Fondazione Caript

14° CONVEGNO NAZIONALE SUI CENTRI DIURNI ALZHEIMER

GRUPPO ITALIANO CENTRI DIURNI ALZHEIMER

Centri Diurni Monteoliveto
Pistoia

11-12 ottobre 2024

Gli anticorpi monoclonali per la malattia di Alzheimer: prospettive realistiche e ostacoli

Camillo Marra

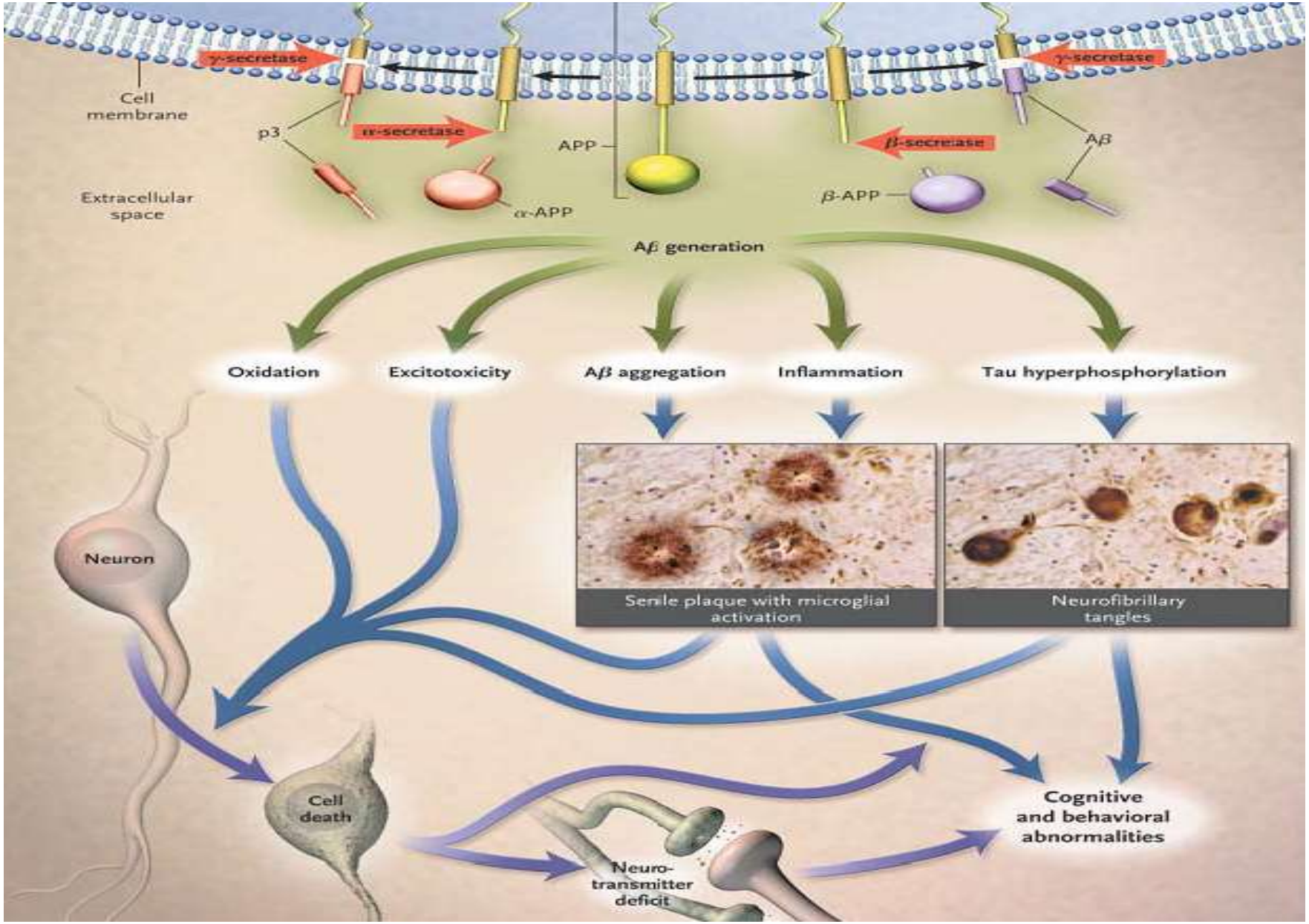
Clinica della Memoria

Fondazione Policlinico Agostino Gemelli- IRCCS

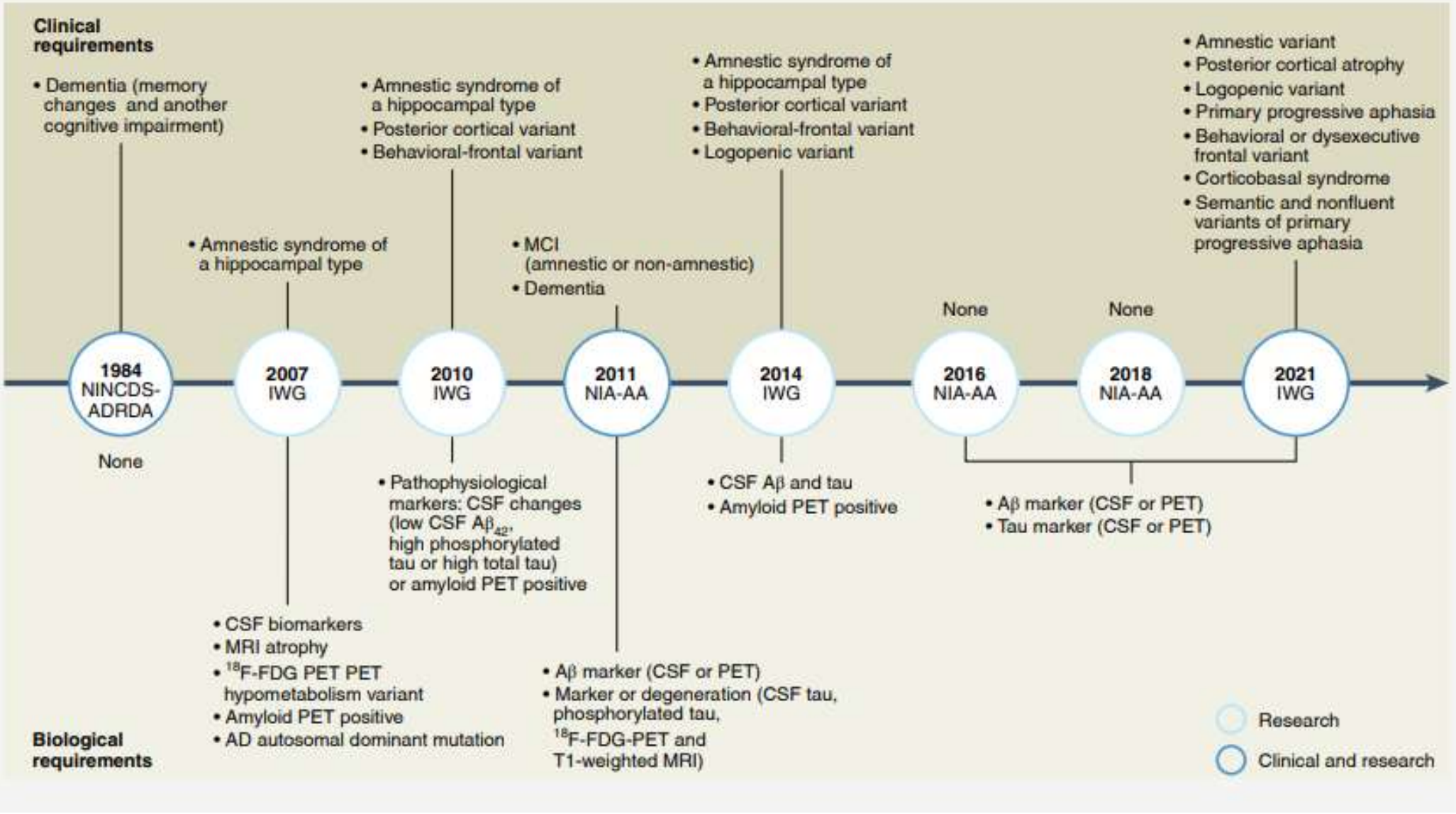
UCSC – Roma-Milano

Disclosures

- Camillo Marra è membro del Tavolo Nazionale Demenze e partecipa alla redazione del nuovo Piano Nazionale Demenze
- È membro del Panel on Dementia dell'EAN.
- Ha ricevuto fondi di supporto alla ricerca da Ministero della Salute, AIFA, EU commission Horizon Program, EU Joint Programme – Neurodegenerative Disease Research (JPND), PROMIS.
- Ha ricevuto compensi come speaker per EISAI, BIOGEN, ELI LILLY, NOVONORDISK, ANGELINI, ROCHE, PIAM, LUNDBECK, NEOPHARMED,
- Ha partecipato a board e tavoli di lavoro per BIOGEN, EISAI, ELI LILLY, NOVONORDISK, PIAM



Hardy J, Selkoe DJ.
The amyloid hypothesis of Alzheimer's disease: progress and problems on the road to therapeutics.
Science 297(5580), 353–356 (2002).



Evolution of the diagnostic criteria for AD

Diagnosing AD: A Paradigm Shift

DA
L'AD come entità clinico-patologica[1]

Diagnosi e trattamento basati principalmente sui sintomi[2]

- [redacted]
- L'AD viene spesso diagnosticato troppo tardivamente, allo stadio di demenza da lieve a moderata[2]
- [redacted]
- Fino a 1 paziente su 6 con diagnosi clinica di probabile AD è risultato essere stato diagnosticato in modo errato[3]

A
L'AD come costrutto clinico-biologico[1]

Diagnosi e trattamento basati su fenotipi clinici e biomarcatori in vivo[2]

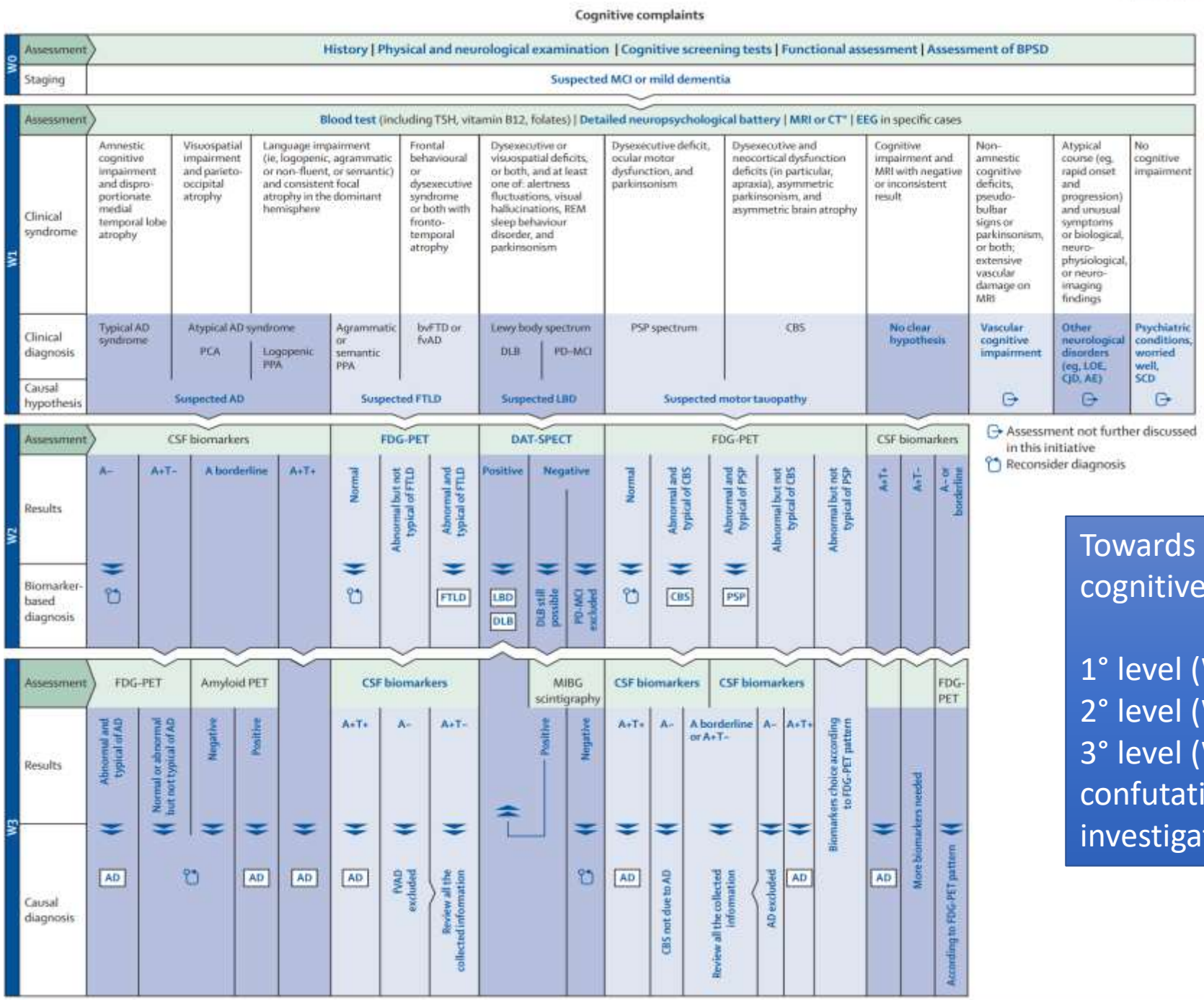
- [redacted]
- L'uso di biomarcatori CSF/PET può aggiungere precisione alla diagnosi e migliorare la fiducia diagnostica dei medici[4-6]
- 
- L'accesso ai dati dei biomarcatori può influire sulle decisioni terapeutiche nei pazienti con MCI o demenza[5,7]

AD=Alzheimer's Disease; CSF=Cerebrospinal Fluid; MCI=Mild Cognitive Impairment; PET=Positron Emission Tomography.

