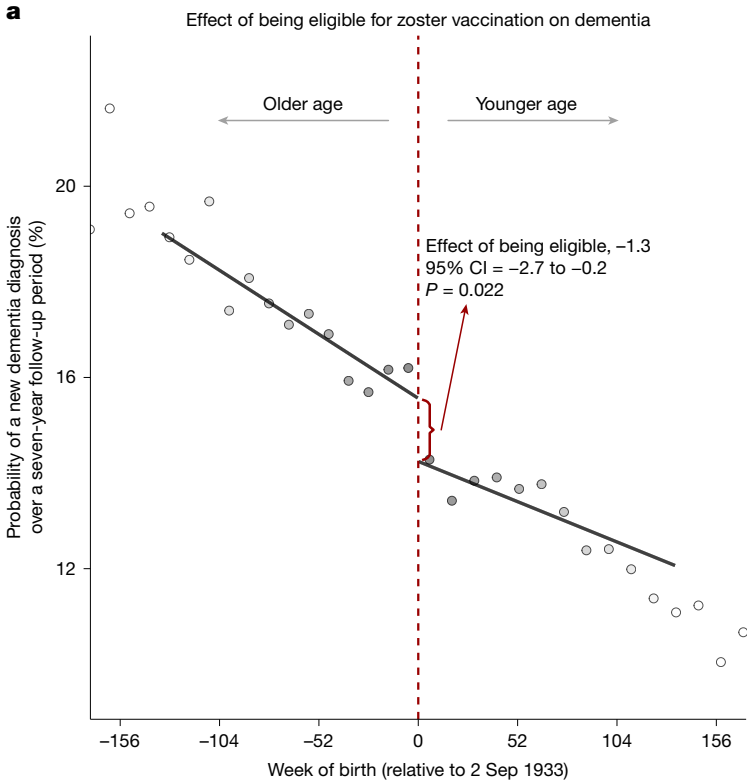
Published online: 03 November 2025

Check for updates

Wai-Ying Wendy Yau[1,2], Dylan R. Kirn[1], Jennifer S. Rabin[3,4,5], Michael J. Properzi[1], Aaron P. Schultz[1,2], Zahra Shirzadi[1,2], Kailee Palmgren[1], Paola Matos[1], Courtney Maa[1], Jeremy J. Pruzin[6], Stephanie A. Schultz[1,2], Rachel F. Buckley[1,2,7], Dorene M. Rentz[1,2], Keith A. Johnson[1,2,8], Reisa A. Sperling[1,2] & Jasmeer P. Chhatwal[1,2]

Yau et al. Nat Med . 2025 Nov 3. doi: 10.1038/s41591-025-03955-6

VZV-Impfung (Wales)



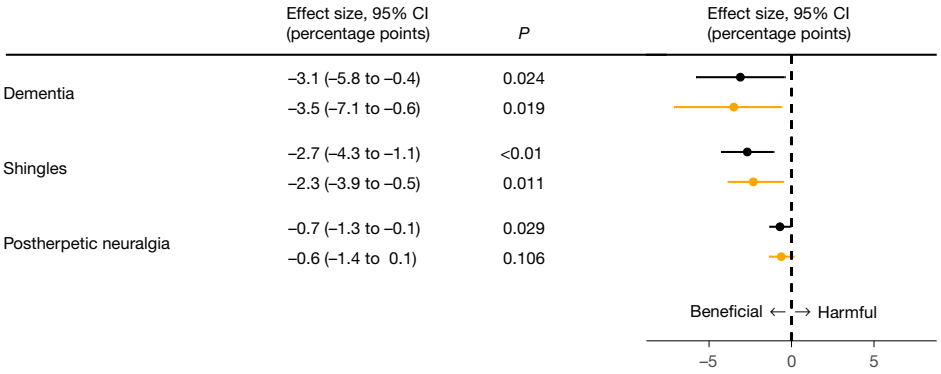
Article

A natural experiment on the effect of herpes zoster vaccination on dementia

https://doi.org/10.1038/s41586-025-08800-x
Received: 4 November 2023
Accepted: 18 February 2025
Published online: 2 April 2025
Open access

Markus Eyting[1,2,3,9], Min Xie[1,4,9], Felix Michalik[1,4], Simon Heß[5], Seunghun Chung[1] & Pascal Geldsetzer[1,6,7,8]

Neurotropic herpesviruses may be implicated in the development of dementia[1–5]. Moreover, vaccines may have important off-target immunological effects[6–9]. Here we aim to determine the effect of live-attenuated herpes zoster vaccination on the



VZV-Impfung (Australien)

JAMA | Original Investigation

Herpes Zoster Vaccination and Dementia Occurrence

Michael Pomirchy, PhD; Christian Bommer, PhD; Fabienne Pradella, PhD; Felix Michalik, MS; Ruth Peters, PhD; Pascal Geldsetzer, ScD, MBChB, MPH

STIKO | Impfkalender

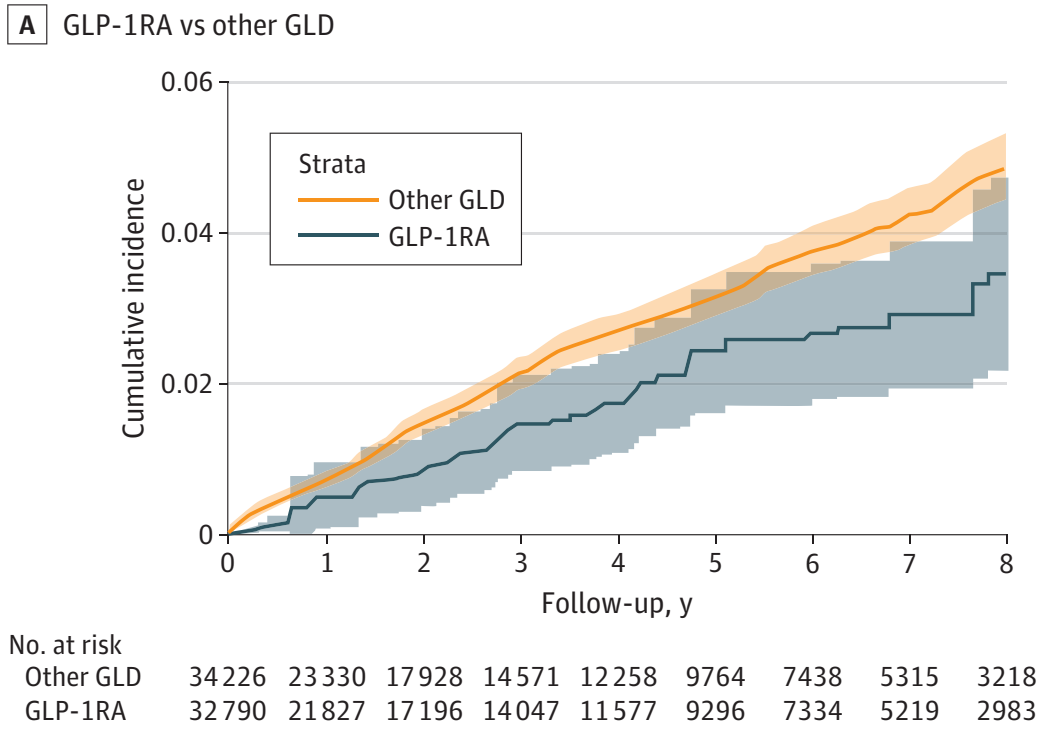
B – Kinder ≥ 5 Jahre, Jugendliche und Erwachsene

Impfung	Alter in Jahren							
	5–6	7–8	9–14	15–16	17	ab 18	60–74	ab 75
	U9	U10	U11/J1		J2			
Tetanus	A1		A2			A[h]		
Diphtherie	A1		A2			A[h]		
Pertussis	A1		A2			A3[h]		
Poliomyelitis			A1					
Hepatitis B								
HPV – Humane Papillomviren			G1[g]	G2[g]				
Meningokokken C								
Masern						S[i]		
Mumps, Röteln								
Varizellen								
Pneumokokken							S[k]	
Herpes zoster							G1[l] G2[l]	
Influenza							S (jährlich)[m]	
COVID-19						Gx[j]	S (jährlich)[m]	
Respiratorische Synzitial Viren								S[n]

- 2 Impfstoffdosen des adjuvantierten Herpes zoster Untereinheiten-Totimpfstoff im Abstand von 2 - 6 Monaten.
  - Shingrix®: in Deutschland zugelassen seit 2018 für Personen ≥18 Jahre.
- Zusätzlich Indikationsimpfung für Personen ≥ 50 Jahre mit einer erhöhten gesundheitlichen Gefährdung infolge einer Grunderkrankung oder für Personen mit angeborener bzw. erworbener Immundefizienz.

