Amsterdam UMC
Universitair Medische Centra

Differentiaal diagnostiek van dementie op jonge leeftijd

YOD-COHORT
a Dutch cohort for people with young-onset dementia and their family

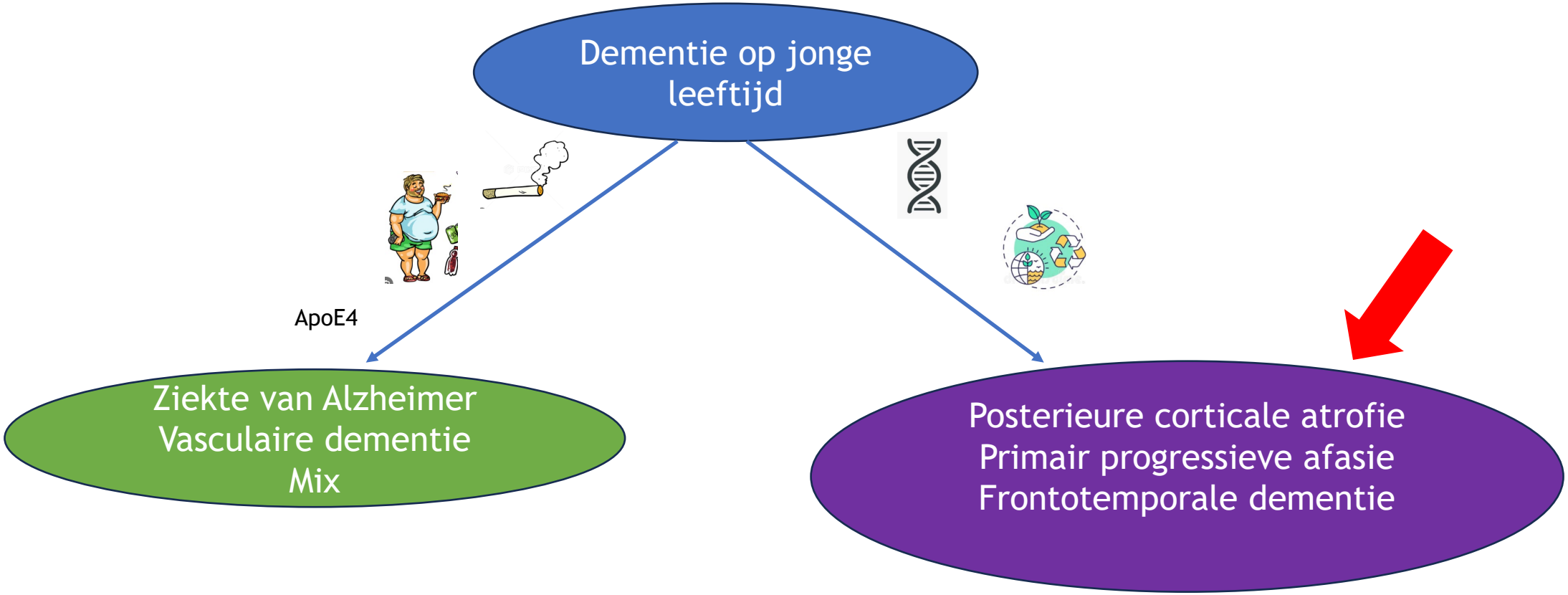
YOD-INCLUDED

Prof. Dr. Yolande Pijnenburg

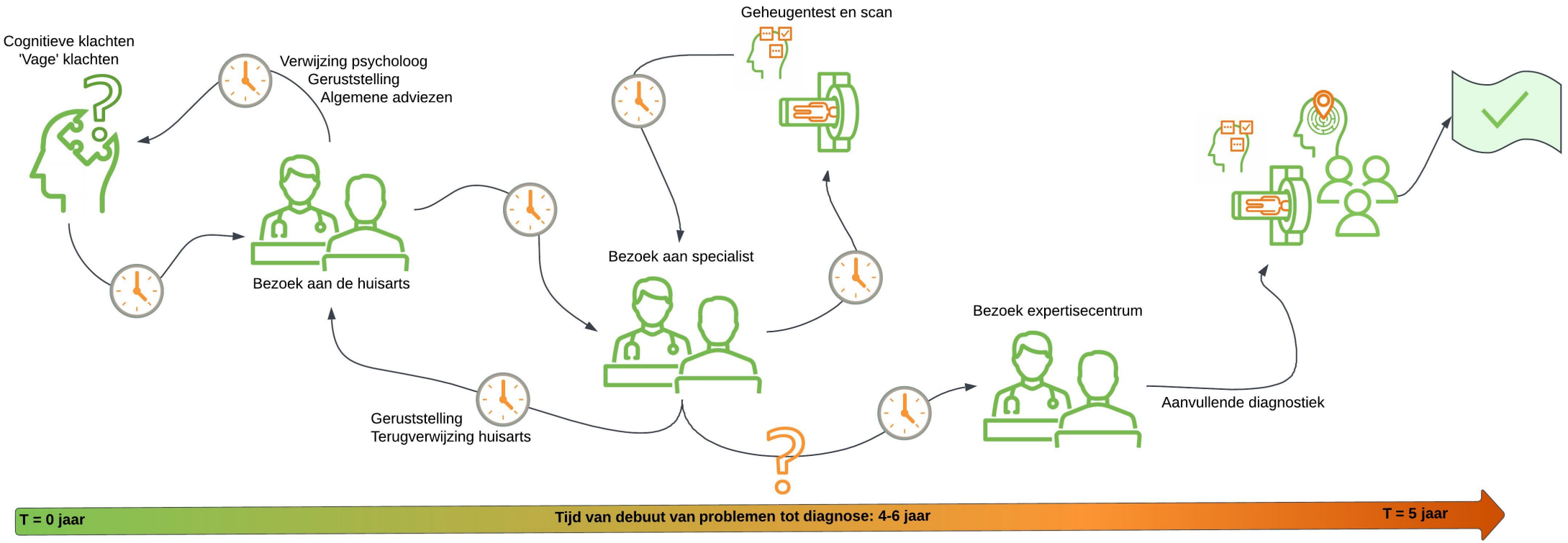
Wat zijn de belangrijkste ontwikkelingen in de afgelopen 10 jaar?