1. Dubois B, et al. *Lancet Neurol*. 2021;20(6):484-496. 2. Hampel H, et al. *Nat Aging*. 2022;2:692-703. 3. Beach TG, et al. *J Neuropathol Exp Neurol*. 2012;71:266-273. 4. Mouton-Liger F, et al. *J Neurol*. 2014;261(1):144-151. 5. Rabinovici GD, et al. *JAMA*. 2019;321(13):1286-1294. 6. Duits FH, et al. *Alzheimers Dement*. 2015;11(5):523-532. 7. de Wilde A, et al. *JAMA Neurol*. 2018;75(9):1062-1070.

European intersocietal recommendations for the biomarker-based diagnosis of neurocognitive disorders

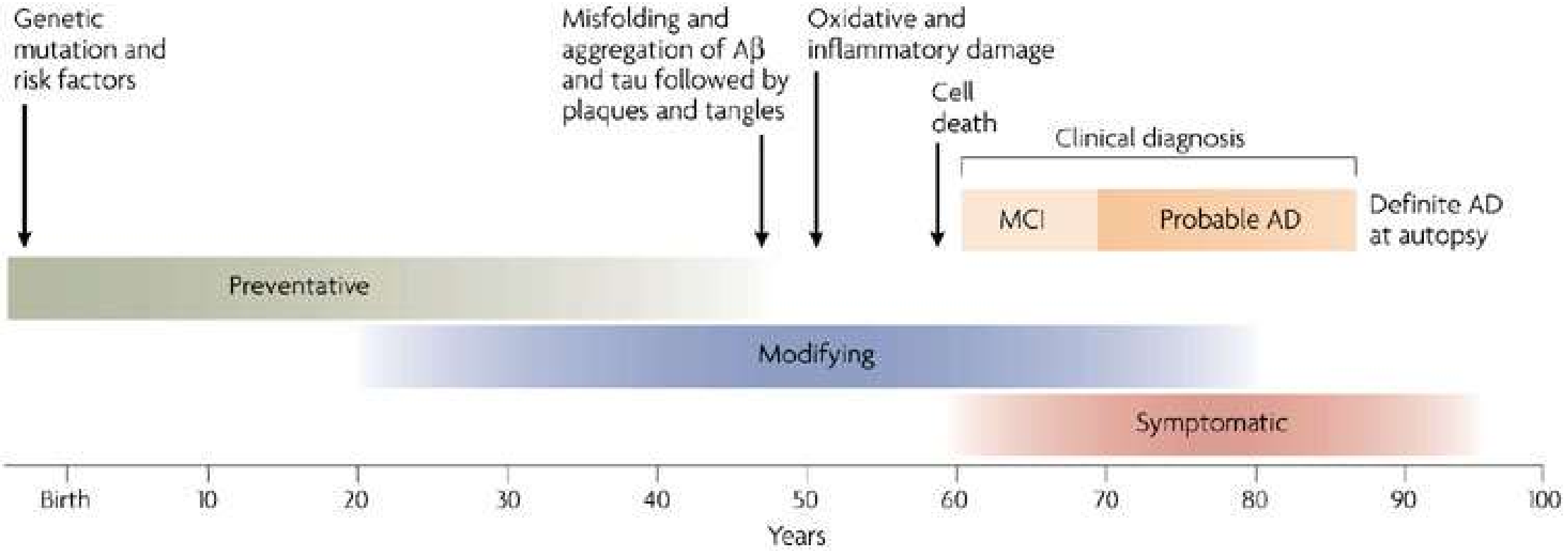
Giovanni B Frisoni, Cristina Festari, Federico Massa, Matteo Cotta Ramusino, Stefania Orini, Dag Aarsland, Federica Agosta, Claudio Babiloni, Barbara Borroni, Stefano F Cappa, Kristian S Frederiksen, Lutz Froelich, Valentina Garibotto, Alexander Hausner, Frank Jessen, Anita Kamondi, Roy PC Kessels, Silvia D Morbelli, John T O'Brien, Markus Otto, Armand Perret-Liaudet, Francesca B Pizzini, Mathieu Vandenbulcke, Rita Vannini, Frans Verhey, Meike W Vernooij, Tarek Yousry, Mercè Boada Rovira, Bruno Dubois, Jean Georges, Oskar Hansson, Craig W Ritchie, Philip Scheltens, Wiesje M van der Flier, Flavio Nobili



Towards a new patient journey of patients with cognitive decline: Delphi consensus in 5 rounds

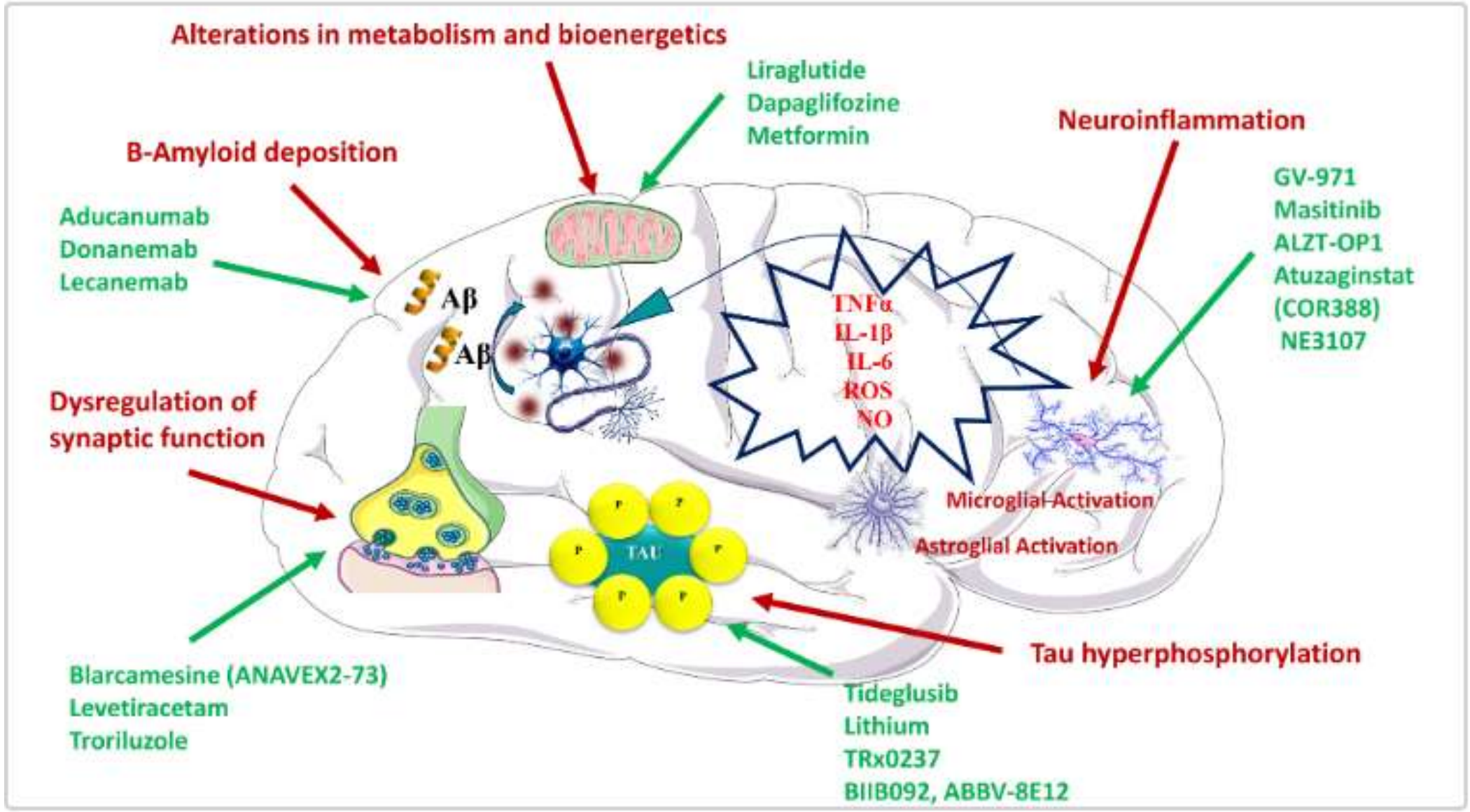
1° level (W1) clinical definition
2° level (W2) first level investigation
3° level (W3) second level investigation and confutational plan for second round 3° level investigation

GB Frisoni et al. Lancet 2024

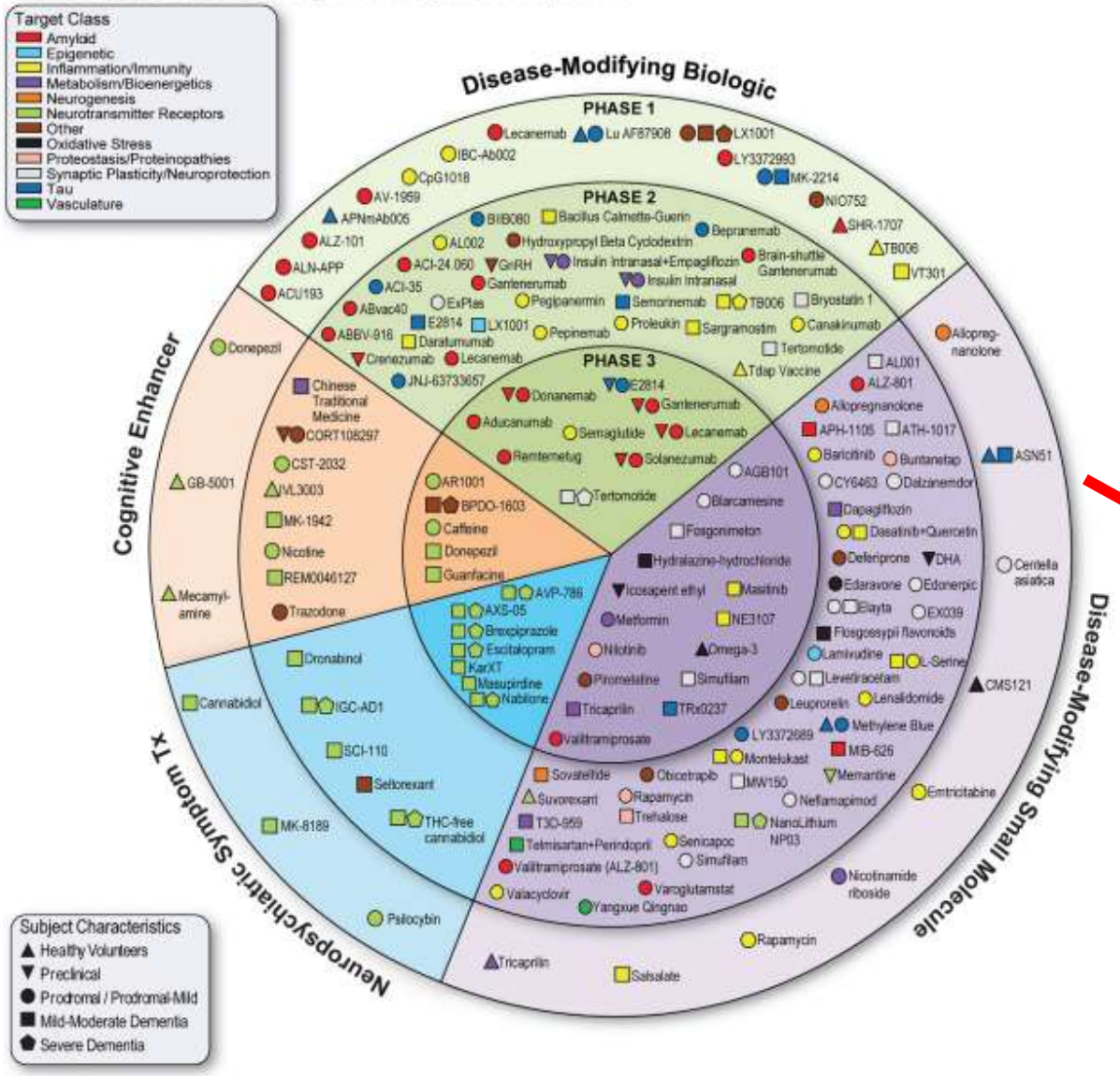


Cronologia ipotetica per l'insorgenza e la progressione della neurodegenerazione e della demenza AD sporadica e familiare. Ci sono pochi biomarcatori predittivi per l'Alzheimer (AD), ad eccezione delle mutazioni genetiche che sono patogene per l'AD familiare, che potrebbero essere misurate

Nature Reviews Drug Discovery May 2007, 6(4):295-303


Alterations in metabolism and bioenergetics
Liraglutide
Dapaglifozine
Metformin
B-Amyloid deposition
Aducanumab
Donanemab
Lecanemab
Aβ
Aβ
Neuroinflammation
GV-971
Masitinib
ALZT-OP1
Atuzaginstat
(COR388)
NE3107
TNFα
IL-1β
IL-6
ROS
NO
Dysregulation of
synaptic function
TAU
Microglial Activation
Astroglial Activation
Blarcamesine (ANAVEX2-73)
Levetiracetam
Troriluzole
Tau hyperphosphorylation
Tideglusib
Lithium
TRx0237
BIIB092, ABBV-8E12