Ständige Impfkommission (STIKO). Epid Bull 2025;4:1- 75 | DOI 10.25646/12971.5

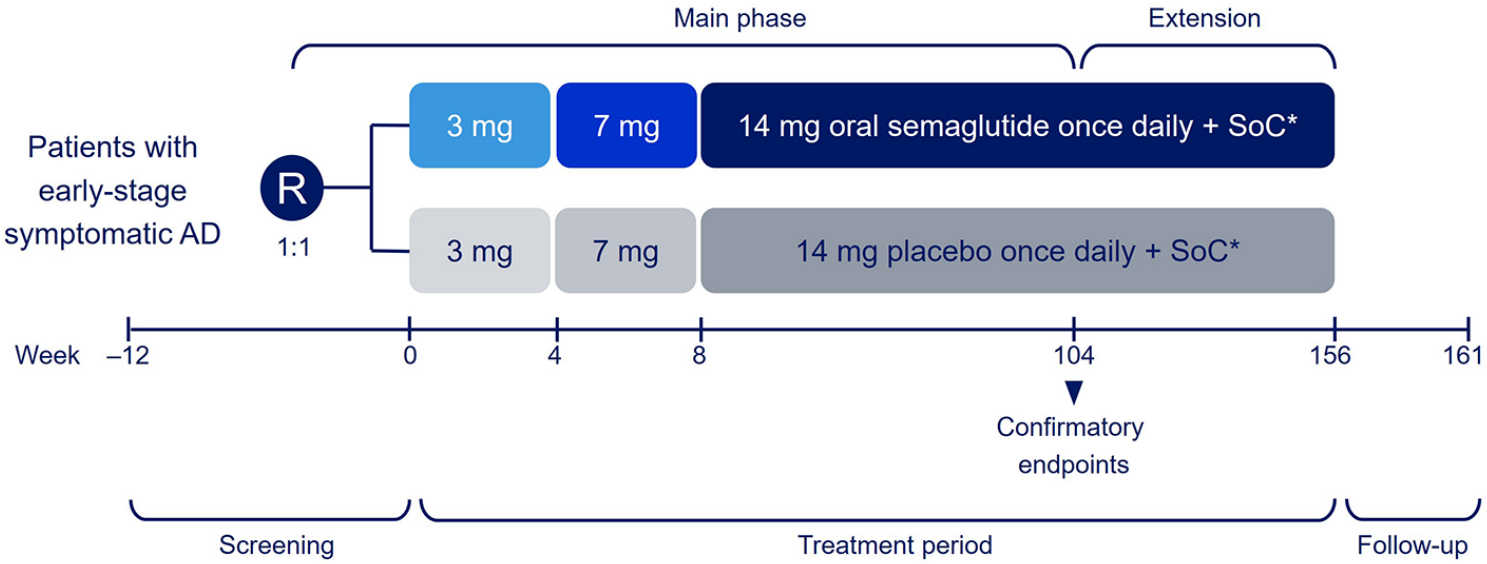
GLP-1RA & Demenz-Inzidenz



Tang et al. JAMA Neurol . 2025 May 1;82(5):439-449

EVOKE (Phase 3) | Semaglutid bei früher Alzheimer-Krankheit

Studiendesign

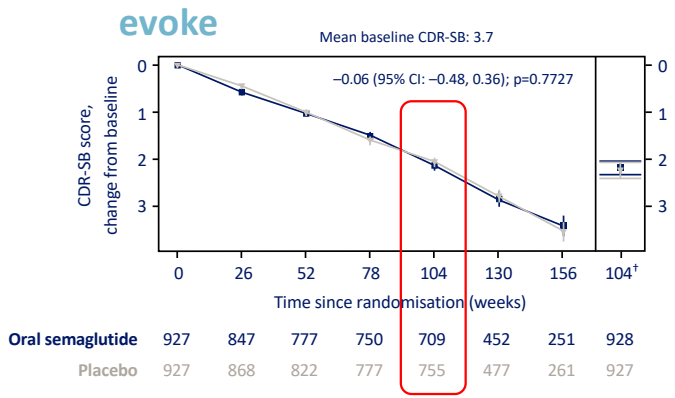


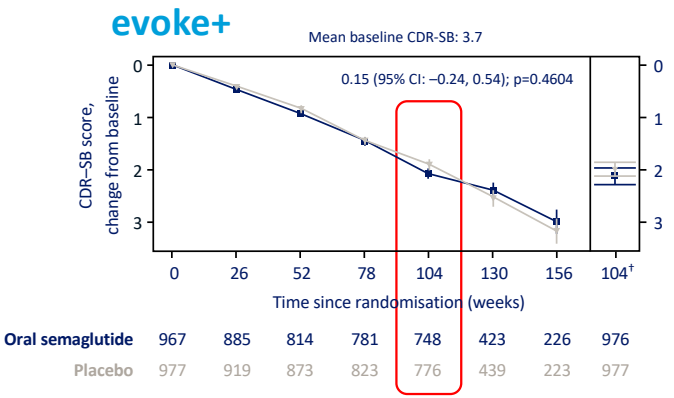
Cummings et al. Alzheimers Res Ther . 2025 Jan 8;17(1):14

EVOKE (Phase 3) | Semaglutid bei früher Alzheimer-Krankheit

Primärer Endpunkt: Clinical Dementia Rating – sum of boxes (CDR-SB)

- Change in CDR-SB from baseline to week 104



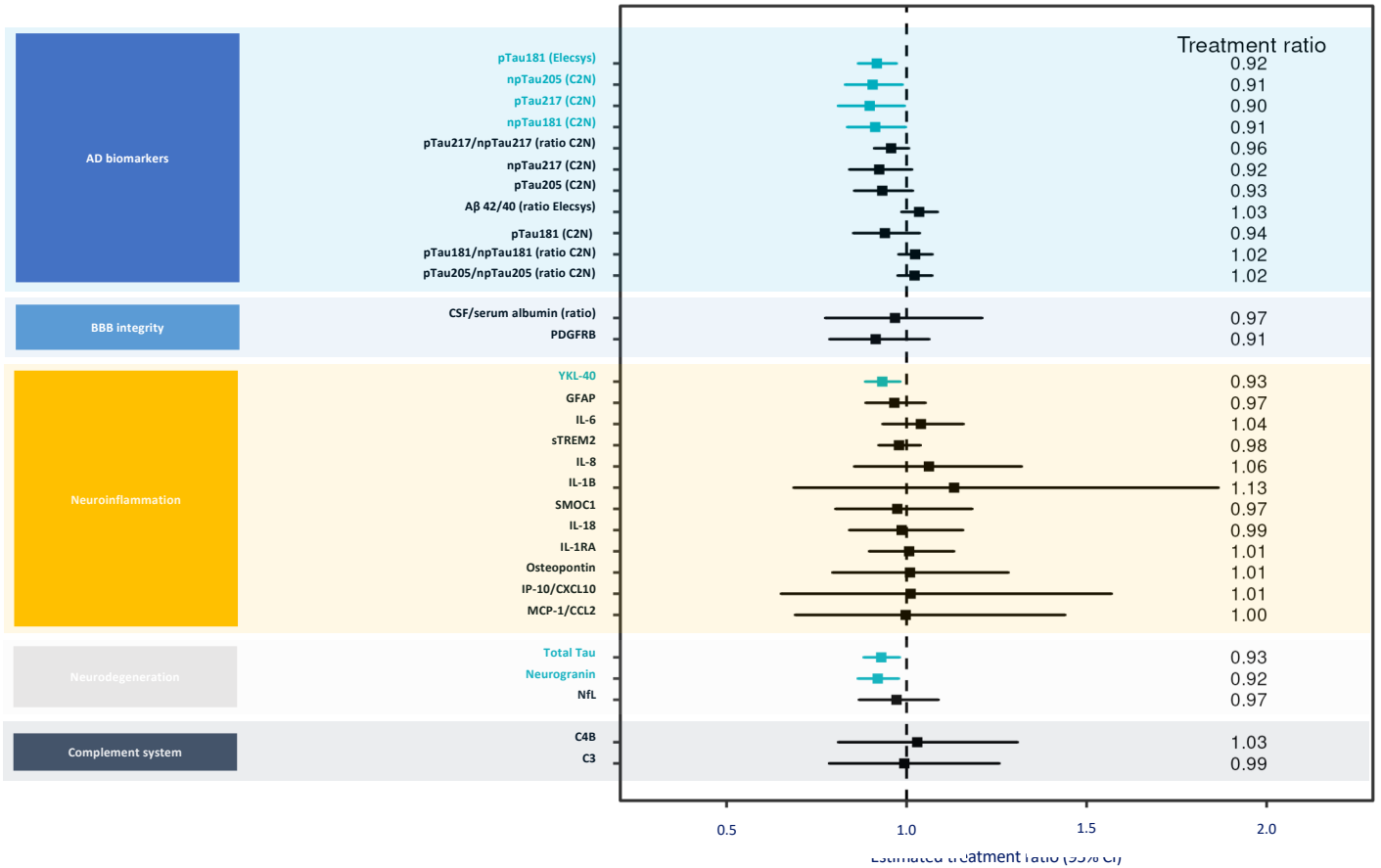


	Estimate†	95% CI	P-value
Oral semaglutide	2.2		
Placebo	2.2		
Oral semaglutide – Placebo	–0.06	–0.48 ; 0.36	0.7727