- Klinisch spectrum
- Ziektemechanismen
- Biomarkers
- Therapie-ontwikkeling

Dementie op jonge leeftijd: begin symptomen < 65 jaar



De reis voor de patiënt…



Een complexe diagnose

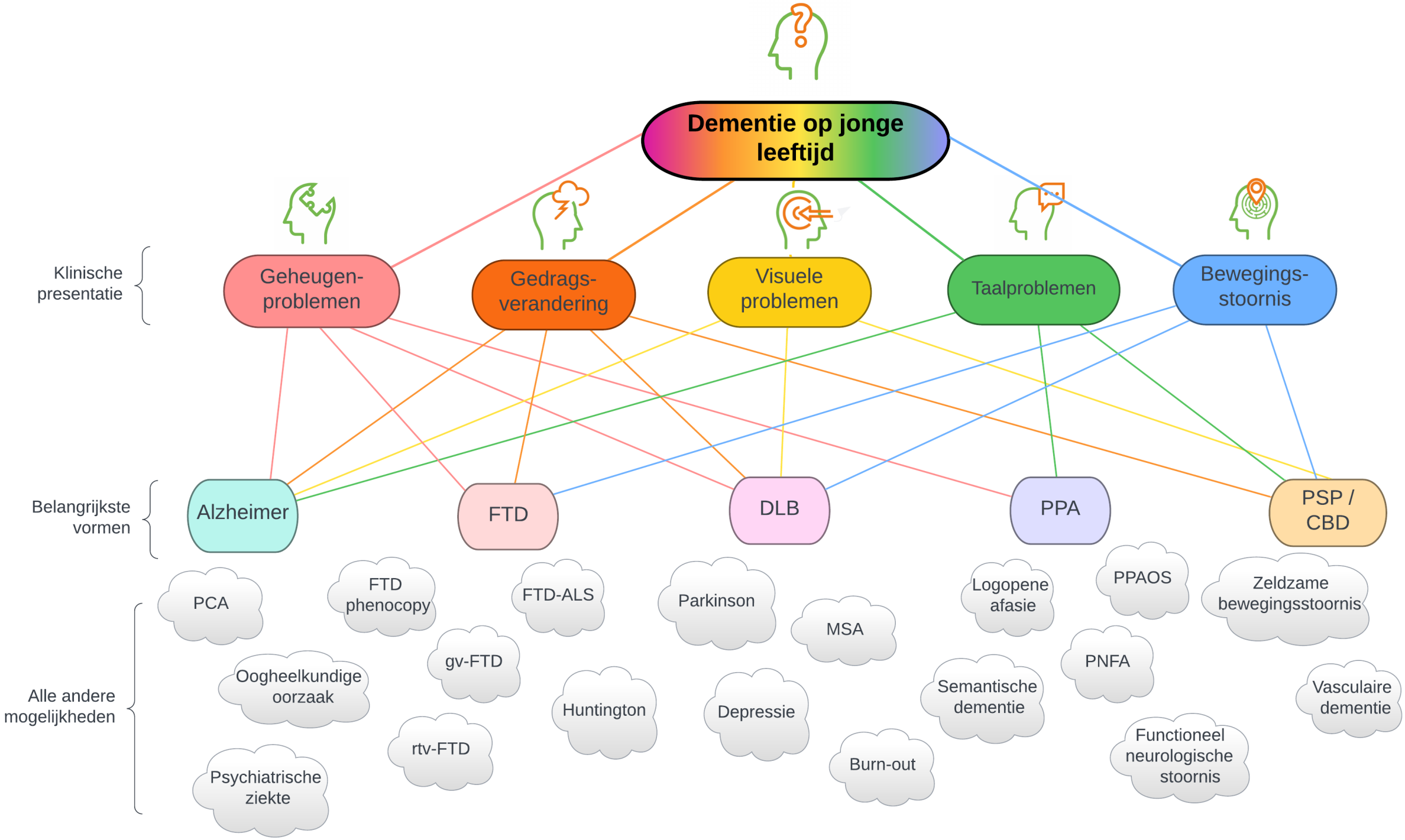
Dementie op jonge leeftijd = vaker lastig

- Geen geheugenklachten
- Bijkomende niet-cognitieve problemen
- Vaker genetisch

- Dementie <65 jaar in Nederland:
  - 14.000-17.000 patiënten
  - Maar misschien: 10% van alle dementie = 29.000 patiënten!

MS = 25.000
Parkinson = 55.000

Klinisch spectrum


Dementie op jonge leeftijd
Klinische presentatie
Geheugen-problemen
Gedrags-verandering
Visuele problemen
Taalproblemen
Bewegings-stoornis
Belangrijkste vormen
Alzheimer
FTD
DLB
PPA
PSP / CBD
Alle andere mogelijkheden
PCA
FTD phenocopy
FTD-ALS
Parkinson
MSA
Logopene afasie
PPAOS
Zeldzame bewegingsstoornis
Oogheelkundige oorzaak
gv-FTD
Huntington
Depressie
Semantische dementie
PNFA
Vasculaire dementie
rtv-FTD
Burn-out
Functioneel neurologische stoornis
Psychiatrische ziekte

Dementie op jonge leeftijd / atypische dementiesyndromen

- Herkennen van de ‘niet geheugen’ symptomen
- Herkennen van de niet-cognitieve symptomen
- Herkennen van vroege symptomen
- Differentiatie van condities die niet tot dementie leiden

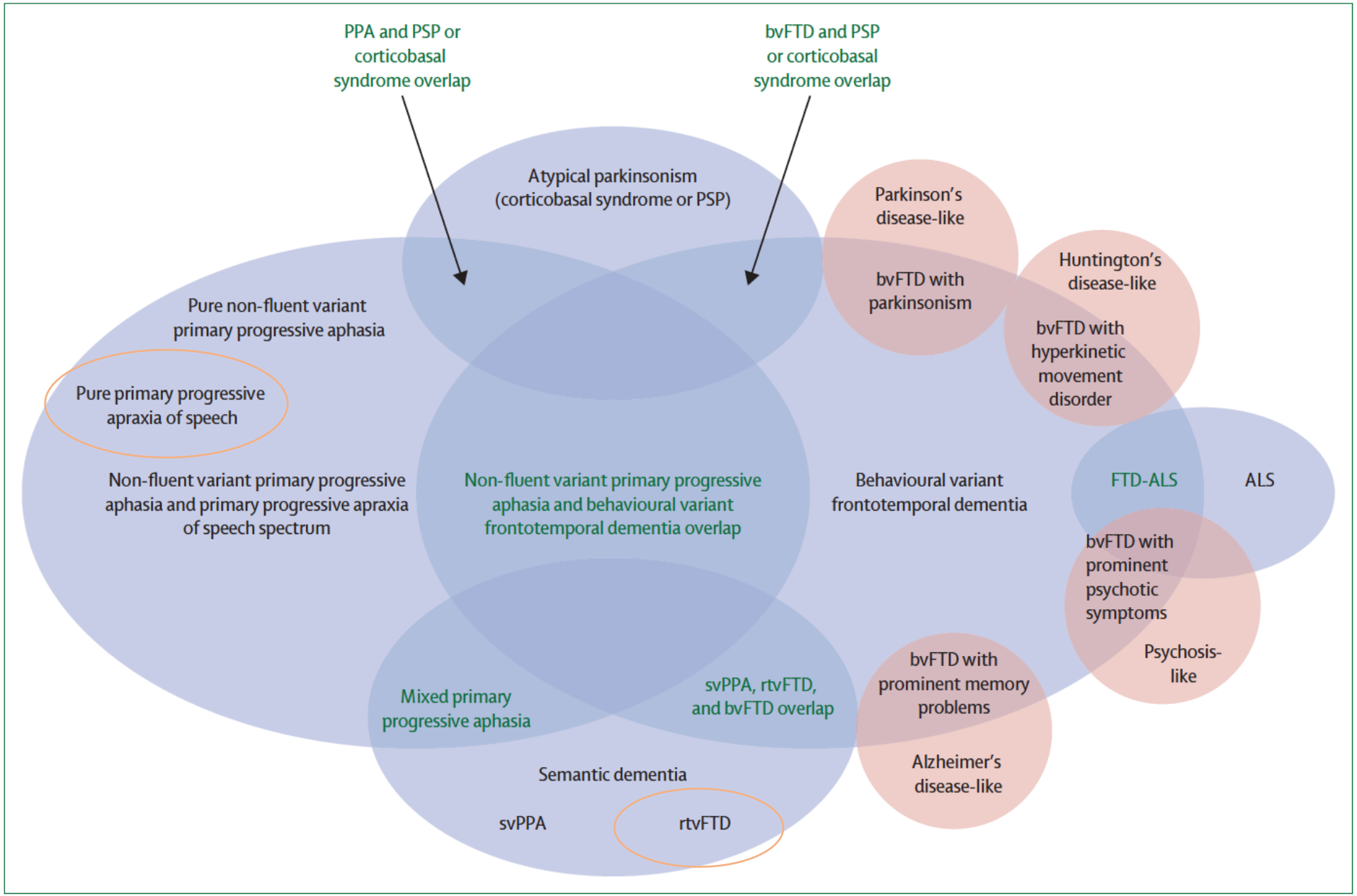
Review

Advances and controversies in frontotemporal dementia: diagnosis, biomarkers, and therapeutic considerations