2023 Alzheimer's Drug Development Pipeline

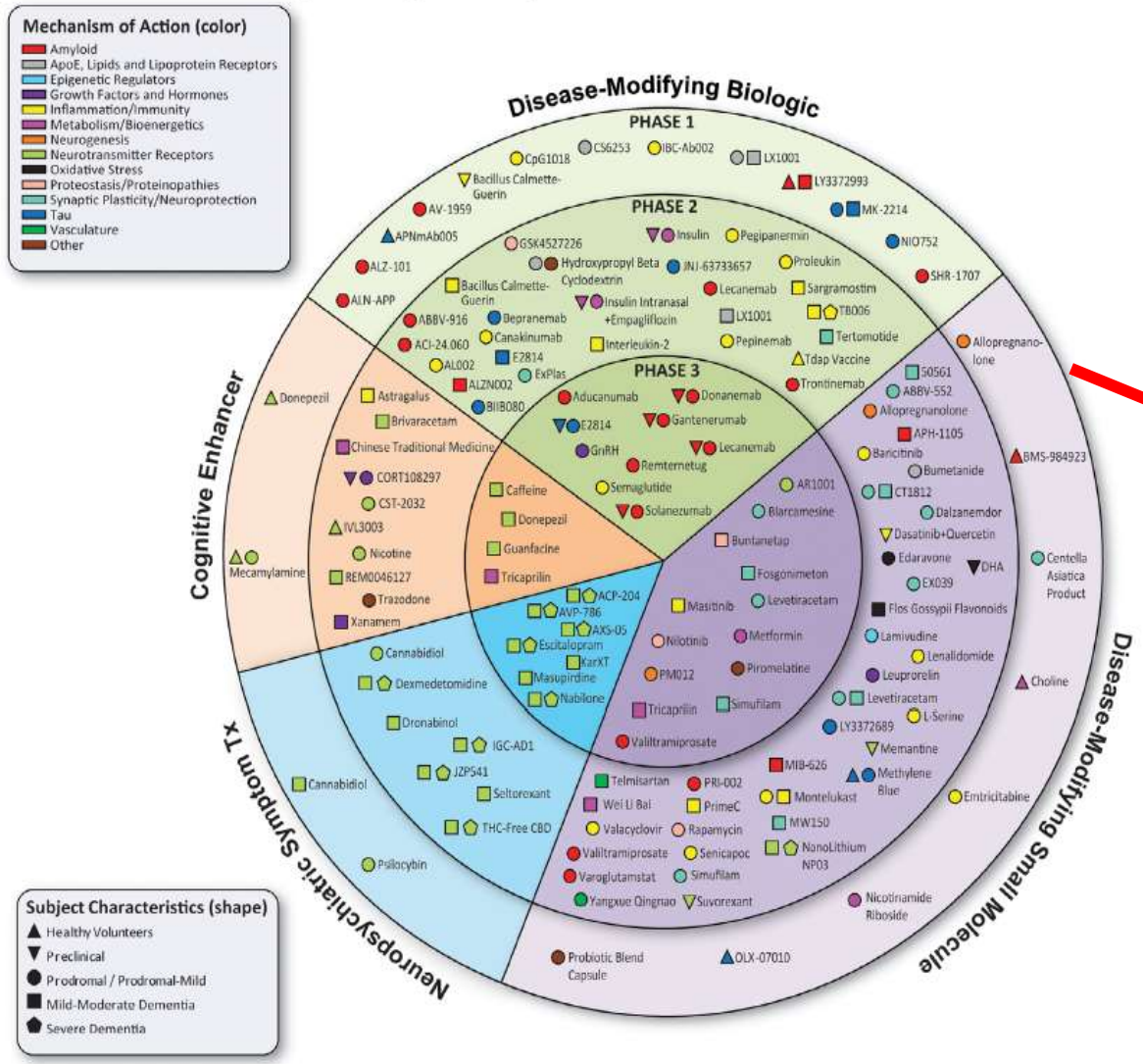


HIGHLIGHTS

- There are currently 187 trials assessing 141 drugs for the treatment of Alzheimer's disease (AD).
- Drugs in the AD pipeline address a variety of pathological processes.
- More than 57,000 participants will be required to populate all currently registered trials.

Cummings JL. Translational research and clinical interventions

2024 Alzheimer's Drug Development Pipeline



Highlights

- In the 2024 Alzheimer's disease drug development pipeline, there are 164 clinical trials assessing 127 drugs.
- The 2024 Alzheimer's disease drug development pipeline has contracted compared to the 2023 Alzheimer pipeline with fewer trials, fewer drugs, and fewer new chemical entities.

Cummings JL. Translational research and clinical interventions

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WSJ BLOGS

Health Blog

WSJ's blog on health and the business of health.

July 19, 2011, 12:05 PM

AAIC: Cognitive Impact From Lilly's Semagacestat Didn't Reverse

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Alzheimer's Disease Latest N

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Beta-Amyloid Inhibitor Fails in Alzheimer's Trial

By John Gever, Senior Editor, MedPage Today
Published: December 15, 2009

Reviewed by Zalman S. Agus, MD; Emeritus Professor
University of Pennsylvania School of Medicine and Dorothy Caputo, MA, RN, BC-ADM, CDE

investigational drug to reduce beta-
yloid protein deposition failed to prevent
heimer's disease progression in a Phase III
dy, after the drug had shown promise in an
lier trial.

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AAN: Tramiprosate Ineffective in Alzheimer's Disease

By Kristina Fiore, Staff Writer, MedPage Today
Published: April 30, 2009

Reviewed by Dori F. Zaleznik, MD; Associate Clinical Professor of

SEATTLE, April 30 -- Tramiprosate (Alzhemed) appears to hold no benefit for patients with mild-to-moderate Alzheimer's disease, researchers said here.

A randomized, controlled trial of more than 1,000 patients found no significant difference in cognitive functioning or dementia between treatment and control patients.

"There were no beneficial effects on tests of cognitive functioning or dementia," said Paul Aisen, M.D., of Georgetown University Hospital, who presented the findings at a late-breaking session of the American Academy of

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Performing your original search, ***an1792***, in PubMed will retrieve *98* records.

Neurology. 2005 May 10;64(9):1553-62.

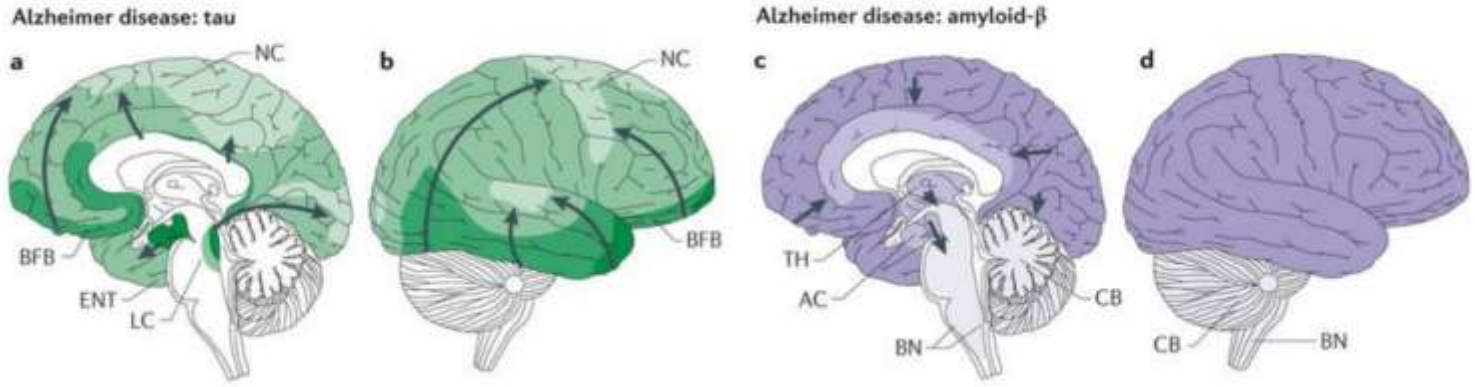
Clinical effects of Abeta immunization (AN1792) in patients with AD in an interrupted trial.

Gilman S, Koller M, Black RS, Jenkins L, Griffith SG, Fox NC, Eisner L, Kirby L, Rovira MB, Forette F, Orgogozo JM; AN1792(QS-21)-201 Study Team.

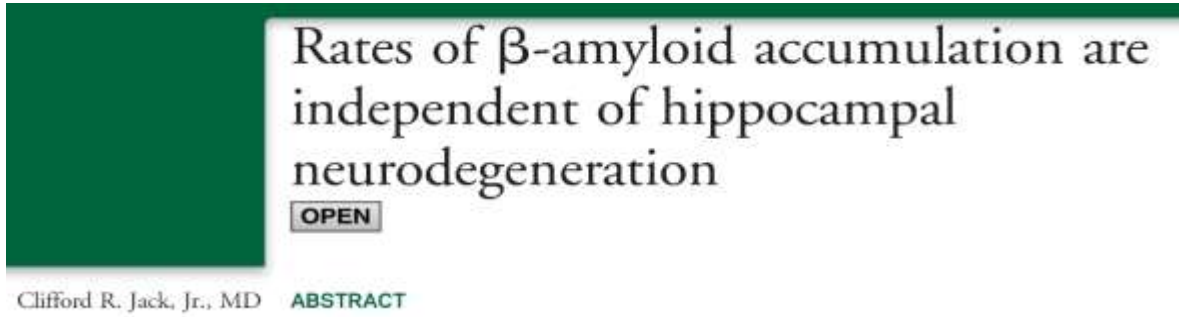
Department of Neurology, University of Michigan, 300 N. Ingalls 3D15, Ann Arbor, MI 48109-0489, USA. sgilman@umich.edu

Criticità

- Diversa distribuzione delle lesioni tau e dell'attivazione infiammatoria rispetto alla deposizione di Beta amiloide
- **(ipotesi driver)**



- Tempo Variabile dall'esordio della patologia amiloidea e lo sviluppo di neurodegenerazione non determinato e prevedibile sebbene la beta amiloide accelleri la neurodegenerazione
- **(ipotesi trigger)**


Rates of β-amyloid accumulation are independent of hippocampal neurodegeneration

OPEN

Clifford R. Jack, Jr., MD ABSTRACT

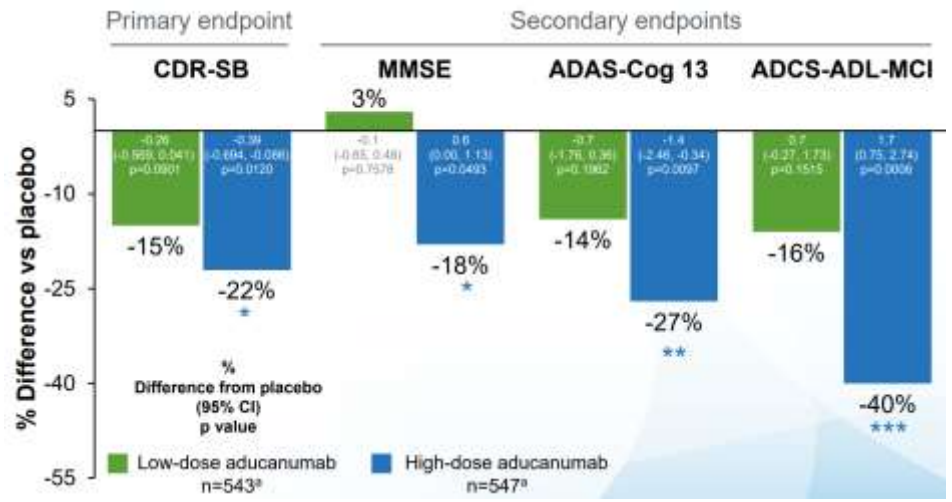
- Ruolo dell'amiloide nella età avanzata che da patogeno diventa parafisiologico e non correlato alla neurodegenerazione o possibilità di neurodegenerazione senza amiloide.
- **(Ipotesi treshold)**

Aducanumab's rise, fall and resurrection

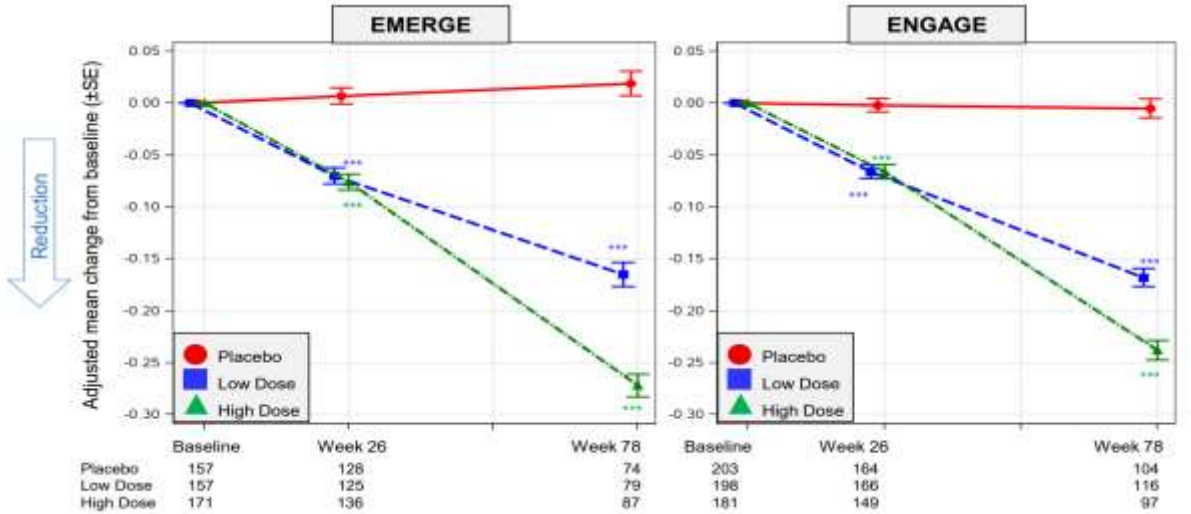
221AD301 Phase 3 Study of Aducanumab (BIIB037) in Early Alzheimer's Disease (ENGAGE)

221AD302 Phase 3 Study of Aducanumab (BIIB037) in Early Alzheimer's Disease (EMERGE)