	Estimate†	95% CI	P-value
Oral semaglutide	2.1		
Placebo	2.0		
Oral semaglutide – Placebo	0.15	–0.24 ; 0.54	0.4604

Cummings et al. Präsentation bei CTAD- Dec 3, 2025, San Diego, US

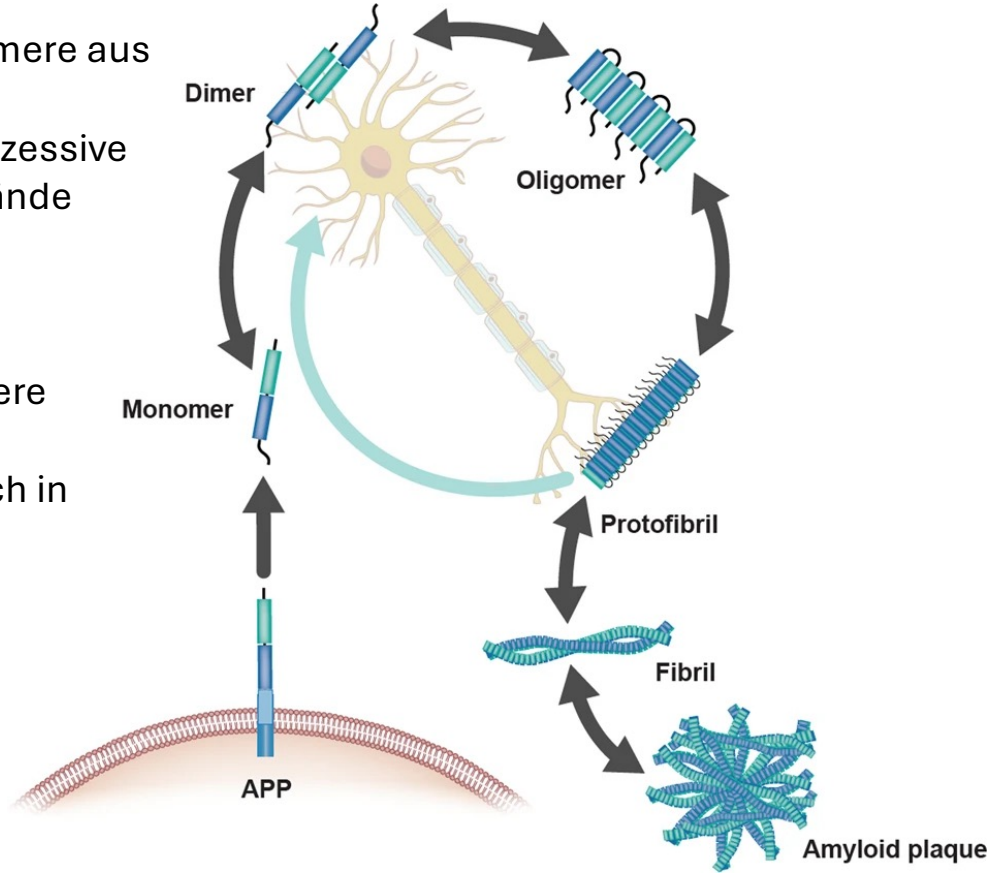
EVOKE (Phase 3) | Semaglutid bei früher Alzheimer-Krankheit



Cummings et al. Präsentation bei CTAD- Dec 3, 2025, San Diego, US

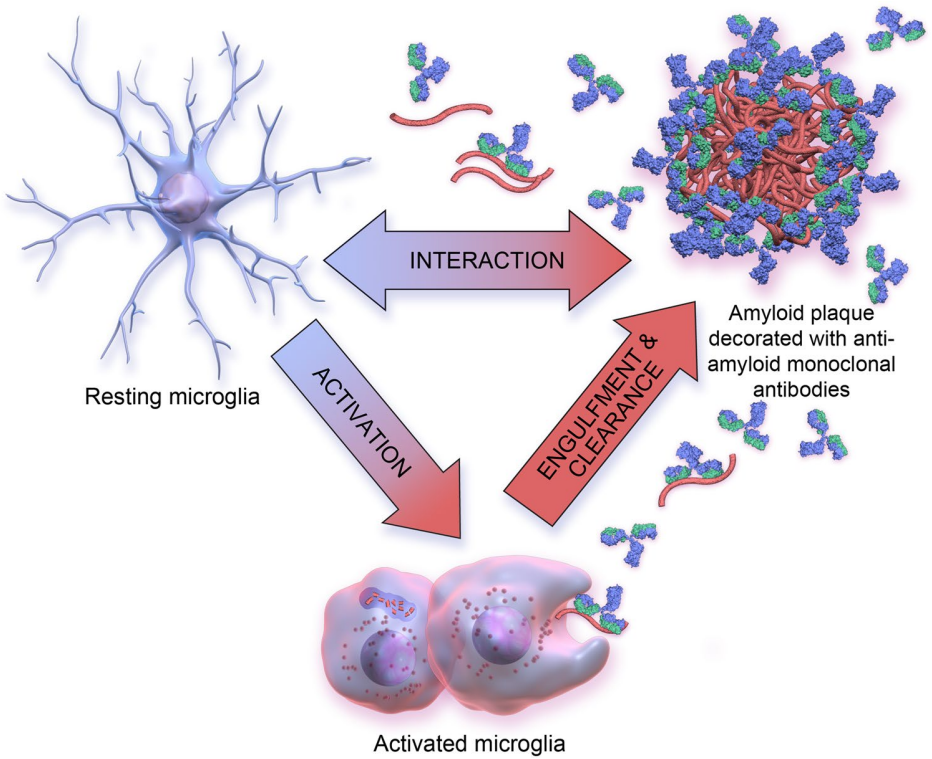
Amyloid-beta

- Aβ wird in Form löslicher Monomere aus APP erzeugt.
- Aus Aβ Monomeren können sukzessive intermediäre Aggregationszustände entstehen, darunter
  - Dimere
  - Oligomere
    - Trimere, …, Dodecamere
  - Protofibrillen
  - Fibrillen, die sich schließlich in
  - Plaques ansammeln.



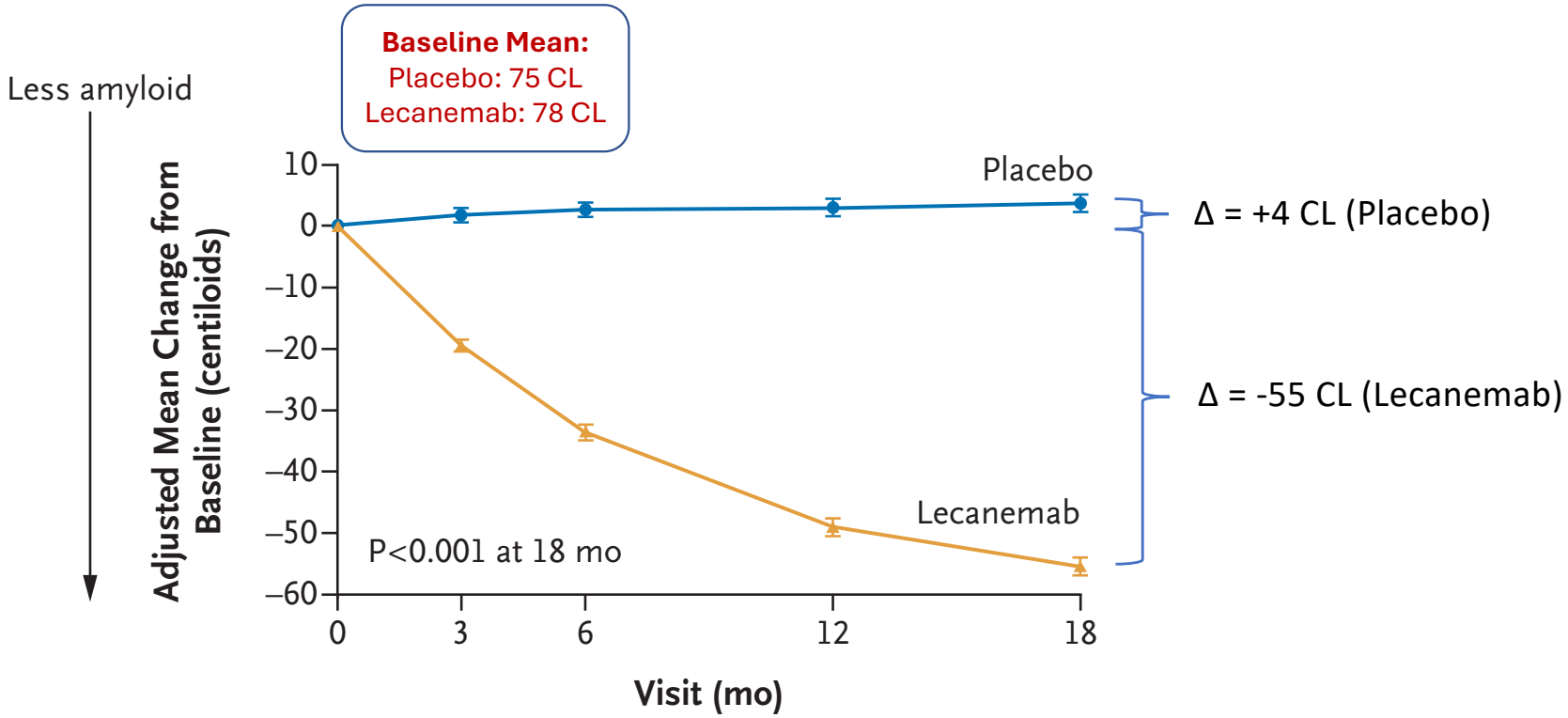
Hampel et al. Mol Psychiatry. 2021 Oct;26(10):5481-5503