Bradley F Boeve, Adam L Boxer, Fiona Kumfor, Yolande Pijnenburg, Jonathan D Rohrer

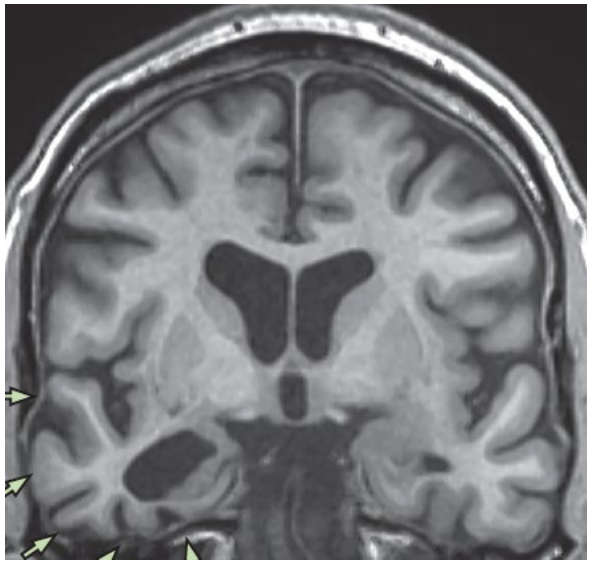
Lancet Neurol 2022; 21: 258–72

Frontotemporal dementia comprises a group of clinical syndromes that are characterised by progressive changes in



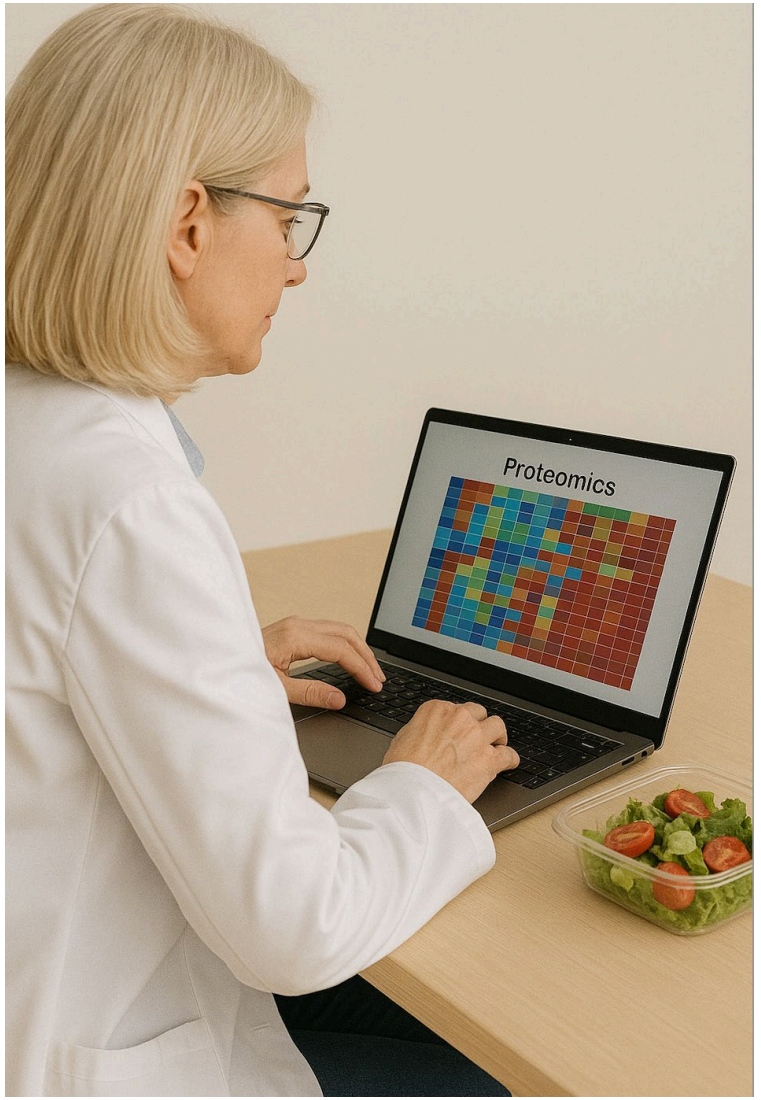
Prodromal: MCBMI

Rechts temporale variant FTD



- Non-verbale semantische stoornis
- Socio-emotionele stoornis
- Veranderde prioritering
- Relatief gespaarde functies: visuospatieel
  aandacht/ executief
  episodisch geheugen
  verbaal semantisch geheugen

Ziektemechanismen



Ziektemechanismen in dementie op jonge leeftijd

- Meerdere ziekteprocessen spelen een rol bij Alzheimer
- Pathologische eiwitneerslagen komen vaak samen voor
- Pathologische eiwitneerslagen worden ook elders in het lichaam gevonden
- Ziektemechanismen van FTD en ALS overlappen sterk

Alzheimer: meer dan 1 ziekte?

nature aging

Letter

https://doi.org/10.1038/s43587-023-00550-7

Cerebrospinal fluid proteomics in patients with Alzheimer's disease reveals five molecular subtypes with distinct genetic risk profiles