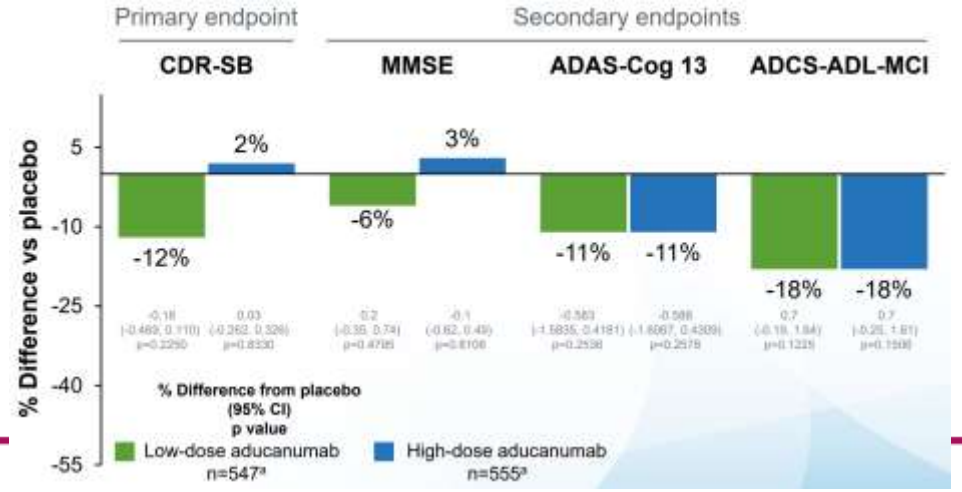
Endpoints – EMERGE (larger dataset)



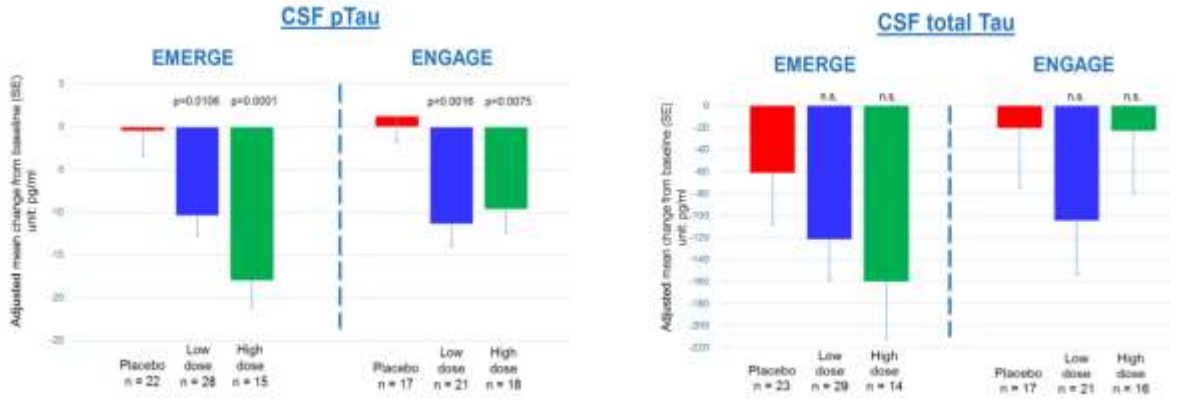
Dose- and time-dependent reduction in β-amyloid pathology



Endpoints – ENGAGE (larger dataset)



Reduction in CSF biomarkers of tau pathology and neurodegeneration at 18 months



CSF pTau and CSF total Tau measured at 18 months (data analyzed using ANCOVA); n.s. = not significant

Aducanumab's rise, fall and resurrection

FDA's Decision to Approve New Treatment for Alzheimer's Disease

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Today FDA approved Aduhelm (aducanumab) to treat patients with Alzheimer's disease using the Accelerated Approval pathway, under which the FDA approves a drug for a serious or life-threatening illness that may provide meaningful therapeutic benefit over existing treatments when the drug is shown to have an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit to patients and there remains some uncertainty about the drug's clinical benefit.

This approval is significant in many ways. Aduhelm is the first novel therapy approved for Alzheimer's disease since 2003. Perhaps more significantly, Aduhelm is the first treatment directed at the underlying pathophysiology of Alzheimer's disease, the presence of amyloid beta plaques in the brain. The clinical trials for Aduhelm were the first to show that a reduction in these plaques—a hallmark finding in the brain of patients with Alzheimer's—is expected to lead to a reduction in the clinical decline of this devastating form of dementia.

We are well-aware of the attention surrounding this approval. We understand that Aduhelm has garnered the attention of the press, the Alzheimer's patient community, our elected officials, and other interested stakeholders. With a treatment for a serious, life-threatening disease in the balance, it makes sense that so many people were following the outcome of this review. Further, the data included in the applicant's submission were highly complex and left residual uncertainties regarding clinical benefit. There has been considerable public debate on whether Aduhelm should be approved. As is often the case when it comes to interpreting scientific data, the expert community has offered differing perspectives.

At the end of the day, we followed our usual course of action when making regulatory decisions in situations where the data are not straightforward. We examined the clinical trial findings with a fine-tooth comb, we solicited input from the Peripheral and Central Nervous System Drugs Advisory Committee, we listened to the perspectives of the patient community, and we reviewed all relevant data. We ultimately decided to use the Accelerated Approval pathway—a pathway intended to provide earlier access to potentially valuable therapies for patients with serious diseases where there is an unmet need, and where there is an expectation of clinical benefit despite some residual uncertainty regarding that benefit. In determining that the application met the requirements for Accelerated Approval, the Agency concluded that the benefits of Aduhelm for patients with Alzheimer's disease outweighed the risks of the therapy.

Aduhelm is approved under the accelerated approval pathway, which provides patients with a serious disease earlier access to drugs when there is an expectation of clinical benefit despite some uncertainty about the clinical benefit.

Accelerated approval is based upon the drug's effect on a surrogate endpoint — an endpoint that reflects the effect of the drug on an important aspect of the disease — where the drug's effect on the surrogate endpoint is expected, but not established, to predict clinical benefit. In the case of Aduhelm, the surrogate endpoint is the reduction of amyloid beta plaque. The accelerated approval pathway requires the company to verify clinical benefit in a post-approval trial. If the sponsor cannot verify clinical benefit, FDA may initiate proceedings to withdraw approval of the drug.

June 10, 2021 By this date, three standing members of the FDA PCNS Drugs Advisory Committee had resigned in protest over aducanumab's approval

July 13, 2021 A number of US private health insurance companies announced they would not cover Aduhelm, as they considered that a clinical benefit was not established

July 14, 2021 The Cleveland Clinic medical center and Mount Sinai health system announced they will not administer Aduhelm to patients until the HHS-OIG affirms the integrity of the FDA–Biogen relationship and reaffirms the FDA's basis for approving the drug

June 25, 2021 Two US House of Representatives committees launched an investigation into the approval and pricing of Biogen's aducanumab

An Observational Study of Aducanumab-avwa in Participants With Alzheimer's Disease in the US

Official Title: International Collaboration for Real-World Evidence in Alzheimer's Disease (ICARE AD)

Actual Study Start Date : November 18, 2021
Estimated Primary Completion Date : October 1, 2026
Estimated Study Completion Date : October 1, 2026

Aducanumab's rise, fall and resurrection

DIORNI ALZHEIMER

Refusal of the marketing authorisation for Aduhelm (aducanumab)

The European Medicines Agency has recommended the refusal of the marketing authorisation for Aduhelm, a medicine intended for the treatment of Alzheimer's disease.

The Agency issued its opinion on 16 December 2021. The company that applied for authorisation, Biogen Netherlands B.V., may ask for re-examination within 15 days of receiving the opinion.

What were the main reasons for refusing the marketing authorisation?

The European Medicines Agency noted that although Aduhelm reduces amyloid beta in the brain, the link between this effect and clinical improvement had not been established. Results from the main studies were conflicting and did not show overall that Aduhelm was effective at treating adults with early stage Alzheimer's disease.

In addition, the studies did not show that the medicine was sufficiently safe as images from brain scans of some patients showed abnormalities suggestive of swelling or bleeding, which could potentially cause harm. Furthermore, it is not clear that the abnormalities can be properly monitored and managed in clinical practice.

Therefore, the Agency's opinion was that the benefits of Aduhelm did not outweigh its risks and it recommended refusing marketing authorisation.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Update as of 25 February 2022:

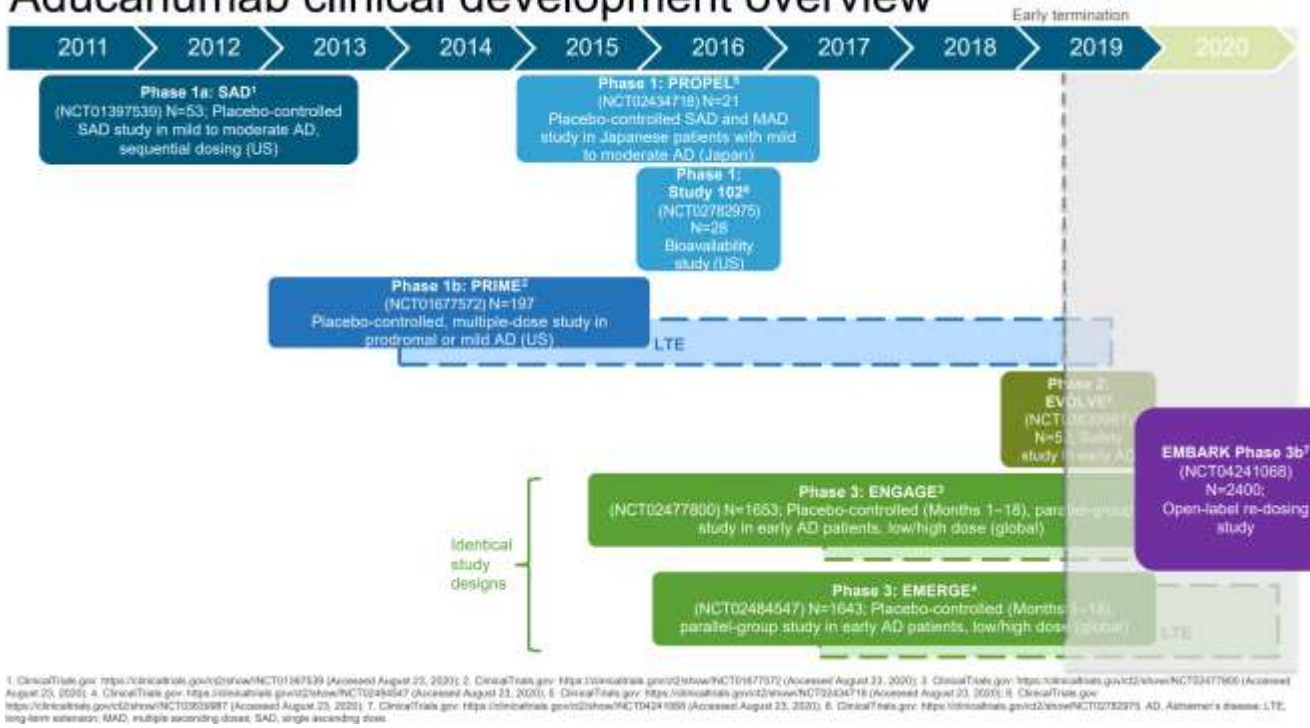
The applicant for Aduhelm has requested a re-examination of EMA's December 2021 opinion. Upon receipt of the grounds of the request, the Agency will re-examine its opinion and issue a final recommendation.

May 2022 Biogen withdraw appeal contra EMA

Aducanumab's rise, fall and resurrection

A Study to Evaluate Safety and Tolerability of Aducanumab in Participants With Alzheimer's Disease Who Had Previously Participated in the Aducanumab Studies 221AD103, 221AD301, 221AD302 and 221AD205

Aducanumab clinical development overview



1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT01397539 (Accessed August 23, 2020); 2. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT01677572 (Accessed August 23, 2020); 3. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02477800 (Accessed August 23, 2020); 4. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02484547 (Accessed August 23, 2020); 5. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02434718 (Accessed August 23, 2020); 6. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02782975 (Accessed August 23, 2020); 7. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04241068 (Accessed August 23, 2020); 8. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03639987 (Accessed August 23, 2020). AD, Alzheimer's disease; LTE, long-term extension; MAD, multiple ascending doses; SAD, single ascending dose.