Aβ-Antikörper | Wirkmechanismus



Cummings et al. BioDrugs. 2024 Jan;38(1):5-22

Lecanemab | CLARITY (Phase 3) | Amyloid-PET

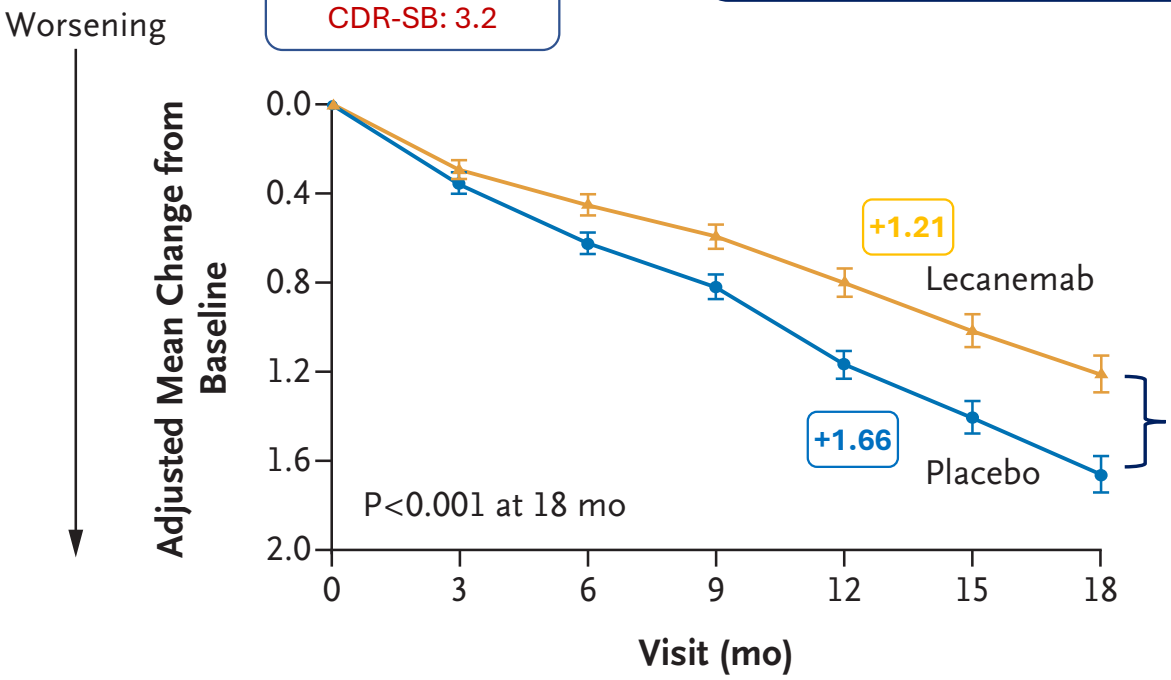


van Dyck et al. N Engl J Med. 2023 Jan 5;388(1):9-21

Lecanemab | CLARITY (Phase 3) | Primärer Endpunkt

CDR-SB
(**C**linical **D**ementia **R**ating – **S**um of **B**oxes)
Range: 0-18 [higher scores = greater deficit]

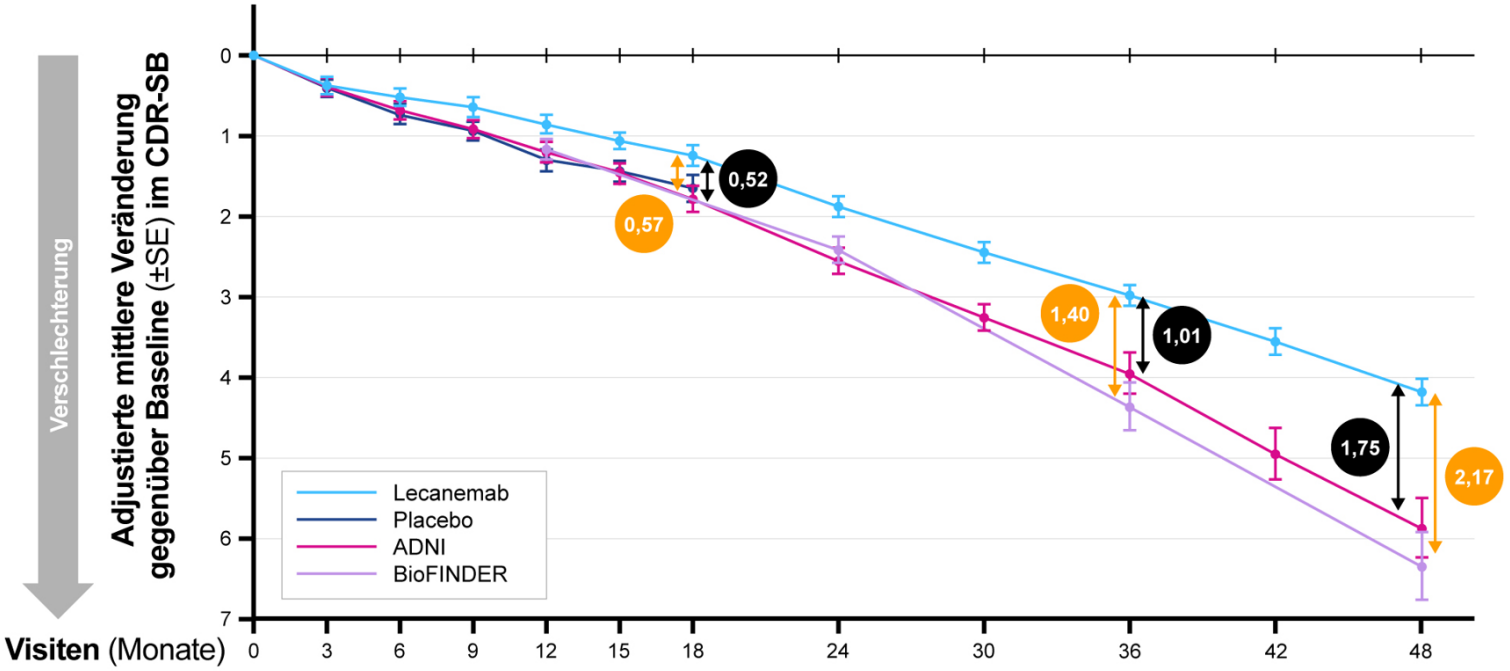
Baseline Mean:
CDR-SB: 3.2



27% geringere CDR-SB Verschlechterung
(Δ = **-0.45**; p=0.00005)