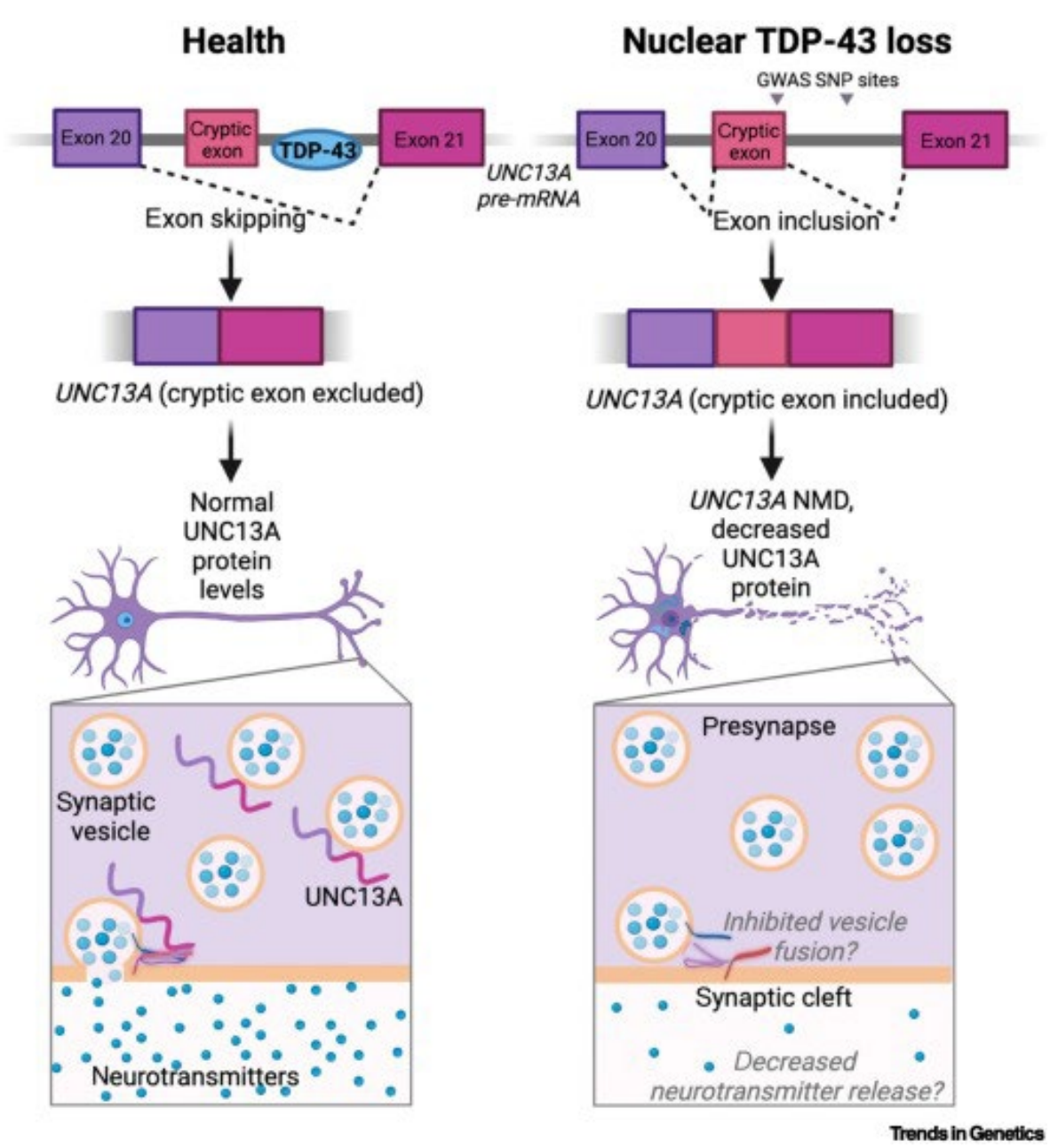
Received: 11 September 2023

Accepted: 29 November 2023

Published online: 9 January 2024

Check for updates

Betty M. Tijms[1,2] ✉, Ellen M. Vromen[1,2], Olav Mjaavatten[3], Henne Holstege[1,2,4], Lianne M. Reus[1,2,5], Sven van der Lee[1,2,6], Kirsten E. J. Wesenhagen[1,2], Luigi Lorenzini[7,8], Lisa Vermunt[2,9], Vikram Venkatraghavan[1,2], Niccoló Tesi[6,10], Jori Tomassen[1,2], Anouk den Braber[1,2,11], Julie Goossens[12], Eugeen Vanmechelen[12], Frederik Barkhof[7,13], Yolande A. L. Pijnenburg[1,2], Wiesje M. van der Flier[1,2,14], Charlotte E. Teunissen[2,9], Frode S. Berven[3] & Pieter Jelle Visser[1,2,15,16]