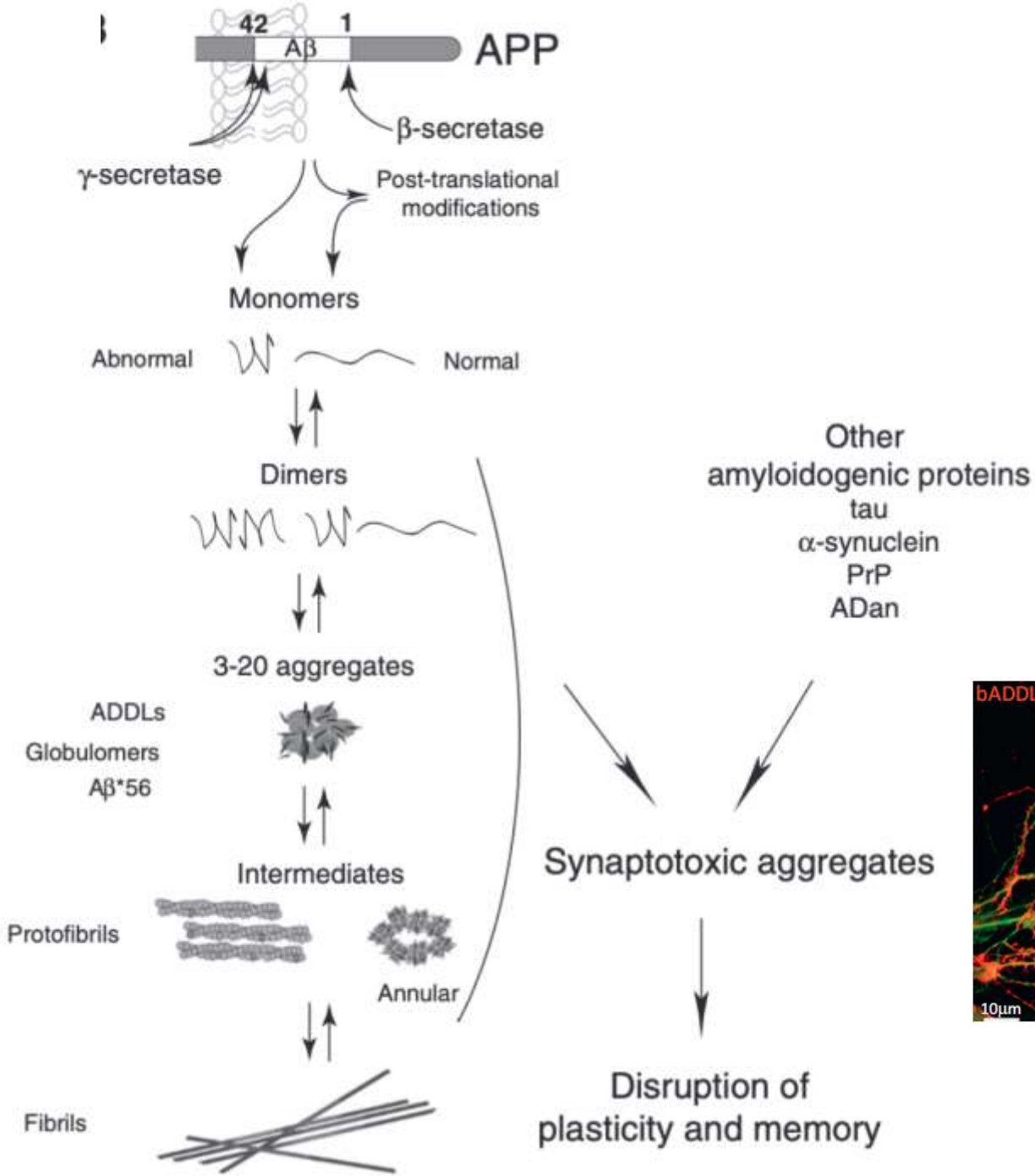
EMBARK will provide a **deeper understanding** of:
1) the occurrence of ARIA after a long treatment gap and re-exposure to aducanumab
and
2) the long-term safety of 10 mg/kg aducanumab

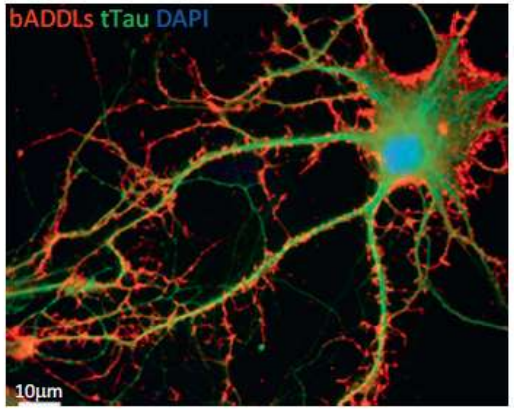
EMBARK will shed light on the **effect of prolonged treatment interruption** and improve our understanding of **the durability of treatment effects**

EMBARK will **inform the effect of aducanumab** on treatment-naïve patients who **initiate treatment at a more advanced stage of Alzheimer's disease**

A **large substudy of imaging and fluid biomarkers** will provide a deeper understanding of the **durability of aducanumab effect** following a treatment gap, after prolonged exposure and, potentially, the correlation between biomarkers and clinical outcomes

Sviluppo di anticorpi per l'immunoterapia passiva: quale forma di Aβ è il miglior target?



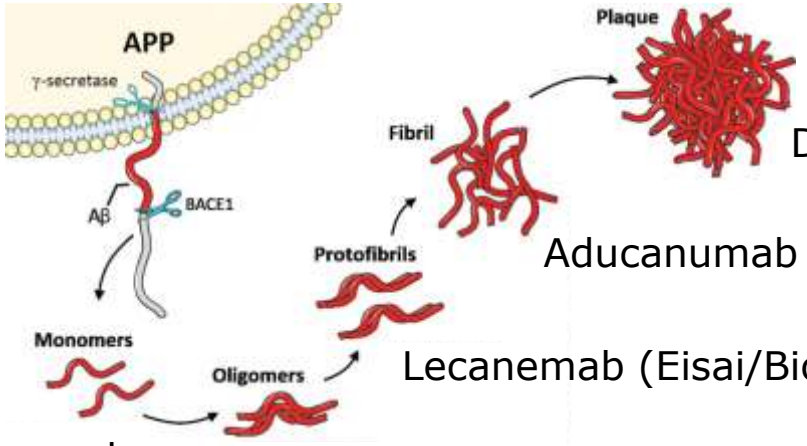


Klyubin et al., 2012

Sviluppo di anticorpi per l'immunoterapia passiva: quale forma di Aβ è il miglior target?

Aβ amino acid numbering	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	IgG class	Monomer/fibril preference
Amino acid	D	A	E	F	R	H	D	S	G	Y	E	V	H	H	Q	K	L	V	F	F	A	E	D	V	G	S	N	K	G	A		
Bapineuzumab																															IgG1	M = F
Lecanemab	Epitope undisclosed but between amino acids 1 and 16																														IgG1	M << F
Gantenerumab																															IgG1	M << F
Aducanumab																															IgG1	M << F
Donanemab																															IgG1	M = F*
Solanezumab																															IgG1	M >>> F
Crenezumab																															IgG4	M > F

Key amino acid epitopes



Donanemab (Lilly)

Aducanumab (Biogen)

Lecanemab (Eisai/Biogen)

Aducanumab (Biogen)

Solanezumab (Lilly)

Karran and De Strooper, 2022

J Prev Alz Dis 2023;4(10):771-777
Published online September 29, 2023, http://dx.doi.org/10.14283/

Original Research

Lecanemab Clarity AD: Quality-of-Life Results from a Randomized, Double-Blind Phase 3 Trial in Early Alzheimer's Disease

Figure 1. EQ-5D-5L Health Today Overall and Item Scores by Subject

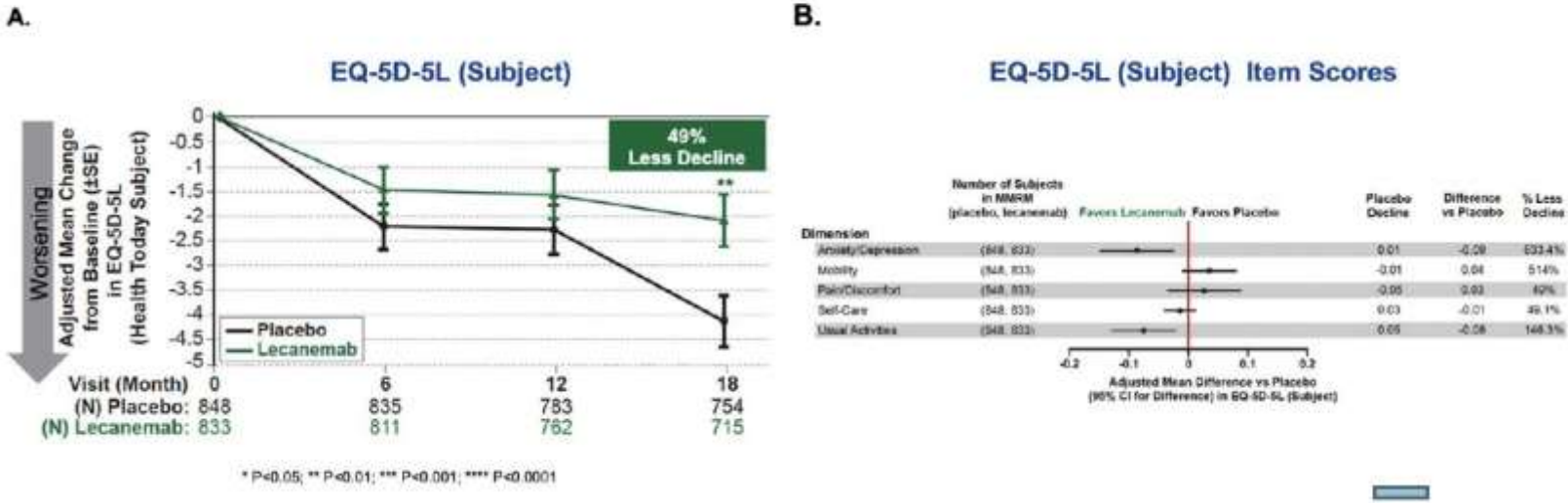
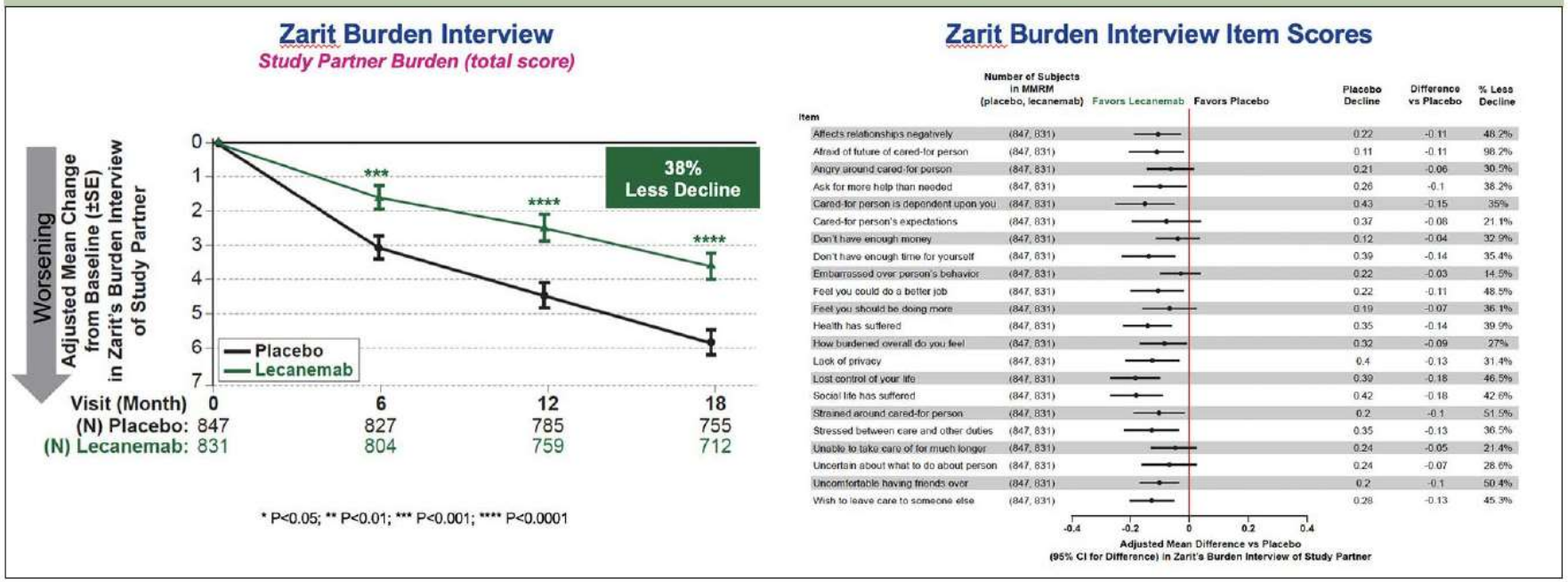


Figure 3. ZBI Overall and Item Scores



Lecanemab was associated with a relative preservation of HRQoL and less increase in caregiver burden, with consistent benefits seen across different quality of life scales and within scale subdomains.

* P<0.05; ** P<0.01; *** P<0.001; **** P<0.0001

LECANEMAB

September 28, 2022

LECANEMAB CONFIRMATORY PHASE 3 CLARITY AD STUDY MET PRIMARY ENDPOINT, SHOWING HIGHLY STATISTICALLY SIGNIFICANT REDUCTION OF CLINICAL DECLINE IN LARGE GLOBAL CLINICAL STUDY OF 1,795 PARTICIPANTS WITH EARLY ALZHEIMER'S DISEASE

Lecanemab treatment met the primary endpoint and reduced clinical decline on the global cognitive and functional scale, CDR-SB, compared with placebo at 18 months by 27%, which represents a treatment difference in the score change of -0.45 (p=0.00005) in the analysis of Intent-to-treat (ITT) population. Starting as early as six months, across all time points, the treatment showed highly statistically significant changes in CDR-SB from baseline compared to placebo (all p-values are less than 0.01). All key secondary endpoints were also met with highly statistically significant results compared with placebo.

Eisai have discussed this data with regulatory authorities in the U.S., Japan and Europe with the aim to file for traditional approval in the US and for marketing authorization applications in Japan, UK, Israel, Australia, Cina, and Europe by the end 2023.

Additionally, Eisai has presented the Clarity AD study results on November 29, 2022, at the Clinical Trials on Alzheimer's Congress (CTAD), and publish the findings in a peer-reviewed medical journal.