van Dyck et al. N Engl J Med. 2023 Jan 5;388(1):9-21

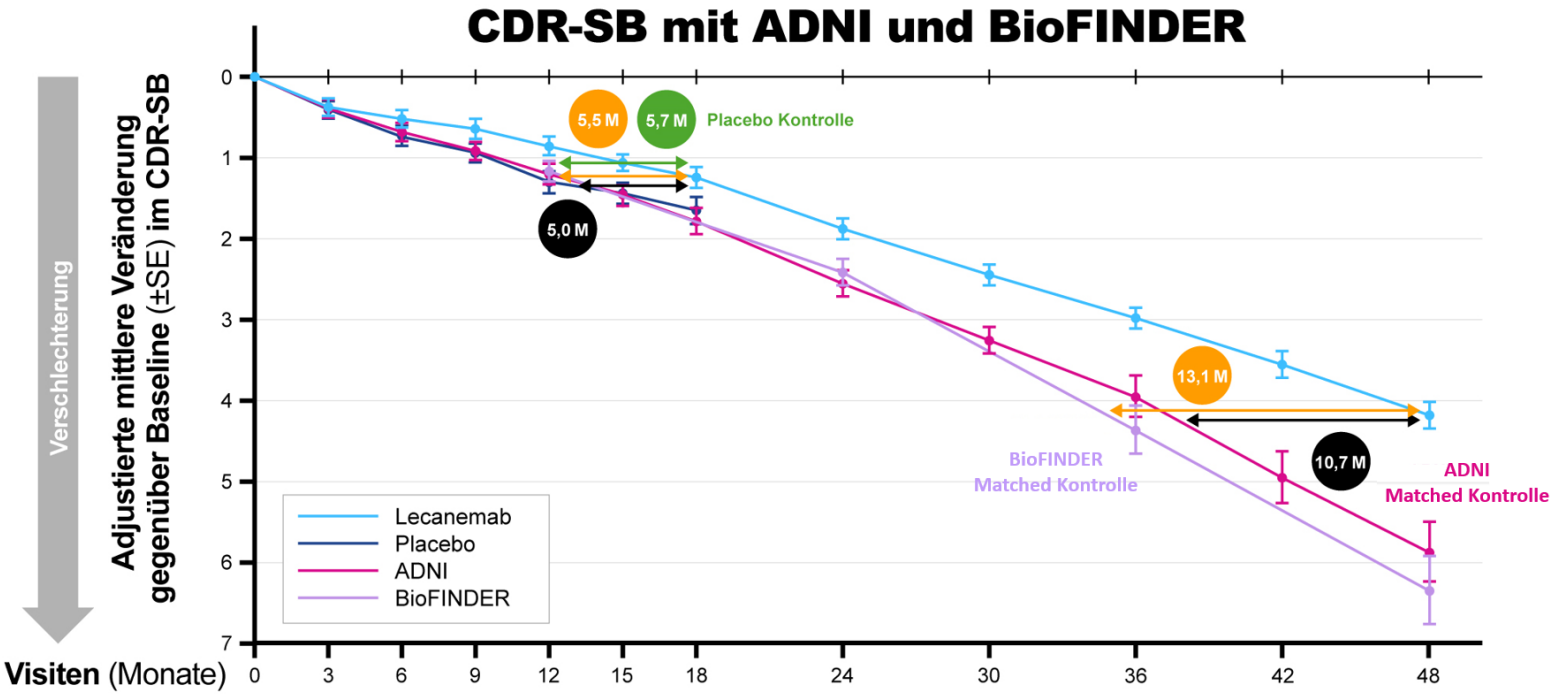
Lecanemab | OLE-Daten (48 Monate): CDR-SB (Δ)



N (Placebo)	875	849	828	813	779	767	757					
N (Lecanemab)	859	824	798	779	765	738	714	659	613	573	527	478
N (ADNI)	436		410		401		121	301	173	173	98	98
N (BioFINDER)	147				139			137		117		112

van Dyck. EISAI. AAIC 2025, Toronto, Canada

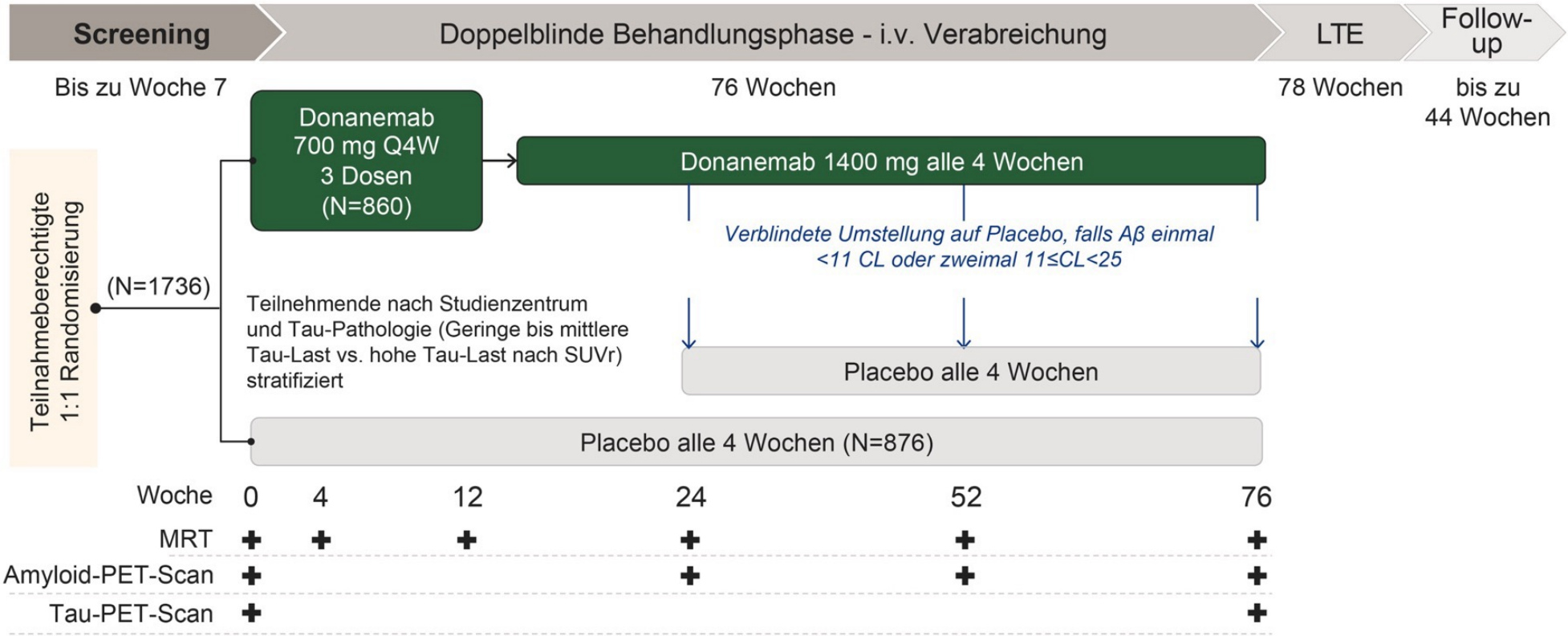
Lecanemab | OLE-Daten (48 Mo.): CDR-SB (Zeit)



N (Placebo)	875	849	828	813	779	767	757					
N (Lecanemab)	859	824	798	779	765	738	714	659	613	573	527	478
N (ADNI)	436		410		401		121	301	173	173	98	98
N (BioFINDER)	147				139			137		117		112

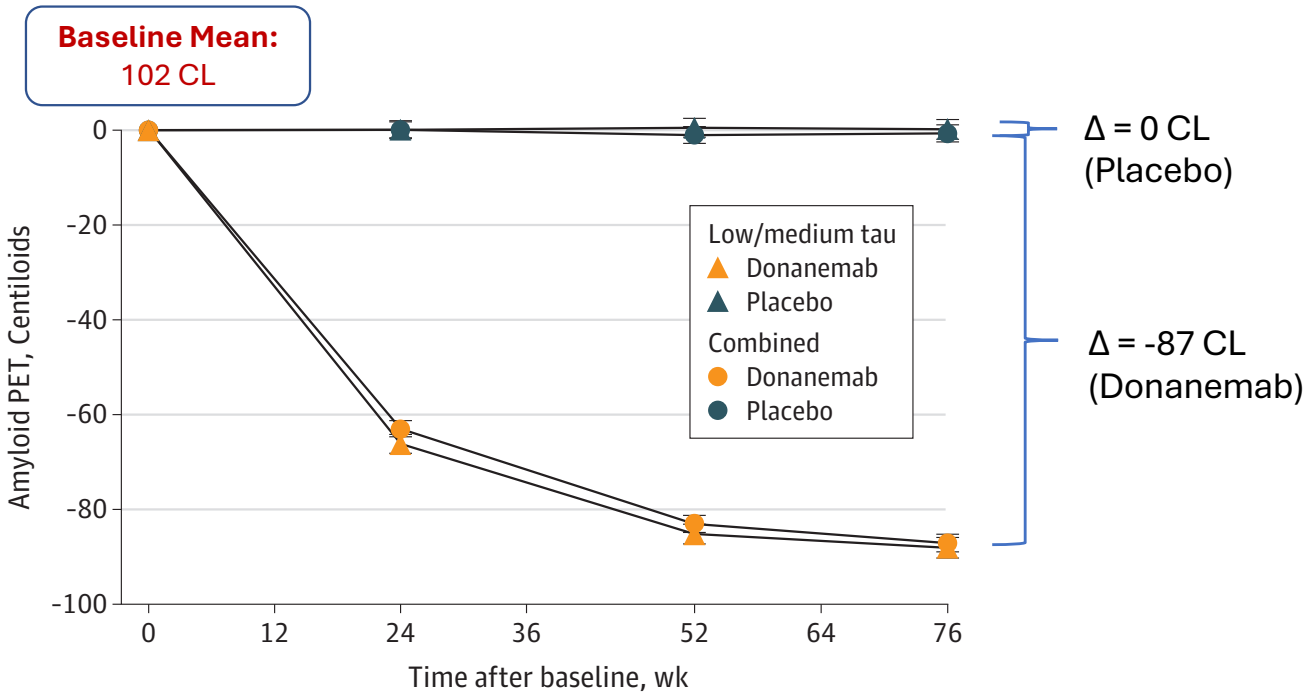
van Dyck. EISAI. AAIC 2025, Toronto, Canada