TDP-43 en rol in cryptic exon splicing

In FTD en ALS

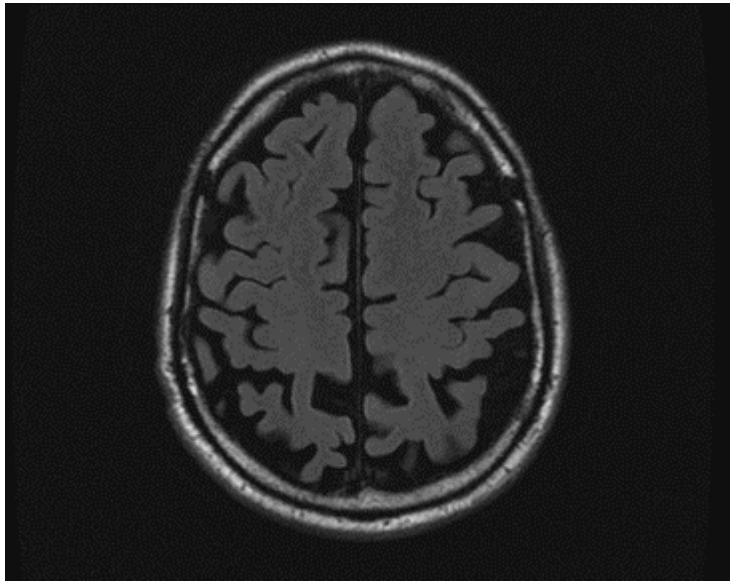
Bademosi et al., 2022

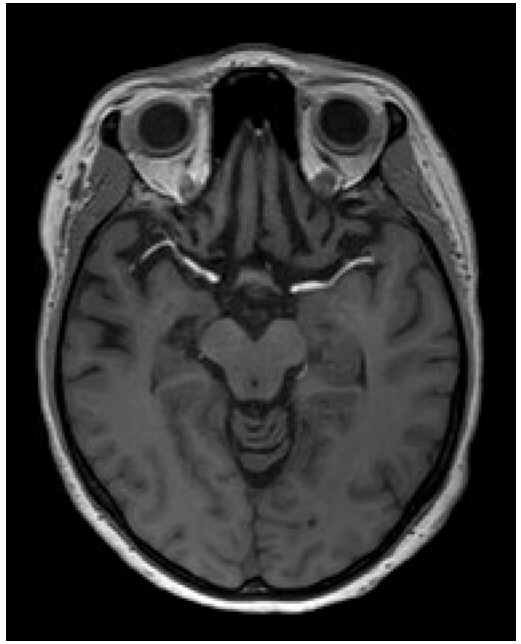
Biomarkers

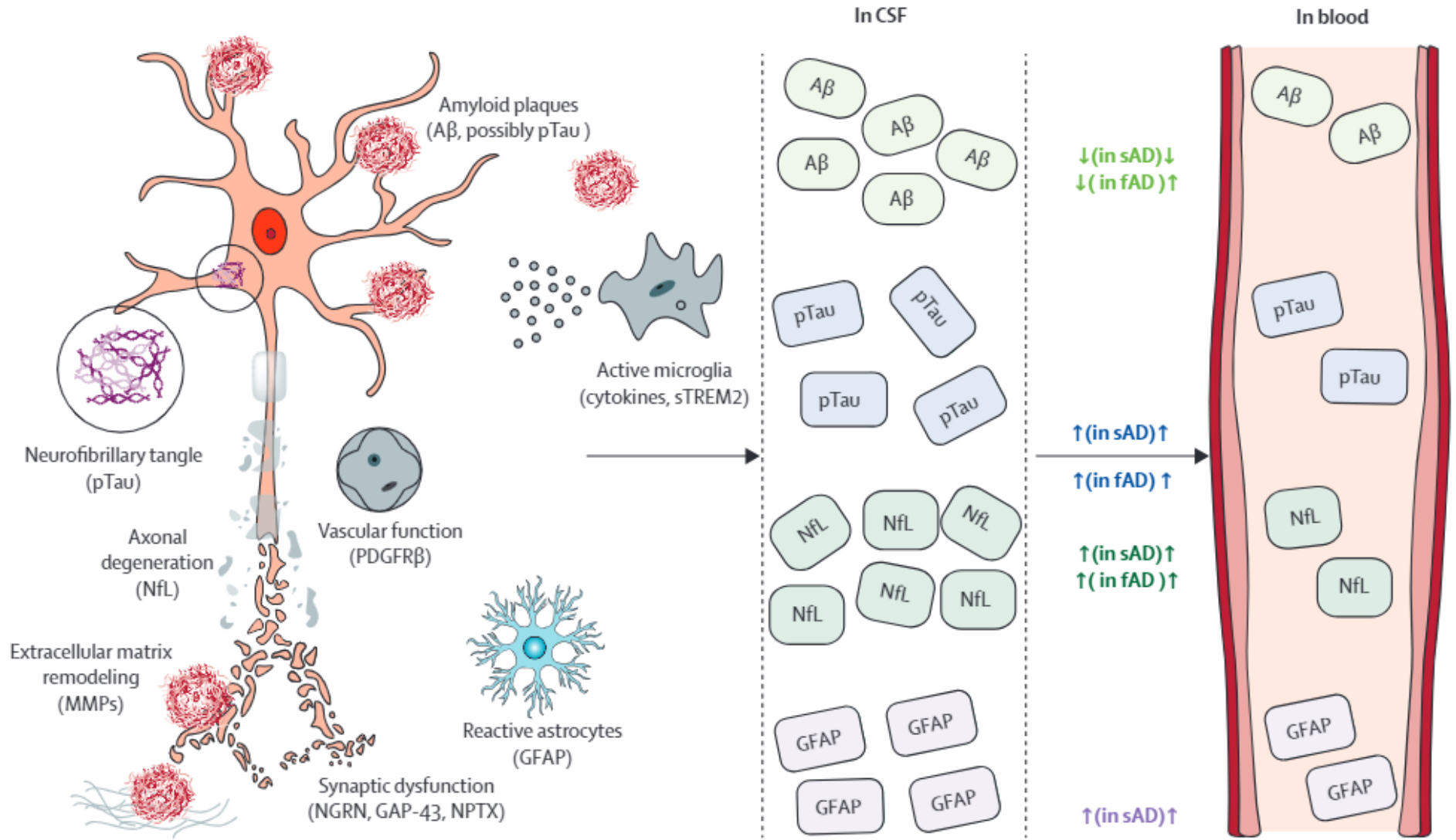
Biomarkers

- MRI-hersenen: patroonherkenning is belangrijk
- Diverse rollen voor PET
- Alzheimer biomarker blijft eerste stap
- Bloedbiomarkers zijn de toekomst?
- Indicaties genetisch onderzoek

Scans: goed kijken !