Fully Approved by FDA in march 2023…..Not approved by EMA July 2024……under revision end 2024

Research

JAMA Neurology | Original Investigation

Association of Amyloid Reduction After Donanemab Treatment With Tau Pathology and Clinical Outcomes
The TRAILBLAZER-ALZ Randomized Clinical Trial

Donanemab

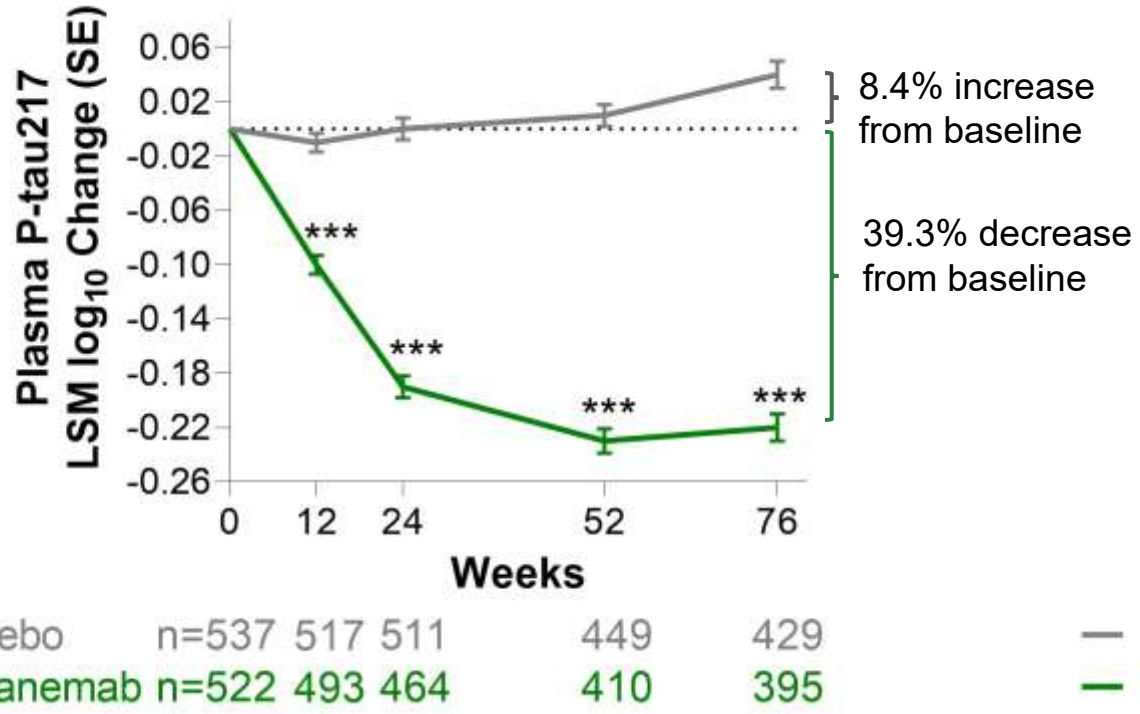
TRAILBLAZER-ALZ, phase 2, placebo-controlled, randomized clinical trial (December 2017, to December 2020, double-blind period of up to 76 weeks and a 48-week follow-up period.
56 centers in the US and Canada.
Participants (60 to 85 years of age with gradual and progressive change in memory function for 6 months or more, early symptomatic Alzheimer disease, elevated amyloid, and intermediate tau levels)

JAMA Neurol. 2022;79(10):1015-1024. doi:10.1001/jamaneurol.2022.2793 Published online September 12, 2022. Corrected on October 17, 2022.

Donanemab treatment rapidly reduced plasma P-tau217

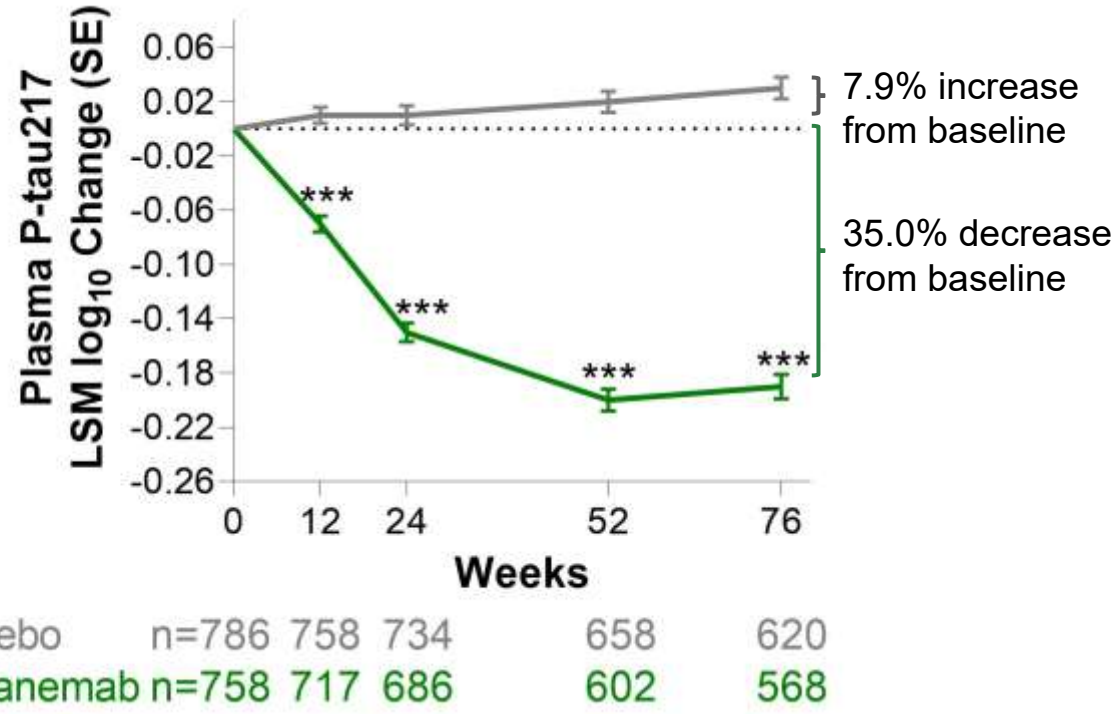
Low-medium Tau Population

39% decrease by donanemab at 76w



Combined Population

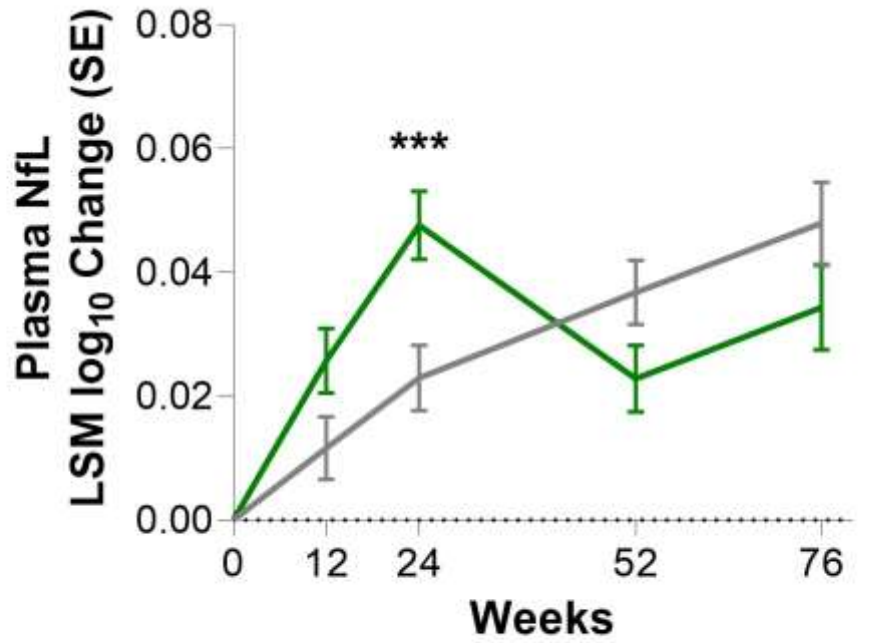
35% decrease by donanemab at 76w



LSM change from baseline, SE, and p-value asterisks are derived using mixed model repeated measures methodology with fixed factors for treatment, visit, treatment-by-visit interaction, and covariates for baseline score, baseline score-by-visit interaction, and age at baseline; ***p<0.0001. C2N was used to assay plasma P-tau217. Abbreviations: LSM=Least Squares Mean; n=number of participants; P-tau217=phosphorylated tau 217; SE=Standard Error

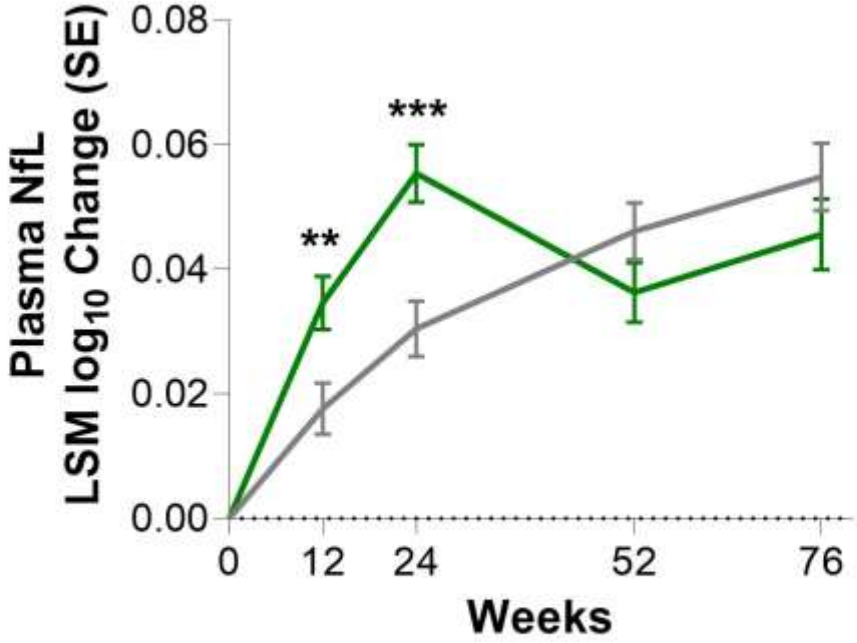
No clear pattern in plasma NfL over 76-week study

Low-medium Tau Population



Placebo	n=560	550	532	477	451
Donanemab	n=538	516	489	438	417

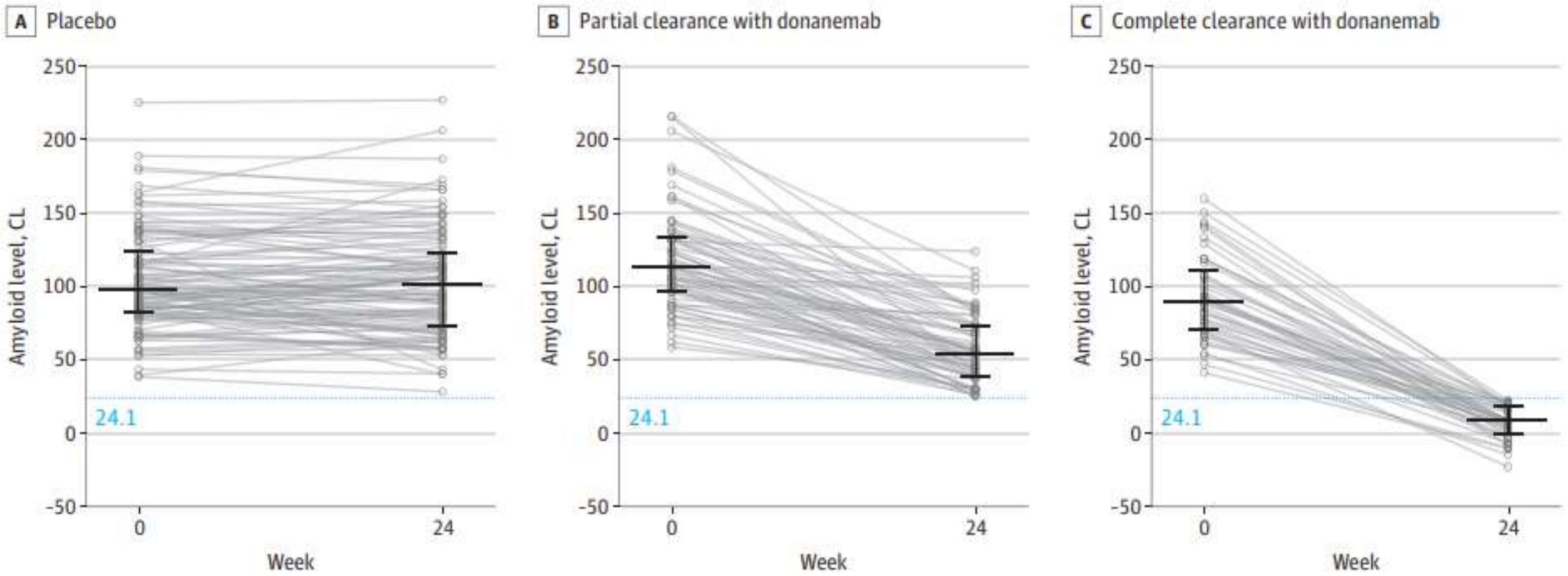
Combined Population



Placebo	n=824	806	772	697	653
Donanemab	n=783	750	719	635	592

LSM change from baseline, SE, and p-value asterisks are derived using mixed model repeated measures methodology with fixed factors for treatment, visit, treatment-by-visit interaction, and covariates for baseline score, baseline score-by-visit interaction, and age at baseline; **nominal p<0.01, ***nominal p≤0.001. Quanterix Simoa® was used to assay plasma NfL. Abbreviations: LSM=Least Squares Mean; NfL=Neurofilament light chain; n=number of participants; SE=Standard Error

Figure 2. Association Between Amyloid Levels and the Magnitude of Amyloid Change at 24 Weeks



Median (IQR) amyloid levels (in centiloid [CL] units) at baseline and 24 weeks for participants receiving placebo (A), donanemab-treated participants with partial amyloid clearance at week 24 (B), and donanemab-treated participants with complete amyloid clearance at week 24 (C) demonstrating the change owing to donanemab treatment. Mean (SD) values along with partial vs complete amyloid clearance and treatment vs placebo comparisons can be found in eTable 2 in Supplement 2. Only participants with follow-up positron emission tomography scans are included.