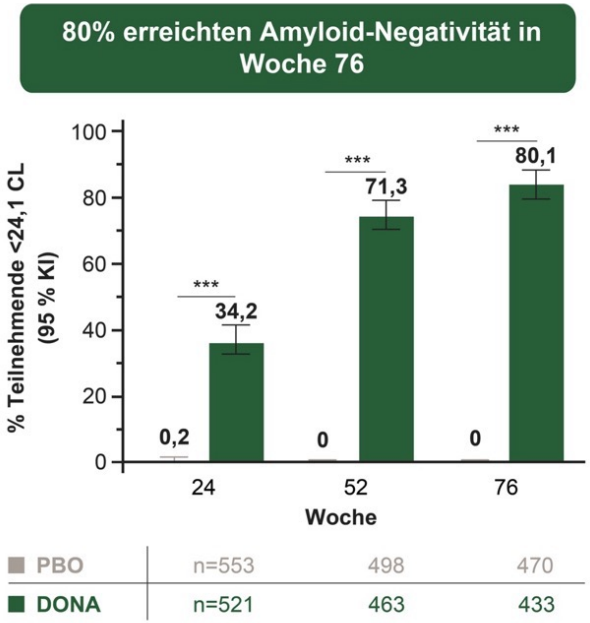
Donanemab | TRAILBLAZER-ALZ2 | Studiendesign



Sims et al. JAMA. 2023 Aug 8;330(6):512-527

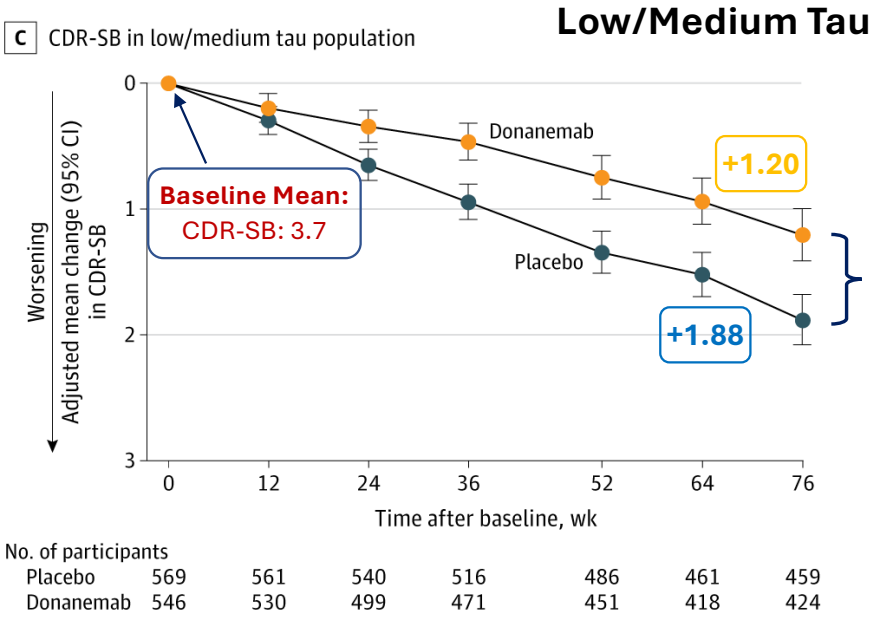
Donanemab | TRAILBLAZER-ALZ2 | Amyloid-PET





Sims et al. JAMA. 2023 Aug 8;330(6):512-527

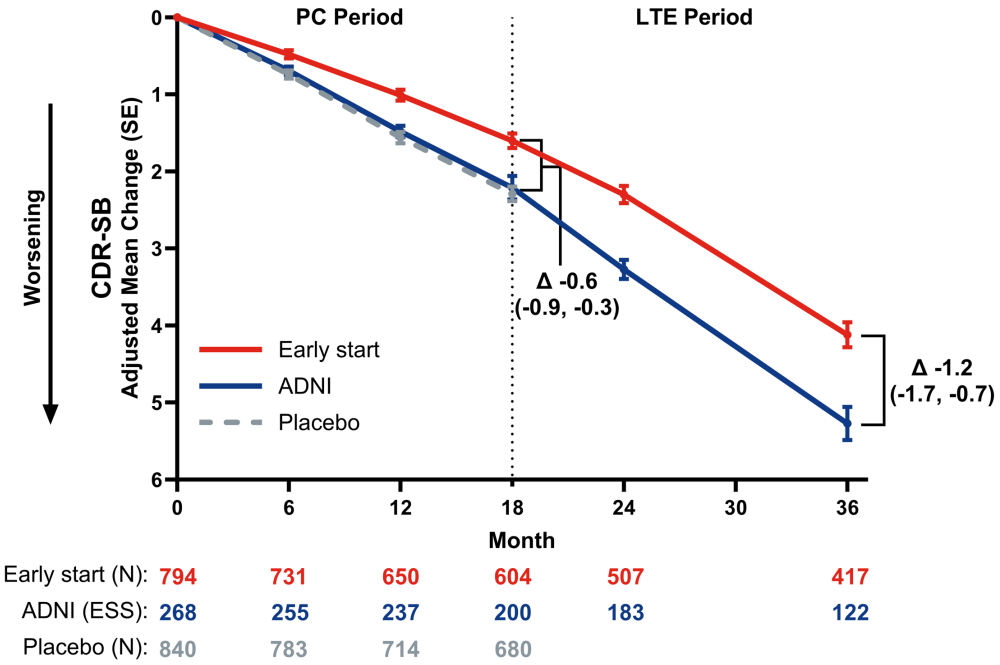
Donanemab | TRAILBLAZER-ALZ2 | Klinischer Endpunkt



36% geringere CDR-SB Verschlechterung
ΔLSM = −0.67 [95% CI, −0.95 to −0.40] p<0.001

Sims et al. JAMA. 2023 Aug 8;330(6):512-527

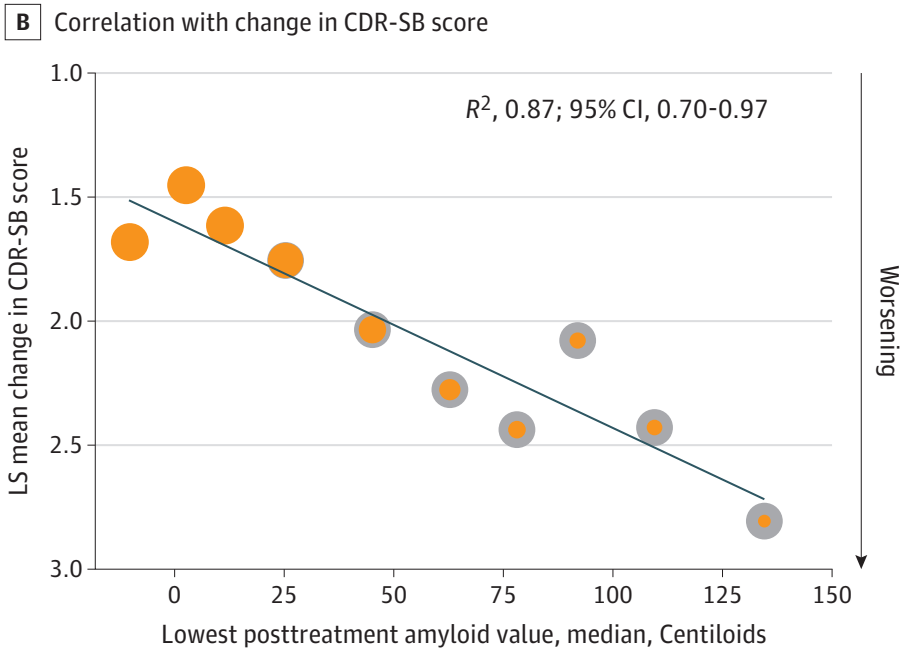
Donanemab | TRAILBLAZER-ALZ2 | long-term extension



- Im Vergleich zur ADNI-Kohorte nahm der Behandlungsvorteil von Donanemab im Verlauf von drei Jahren kontinuierlich zu, mit einem Anstieg des Δ CDR-SB von 0,6 nach 18 Monaten auf 1,2 nach 36 Monaten.
- Der Behandlungsvorteil nahm zu obwohl die Therapie bei den meisten Teilnehmern bereits abgeschlossen war.