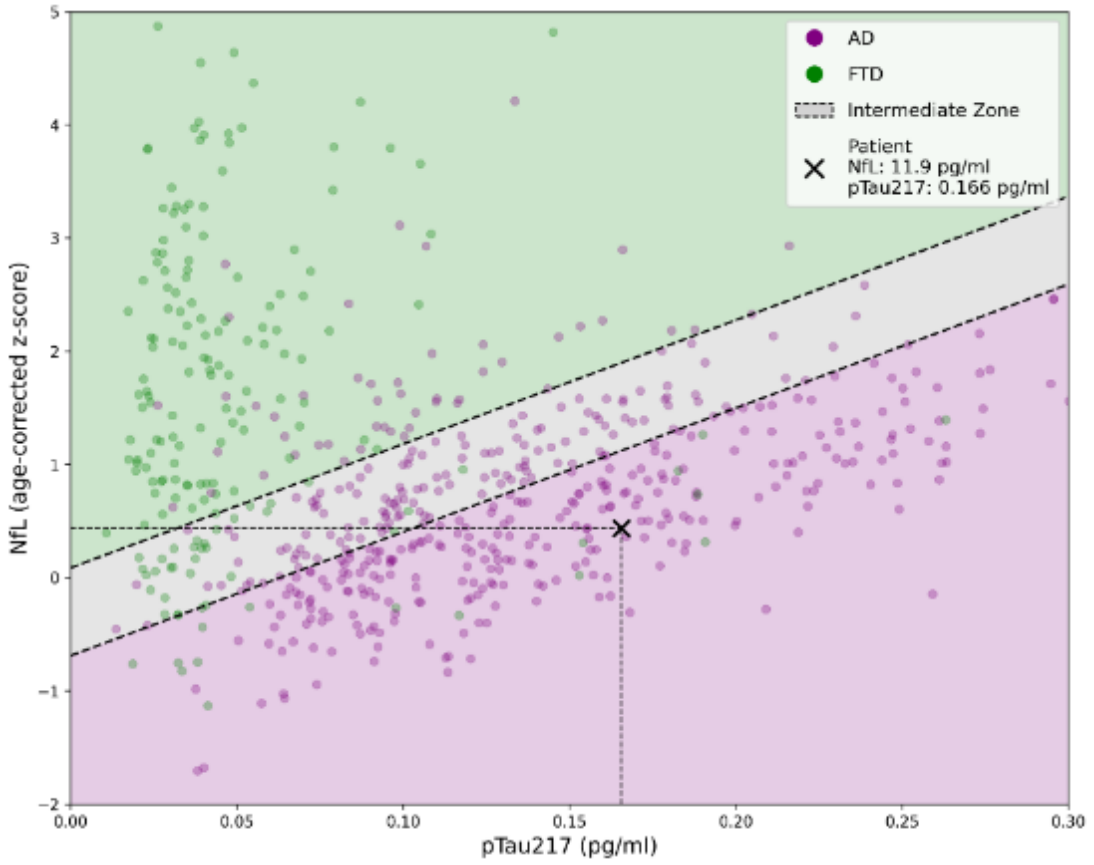


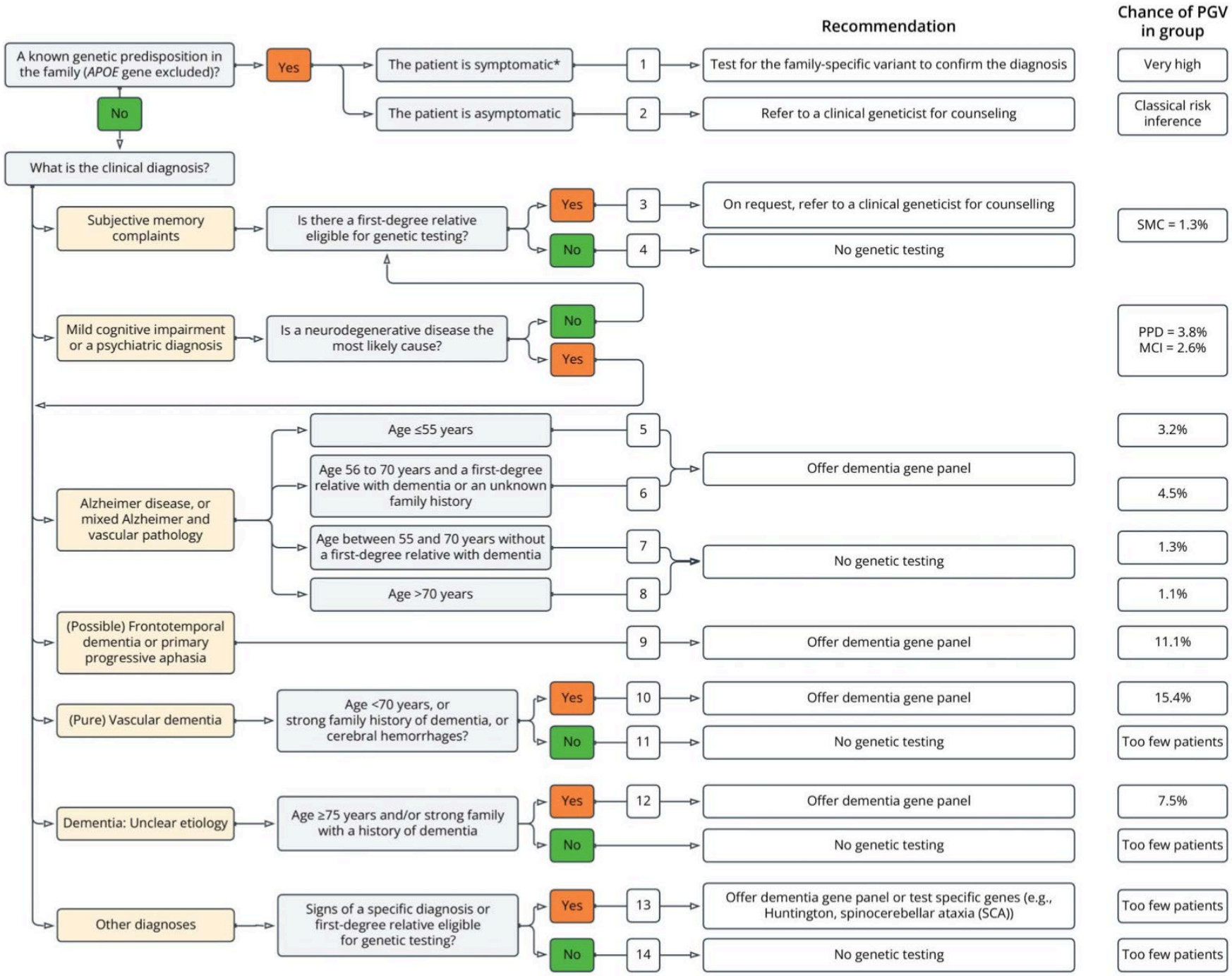




Teunissen CE et al., Lancet Neurol 2022

Bloed biomarkers





Van der Lee et al., 2025

doi:10.1093/brain/awaa018 BRAIN 2020: 0; 1–19 | 1

BRAIN
A JOURNAL OF NEUROLOGY

REVIEW ARTICLE

Recommendations to distinguish behavioural variant frontotemporal dementia from psychiatric disorders

Simon Ducharme,[1,2] Annemiek Dols,[3] Robert Laforce,[4] Emma Devenney,[5] Fiona Kumfor,[5] Jan van den Stock,[6] Caroline Dallaire-Théroux,[7] Harro Seelaar,[8] Flora Gossink,[3] Everard Vijverberg,[9] Edward Huey,[10] Mathieu Vandenbulcke,[11] Mario Masellis,[12] Calvin Trieu,[3] Chiadi Onyike,[13] Paulo Caramelli,[14] Leonardo Cruz de Souza,[14] Alexander Santillo,[15] Maria Landqvist Waldö,[16] Ramon Landin-Romero,[5] Olivier Piguet,[16] Wendy Kelso,[17] Dhamidhu Eratne,[17] Dennis Velakoulis,[17] Manabu Ikeda,[18] David Perry,[19] Peter Pressman,[20] Bradley Boeve,[21] Rik Vandenberghe,[22] Mario Mendez,[23] Carole Azuar,[24] Richard Levy,[24] Isabelle Le Ber,[24] Sandra Baez,[25] Alan Lerner,[26] Ratnavalli Ellayosyula,[27] Florence Pasquier,[28] Daniela Galimberti,[29,30] Elio Scarpini,[29,30] John van Swieten,[8] Michael Hornberger,[31] Howard Rosen,[32] John Hodges,[5] Janine Diehl-Schmid[33] and Yolande Pijnenburg[9]

Aanbevelingen:

- Gebruik standaard schalen / vragenlijsten
- MRI-hersenen
- Bepaling Alzheimer biomarkers
- Bepaling serum neurofilament
- Genetisch testen: in elk geval C9orf
- Rol van FDG-PET

Therapie

Therapie

- Therapie voor monogenetische aandoeningen
- Antilichaam gebaseerde therapie
- In welke fase behandelen?
- Nieuwste ontwikkelingen in Nederland / Europa

Het landschap van geneesmiddelen ontwikkeling bij de ziekte van Alzheimer

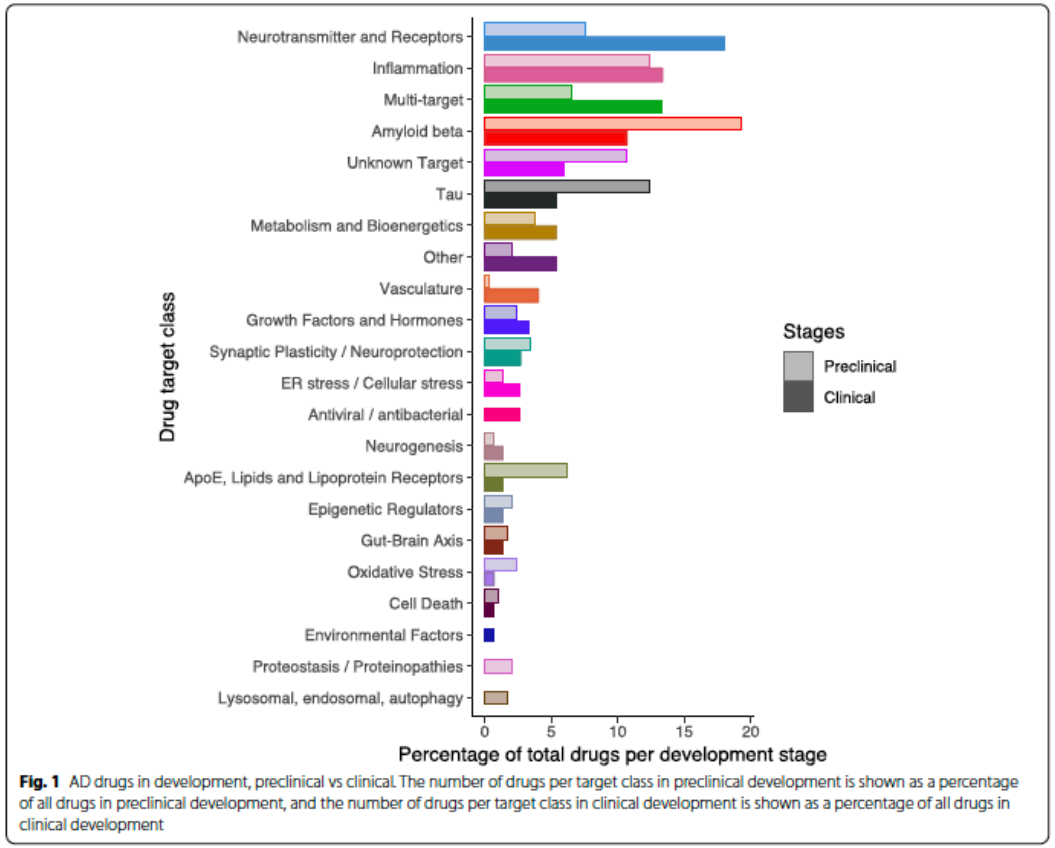
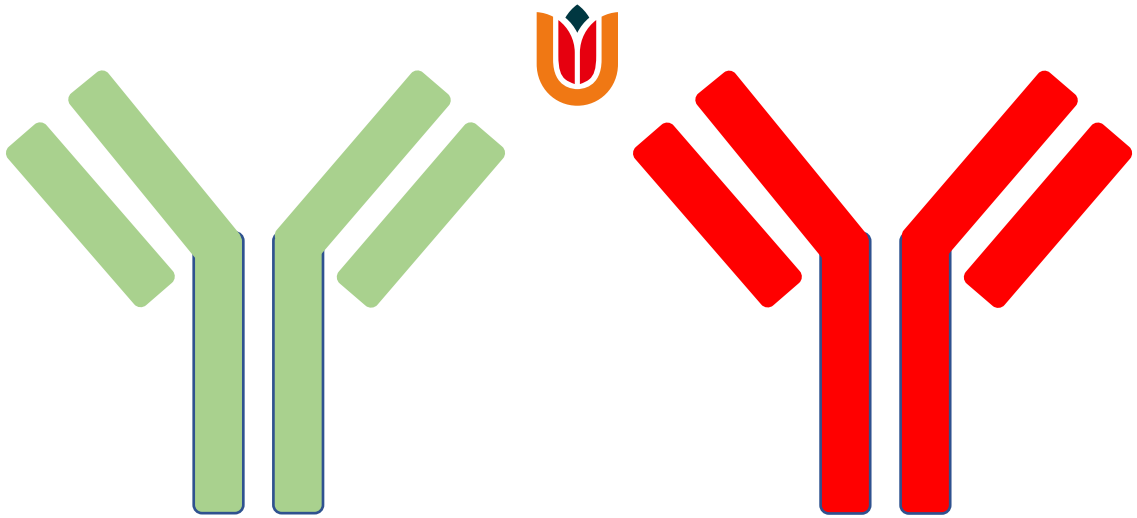