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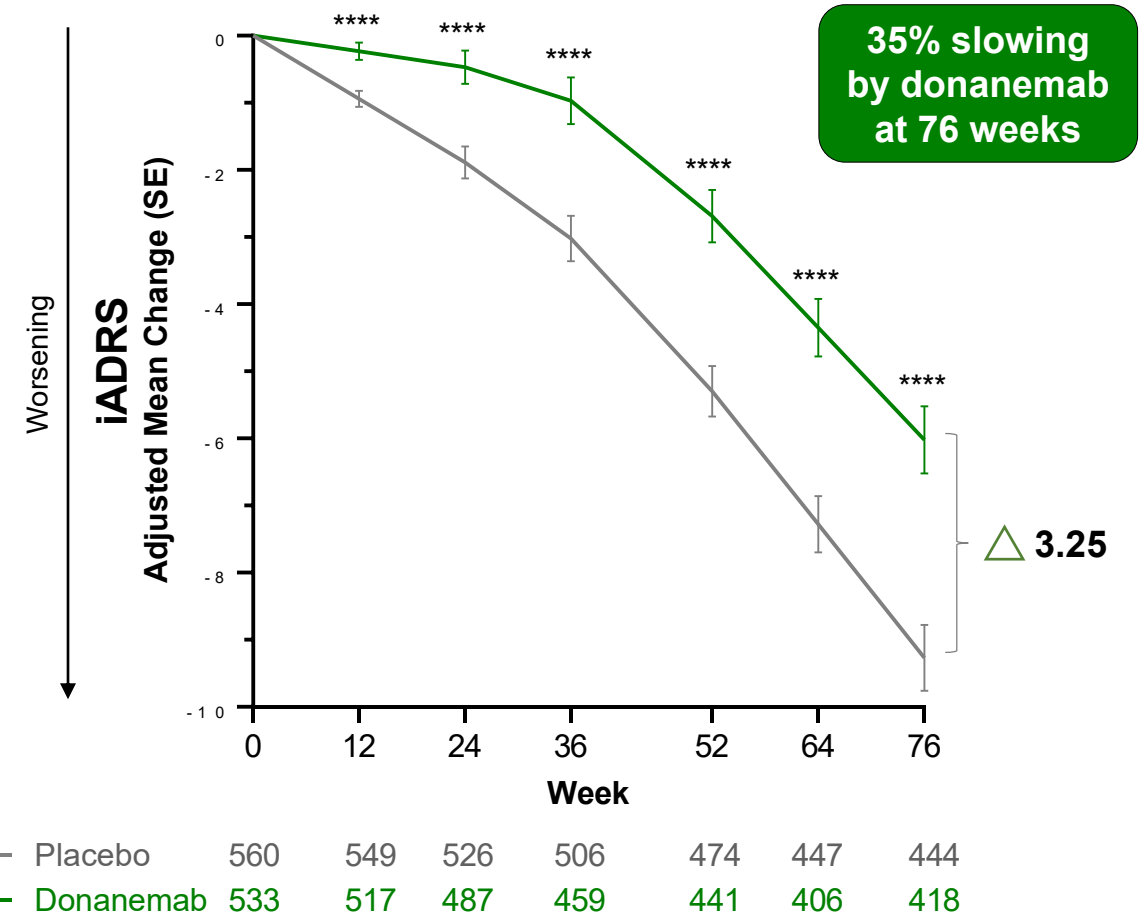
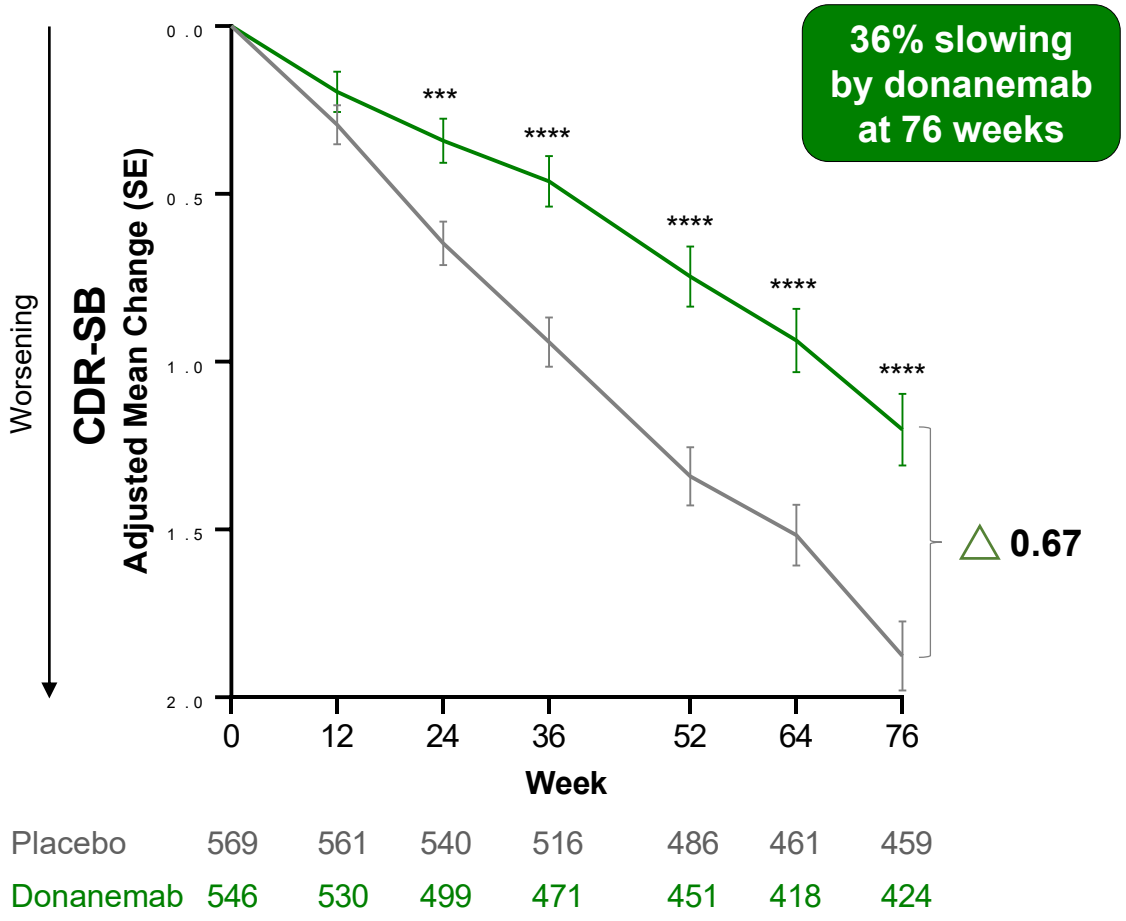
Phase 3 Primary Outcome: iADRS
Consistent with Key Secondary outcome on CDR-SB

iADRS: Low-medium Tau Population



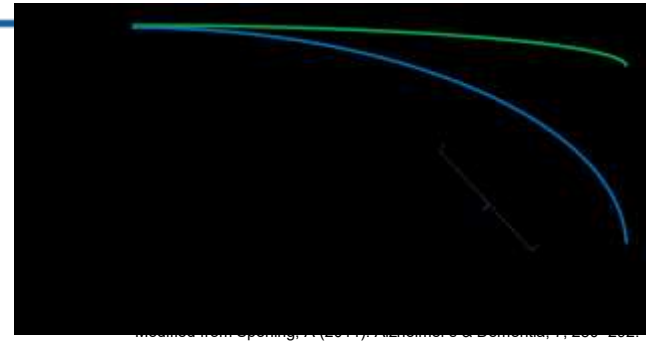
CDR-SB: Low-medium Tau Population



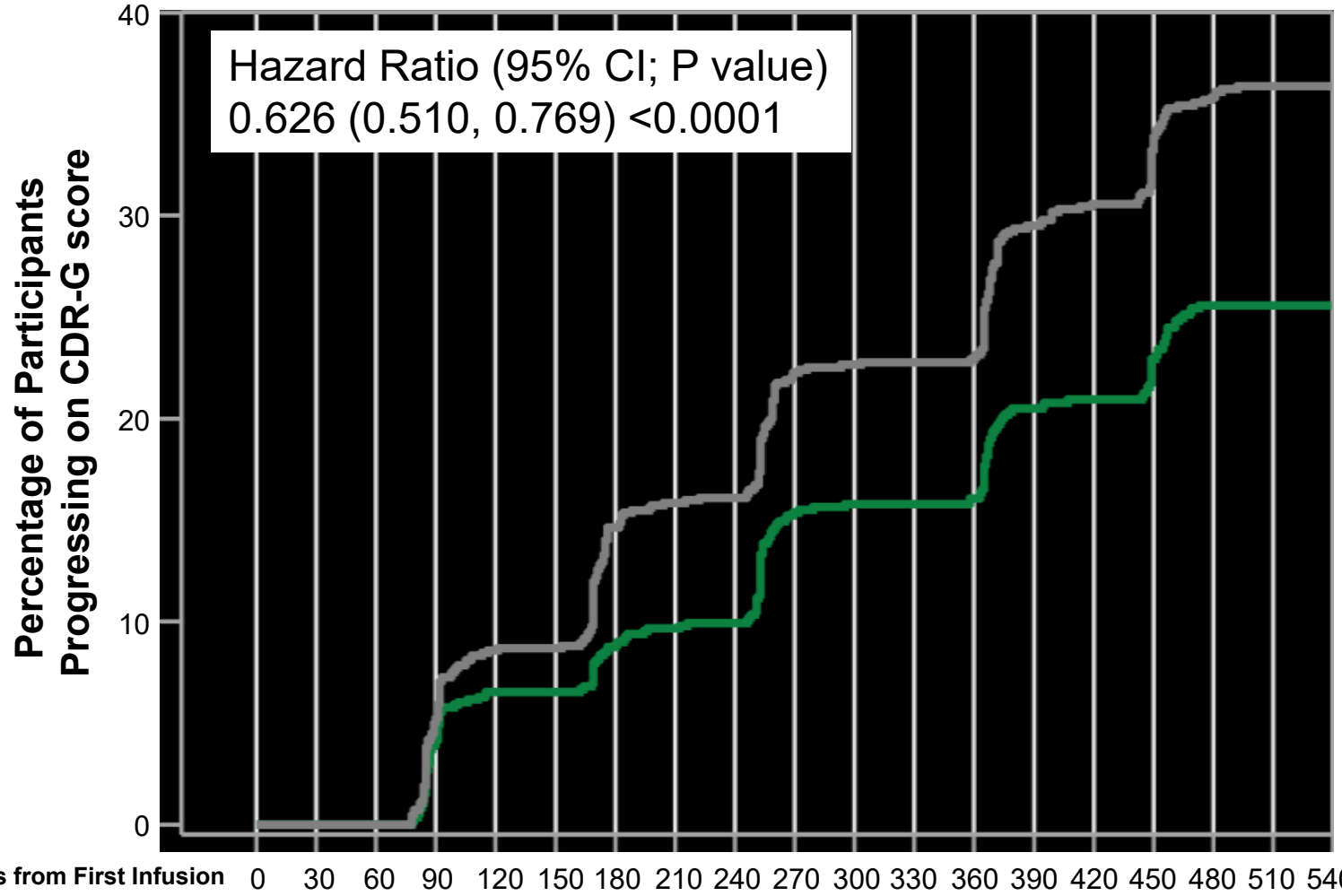
TRAILBLAZER-ALZ 2 primary (iADRS) used the NCS model with 2 degrees of freedom adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, baseline tau level (overall model only), and baseline acetylcholinesterase inhibitor/memantine use. For CDR-SB: adjusted mean change from baseline, SE, 95% CI and p-value are derived using pre-specified mixed model repeated measures methodology with fixed factors for treatment, visit, treatment-by-visit interaction, and covariates for baseline score, baseline score-by-visit interaction, age at baseline, pooled investigator, and baseline acetylcholinesterase inhibitor/memantine use. * P<0.05, ** P<0.01, *** P<0.001, **** P<0.0001. Abbreviations: CDR-SB=Clinical Dementia Rating–Sum of Boxes; iADRS=Integrated Alzheimer's Disease Rating Scale; NCS=natural cubic spline; SE=Standard Error