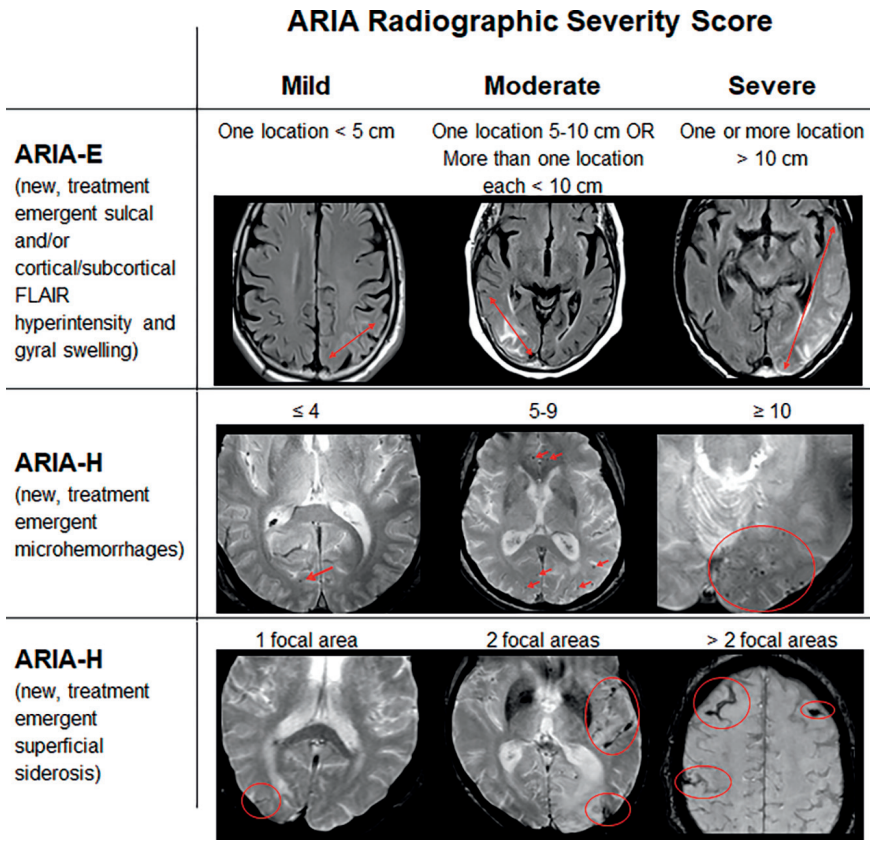
Lilly. AAIC 2025, Toronto, Canada

Donanemab | post-Rx Plaque-Last & klinischer Benefit



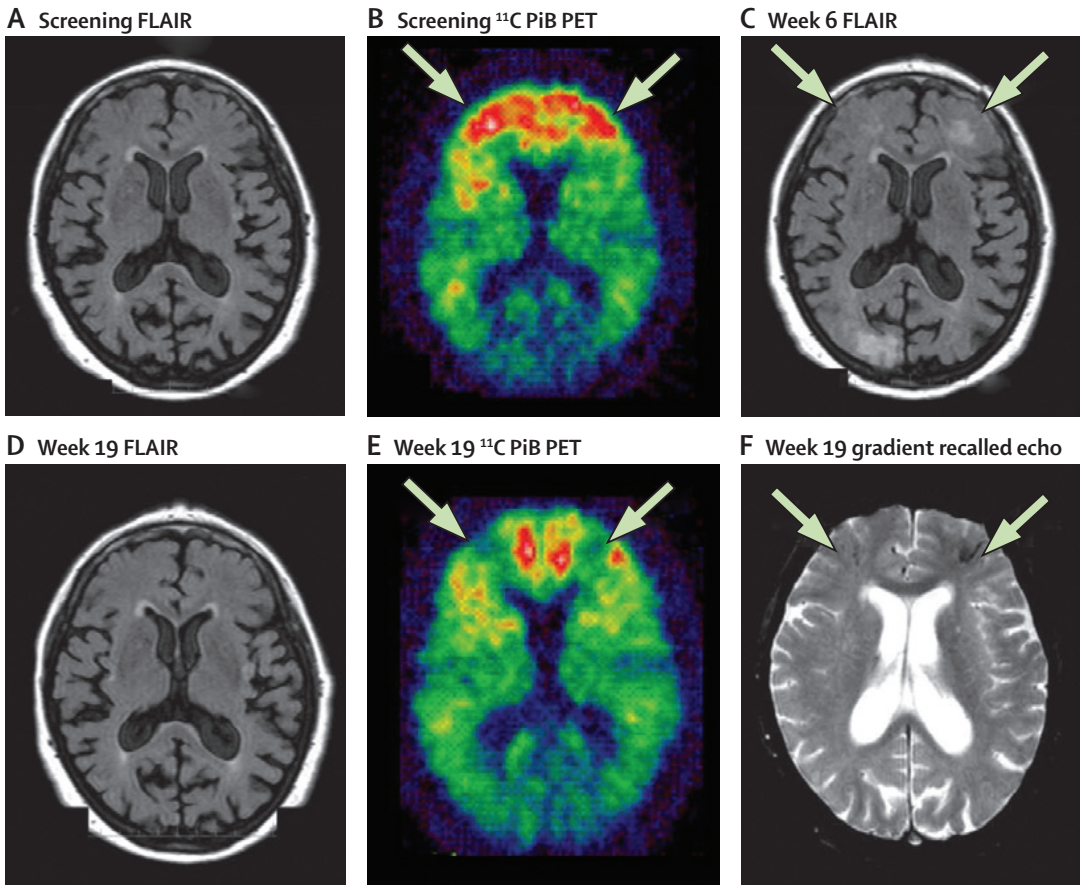
Lu et al. JAMA Neurol . 2025 Oct 13. Epub

Amyloid-related imaging abnormality (ARIA)



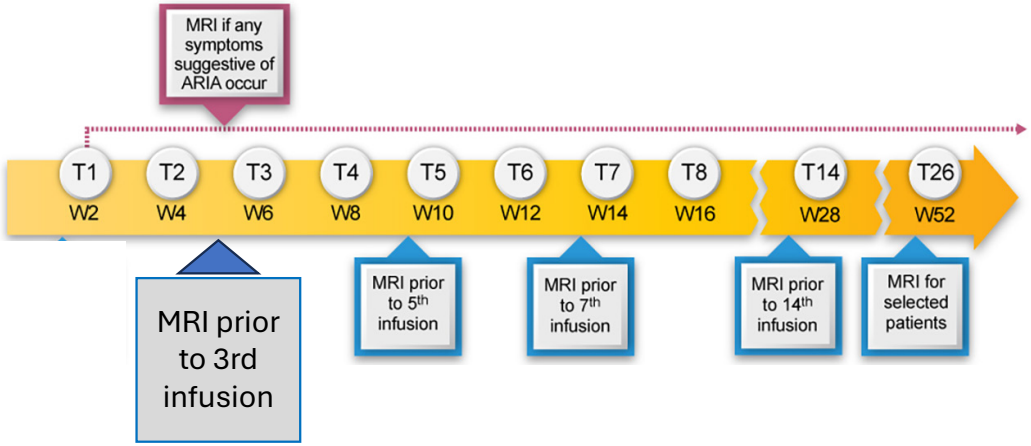
Cogswell et al. AJNR Am J Neuroradiol. 2025 Jan 8;46(1):24-32

Amyloid-related imaging abnormality (ARIA)



Sperling et al. Lancet Neurol. 2012 Mar;11(3):241-9

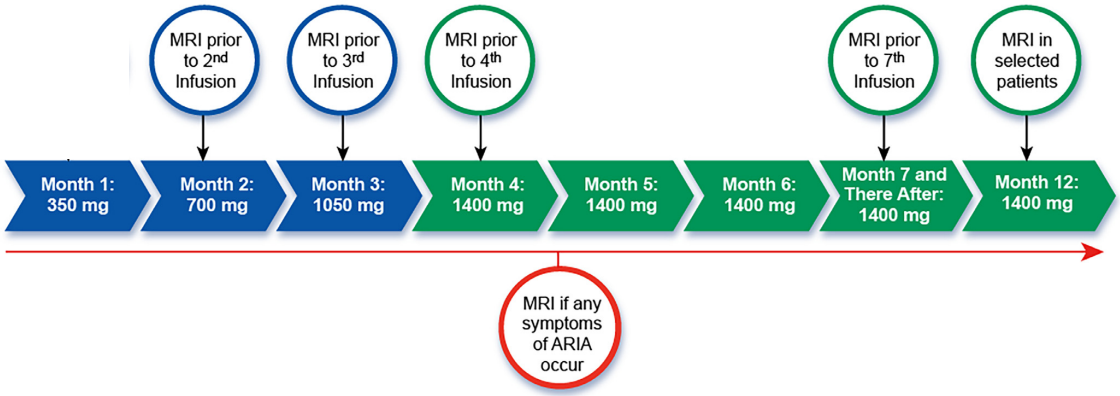
ARIA monitoring



Lecanemab & Donanemab

Baseline-cMRT:
innerhalb von 6 Monaten vor Therapiebeginn.