Fig. 1 AD drugs in development, preclinical vs clinical. The number of drugs per target class in preclinical development is shown as a percentage of all drugs in preclinical development, and the number of drugs per target class in clinical development is shown as a percentage of all drugs in clinical development

RESEARCH Open Access

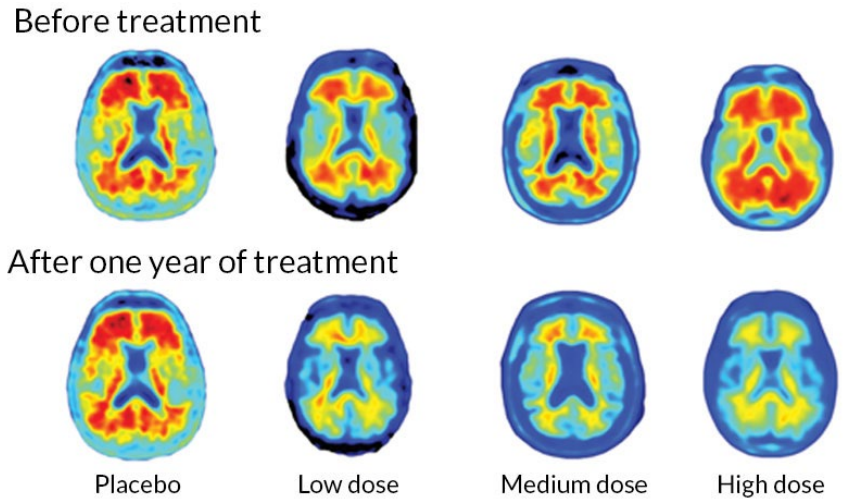
The Alzheimer's disease drug development landscape

Pieter van Bokhoven[1*], Arno de Wilde[2], Lisa Vermunt[3,4], Prisca S. Leferink[1], Sasja Heetveld[1], Jeffrey Cummings[5], Philip Scheltens[2,3] and Everard G. B. Vijverberg[3]