(FDA-Empfehlung vom 28.08.2025)
(Rote Hand Brief vom 26.09.2025)



Cummings et al. J Prev Alzheimers Dis. 2023;10(3):362-377 | Rabinovici et al. J Prev Alzheimers Dis. 2025 May;12(5):100150

cMRT | Technische Anforderungen & Befundbericht

Summary of recommendations based on 3 patient scenarios

	Baseline/Enrollment Evaluation	Asymptomatic Monitoring	Symptomatic Patient on Therapy
Order	MRI brain dementia without IV contrast (indication: AD therapy enrollment)	MRI brain without IV contrast (indication: AD therapy monitoring)	MRI brain without (and with) IV contrast (indication: AD therapy, new symptoms)
Protocol Minimum sequences	AD therapy enrollment 2D or 3D T2 FLAIR GRE[a] ± SWI DWI 3D T1 T2 FSE	AD therapy monitoring 2D or 3D T2 FLAIR GRE[a] ± SWI DWI	AD therapy monitoring 2D or 3D T2 FLAIR GRE[a] ± SWI DWI ± additional sequences
Reporting template Key findings	AD therapy enrollment Microhemorrhages Siderosis White matter hyperintensities Infarcts	AD therapy monitoring ARIA-E (edema, effusion) ARIA-H (new microhemorrhages, siderosis)	AD therapy monitoring ARIA-E ARIA-H Other acute findings
Recommended communication	Standard reporting	Mild ARIA: notification required Moderate or severe ARIA: closed-loop communication	

Cogswell et al. AJNR Am J Neuroradiol. 2025 Jan 8;46(1):24-32

AAT | (Inkomplette) Auswahl der Kriterien zur Patientenselektion

Einschlusskriterien	
Diagnose	Kognitive Defizite infolge Alzheimer-Krankheit
Klinischer Schweregrad	MCI oder leichtgradige Demenz (Stadium 3-4 des Alzheimer-Kontinuums)
Biomarker-Nachweis	Amyloid-PET | CSF
Ausschlusskriterien	
Co-Morbidität (1)	Andere Krankheiten (medizinisch, neurologisch, psychiatrisch) ursächlich für kognitive Defizite
Co-Morbidität (2)	Andere Krankheiten/Medikation, die mit der Therapie interferieren könnten
Schlaganfall / Epilepsie	Schlaganfall innerhalb der letzten 12 Monate oder epilepetischer Anfall
OAK & Blutungsrisiko	Marcumar | DOAKs | Thrombozyten <50.000/µl | INR >1,5 | (Thrombolyse unter Therapie)
cMRT	>4 Mikroblutungen | ≥1 Makroblutung | ≥1 superfizielle Siderose | Leukencephalopathie Fazekas 3
APOE-Genotyp	*APOE*-e4 homozygot

APOE-Genotyp

Der häufigste *APOE*-Genotyp (APOE ε3/ε3): 62 % der kognitiv gesunden Menschen.

APOE ε4/ε4:

- ca. 2 % der kognitiv gesunden Menschen.
- ca. 15 % der Patienten mit Alzheimer-Krankheit.

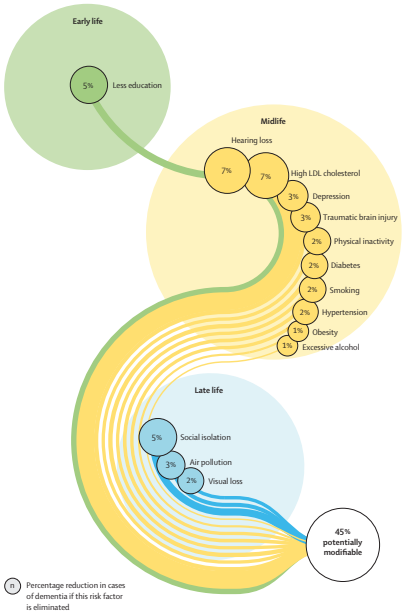
APOE genotype	Frequency in cognitively healthy individuals (%)[286]	Frequency in patients with AD (%)[286]	Odds ratio for AD development[9]	Odds ratio for amyloid positivity at 70 years of age[85]	
				Cognitively healthy	Mild cognitive impairment
*APOE*ε2/ε2*	0.7	0.3	0.56	NA	NA
*APOE*ε2/ε3*	11.0	4.6	0.56	0.34	0.59
*APOE*ε3/ε3*	62.3	34.3	1.00	1.00	1.00
*APOE*ε2/ε4*	1.9	2.6	2.64	4.29	2.38
*APOE*ε3/ε4*	22.2	43.4	3.63	2.94	3.52
*APOE*ε4/ε4*	1.9	14.8	14.49	18.76	14.50

data from: Alzgene. Meta-analysis of all published AD association studies (case-control only) APOE_E2/3/4. Alzgene http://www.alzgene.org/Meta.asp?GeneID=83 (2010).

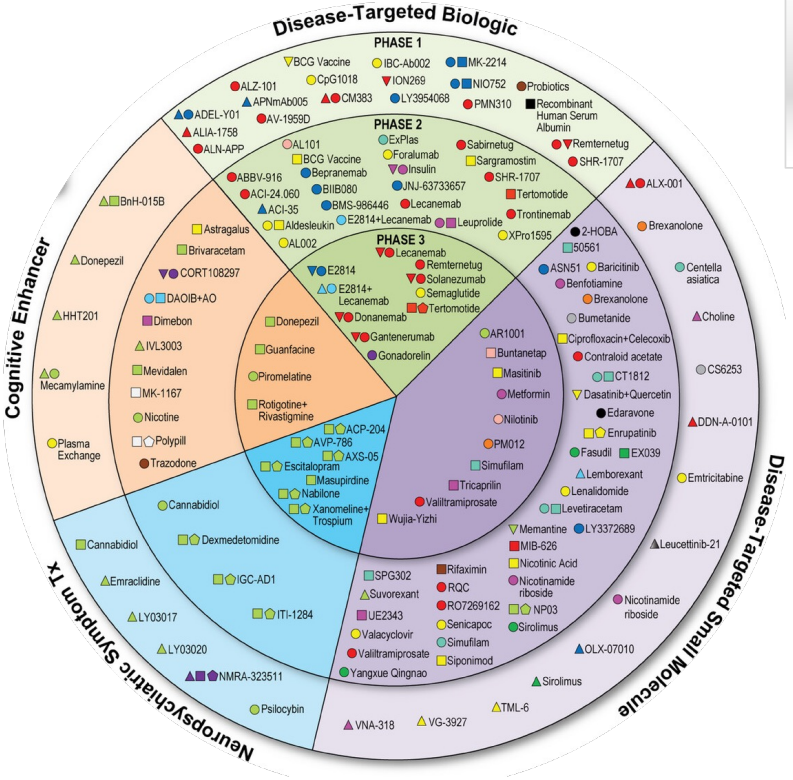
Yamazaki et al. Nat Rev Neurol. 2019 Sep;15(9):501-518

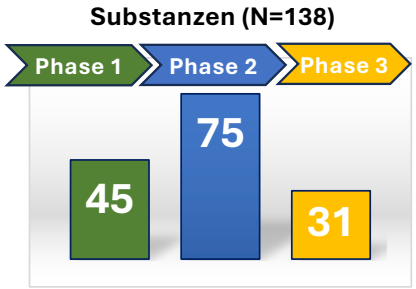
Zusammenfassung | Ausblick

Prävention
Modifizierbare Risikofaktoren



AD Drug Development Pipeline
2025





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matthias.pawlowski@ukmuenster.de