Lecanemab

Donanemab

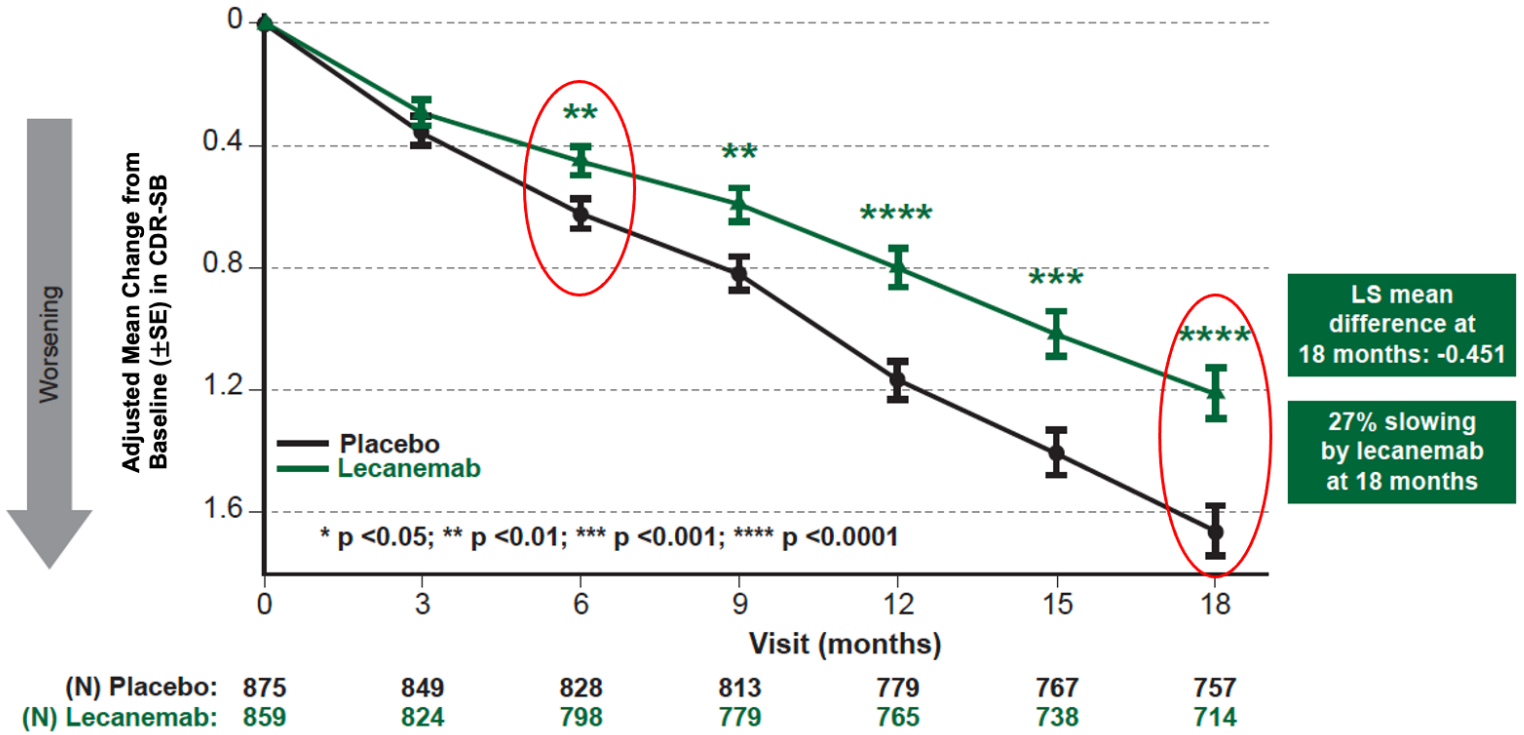


Amyloid PET imaging

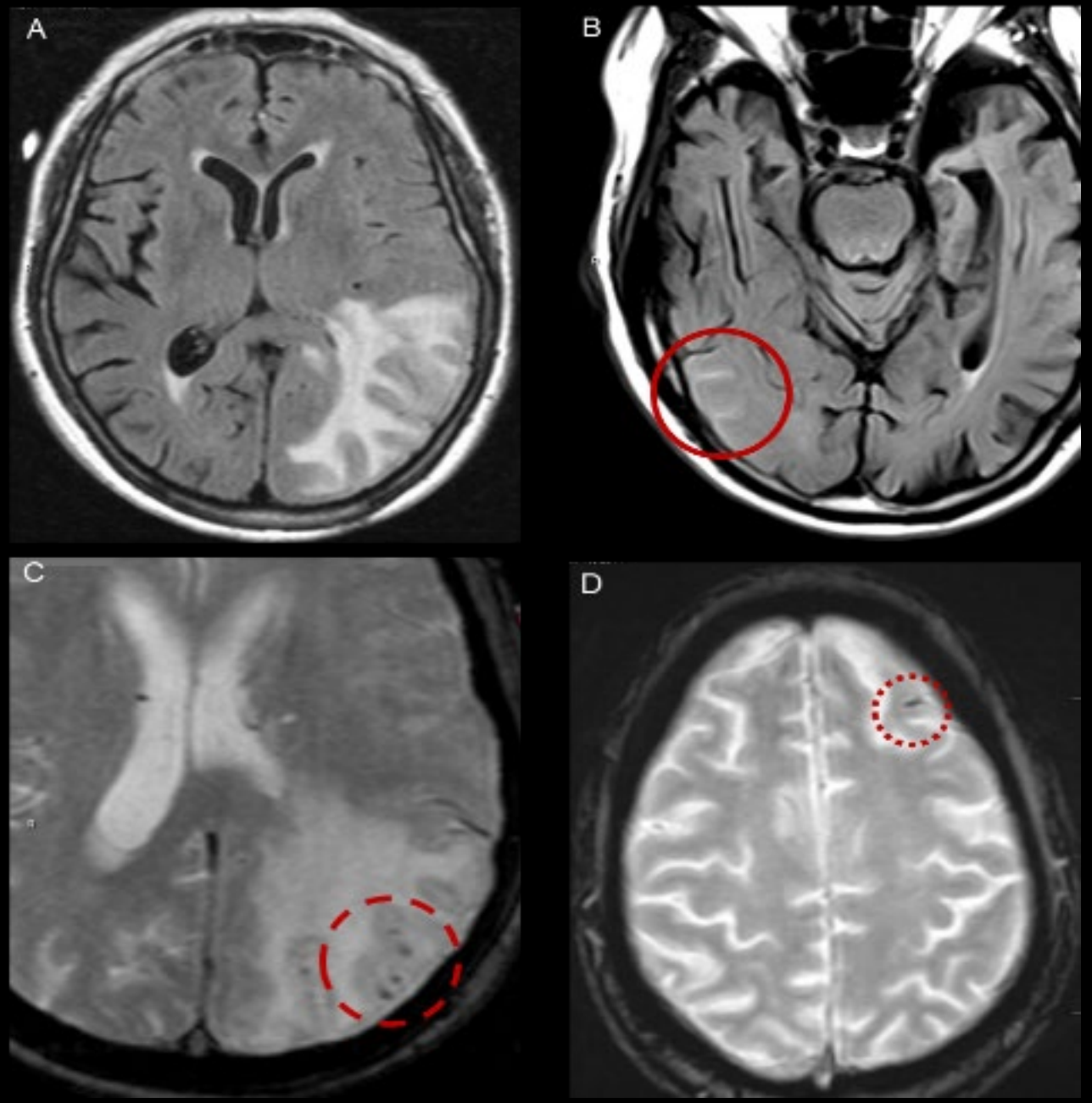
Lecanemab

Clarity AD Primary Endpoint: CDR-SB

Lecanemab Significantly Slowed Disease Progression on CDR-SB by 27% at 18 Months and at All Time Points Beginning at 6 Months



Note: Based on modified intention-to-treat analysis population. Adjusted mean change from baseline, SE and p-value are derived using mixed model repeat measures (MMRM) with treatment group, visit, treatment group by visit interaction, clinical subgroup, use of Alzheimer's disease symptomatic medication at baseline, ApoE4 carrier status, region, baseline value by visit interaction as fixed effects, and baseline value as covariate.
CDR-SB, Clinical Dementia Rating, sum of boxes; LS, least squares; SE, standard error.


A
B
C
D

Gentherapie in FTD

Simultaneous bilateral Infusions

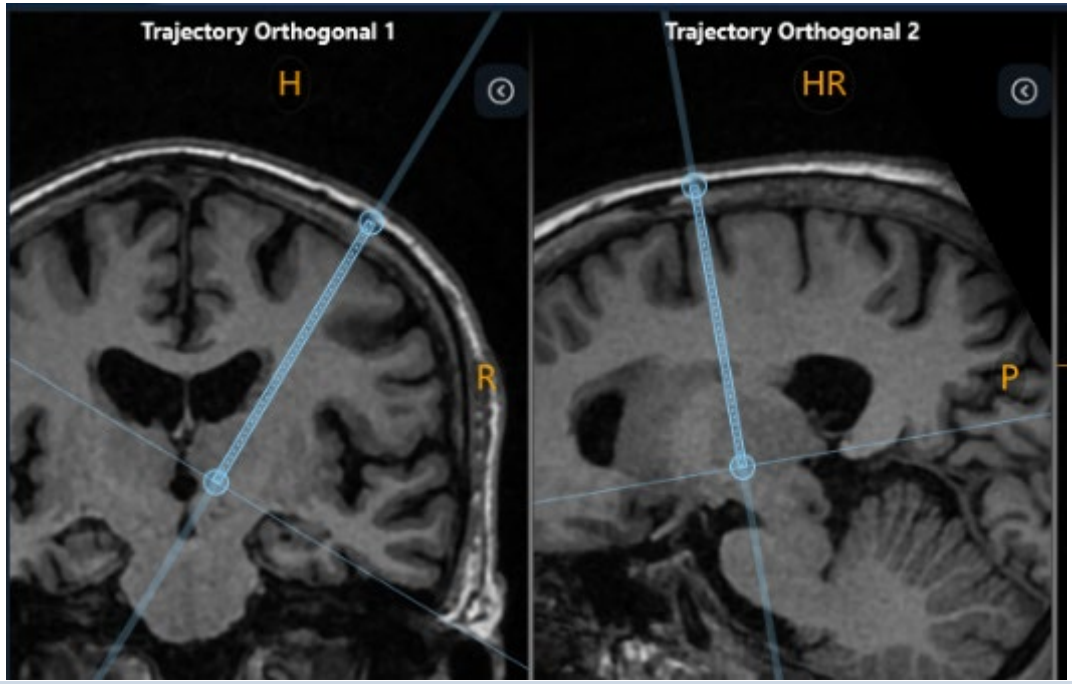
Percutaneously mounted stereotaxic frame

Smartflow™ Neuroventricular Cannula

Trajectory planning for intrathalamic AVB-101

ASPIRE·FTD

Trajectory plans developed based upon **patient-specific** anatomic considerations (atrophy, gyral/sulcal pattern) with review by **global expert neurosurgical committee**



Two frontal trajectories