Risk of Progression: CDR-Global score

Combined Tau population



https://doi.org/10.1016/j.jalz.2011.03.003

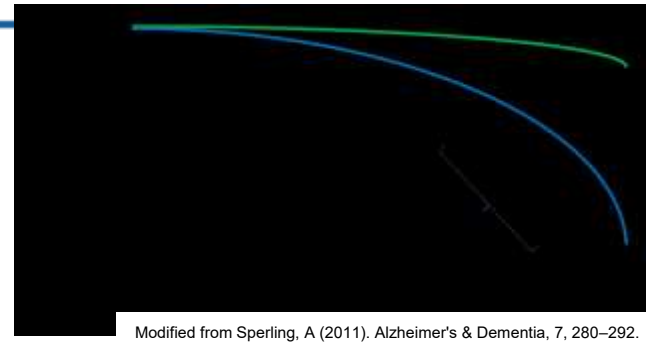


37.4% lower risk of progression over 76 weeks

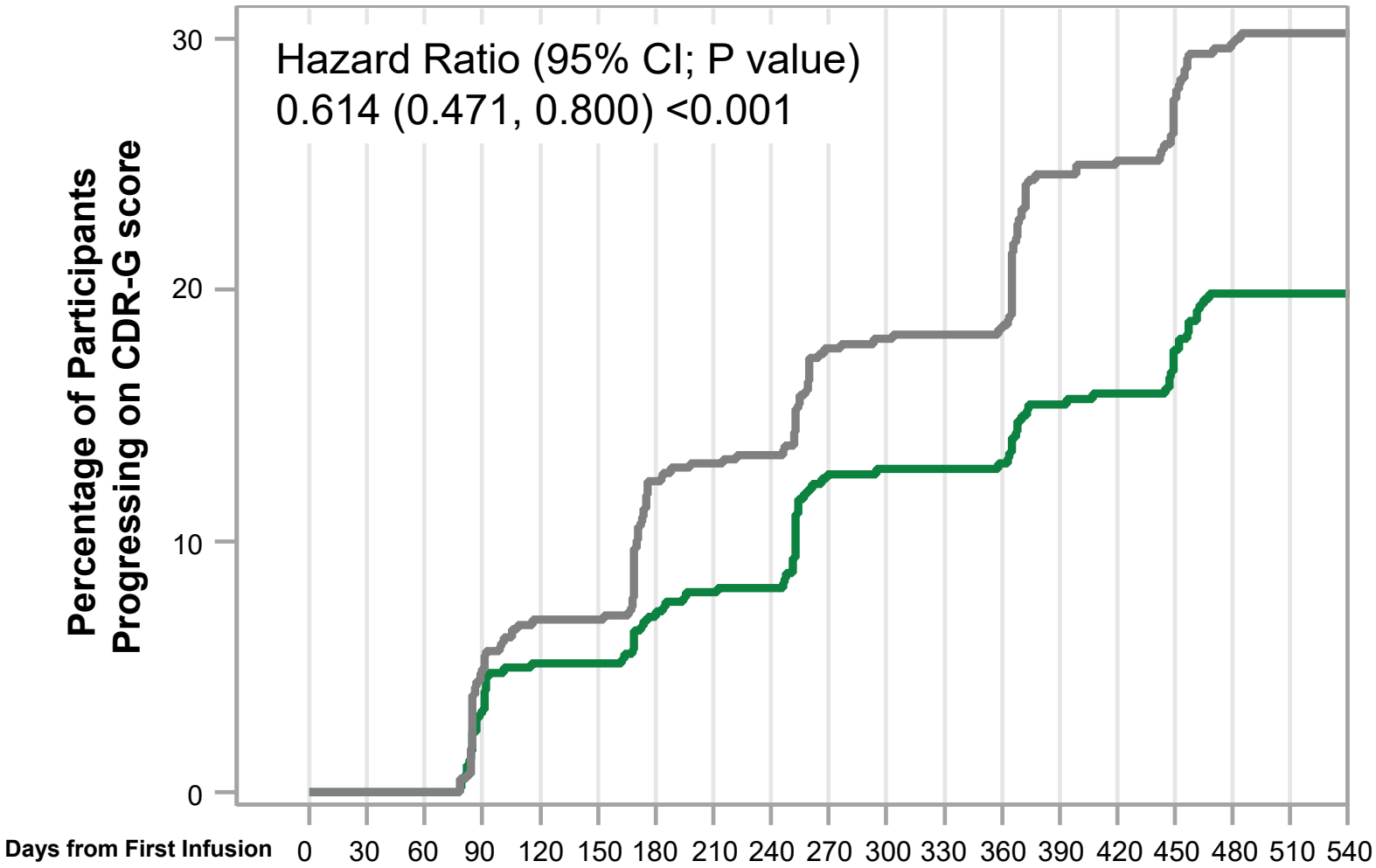
	Placebo	Donanemab
N	844	805
Event	288	186
Time	% (SE) n at risk	% (SE) n at risk
60 days	0.0 (0.00) 840	0.0 (0.00) 801
120 days	8.6 (0.97) 764	6.5 (0.88) 737
180 days	14.6 (1.22) 700	8.9 (1.01) 696
240 days	16.1 (1.27) 671	9.9 (1.07) 668
360 days	23.0 (1.47) 587	16.1 (1.33) 575
480 days	35.8 (1.72) 462	25.6 (1.63) 474

Definition of event: an increase from baseline in CDR-G score at two consecutive visits. Hazard ratio and P-value were generated using a Cox proportional hazards model adjusted for baseline age, baseline value, and baseline acetylcholinesterase inhibitor/memantine use and stratified by pooled investigator and baseline tau level. Abbreviations: CDR-G=Clinical Dementia Rating-Global Scale; CI=confidence interval; MCI=mild cognitive impairment; N=number of participants; SE=standard error

Risk of Progression: CDR-Global score
Low-medium Tau population



Modified from Sperling, A (2011). Alzheimer's & Dementia, 7, 280–292. https://doi.org/10.1016/j.jalz.2011.03.003



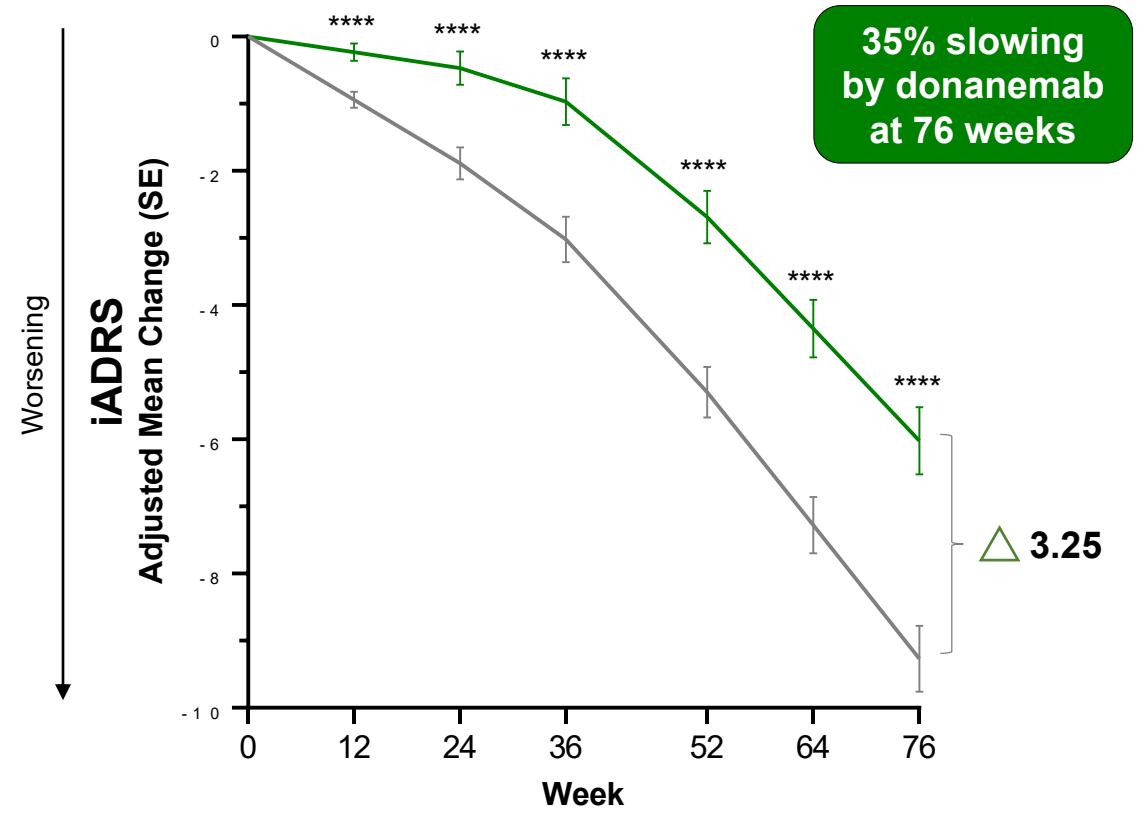
38.6% lower risk of progression over 76 weeks

	Placebo	Donanemab
N	573	555
Event	163	100
Time	% (SE) n at risk	% (SE) n at risk
60 days	0.0 (0.00) 570	0.0 (0.00) 552
120 days	6.8 (1.06) 529	5.1 (0.94) 514
180 days	12.4 (1.38) 489	7.2 (1.11) 492
240 days	13.4 (1.44) 474	8.1 (1.18) 470
360 days	18.6 (1.65) 425	13.1 (1.47) 412
480 days	29.8 (1.98) 345	19.9 (1.79) 335

Definition of event: an increase from baseline in CDR-G score at two consecutive visits. Hazard ratio and P-value were generated using a Cox proportional hazards model adjusted for baseline age, baseline value, and baseline acetylcholinesterase inhibitor/memantine use and stratified by pooled investigator. Abbreviations: CDR-G=Clinical Dementia Rating-Global Scale; CI=confidence interval; MCI=mild cognitive impairment; N=number of participants; SE=standard error

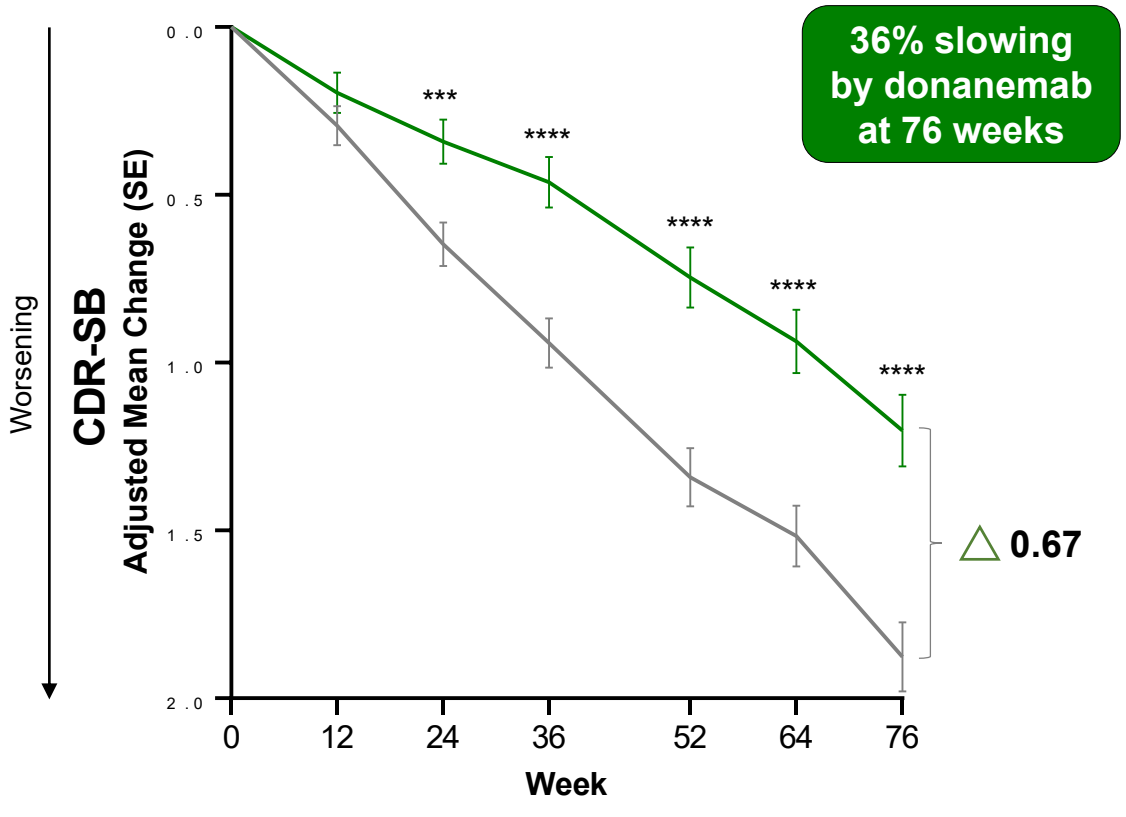
Phase 3 Primary Outcome: iADRS Consistent with Key Secondary outcome on CDR-SB

iADRS: Low-medium Tau Population



Placebo	560	549	526	506	474	447	444
Donanemab	533	517	487	459	441	406	418

CDR-SB: Low-medium Tau Population

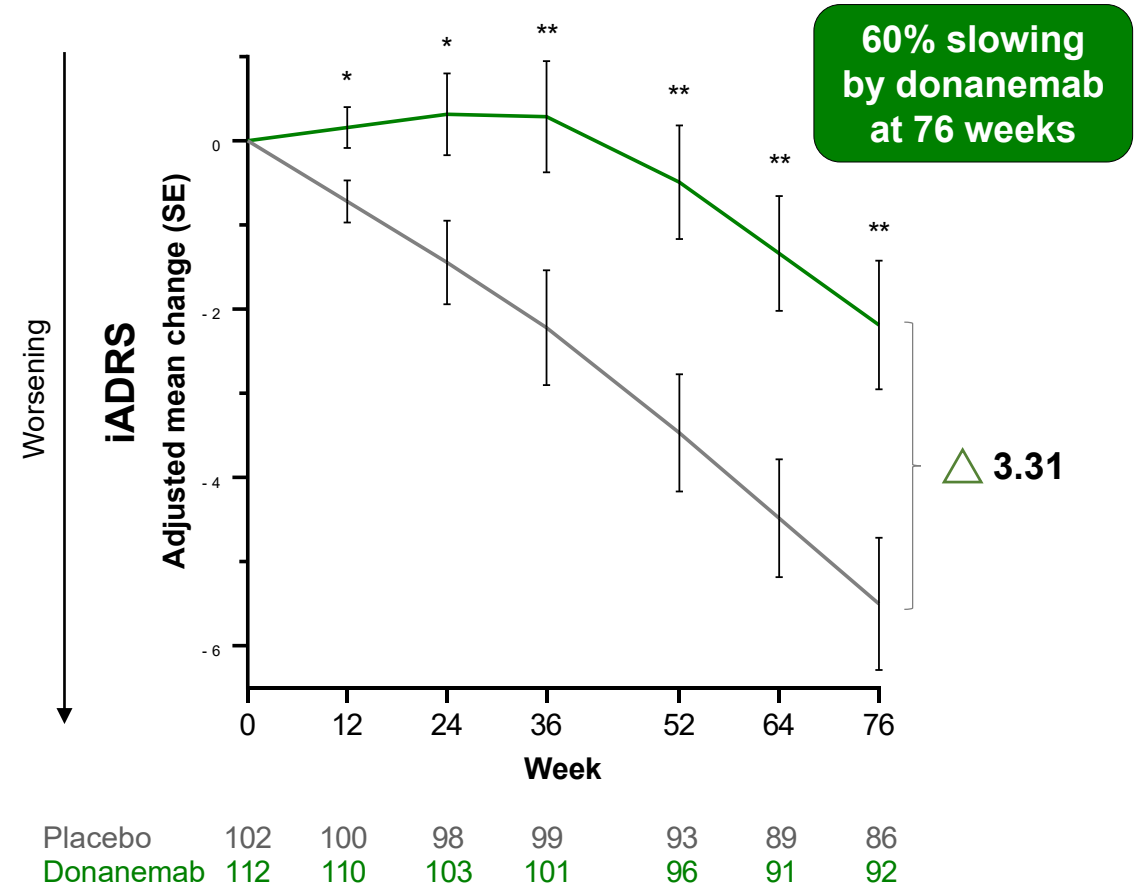


Placebo	569	561	540	516	486	461	459
Donanemab	546	530	499	471	451	418	424

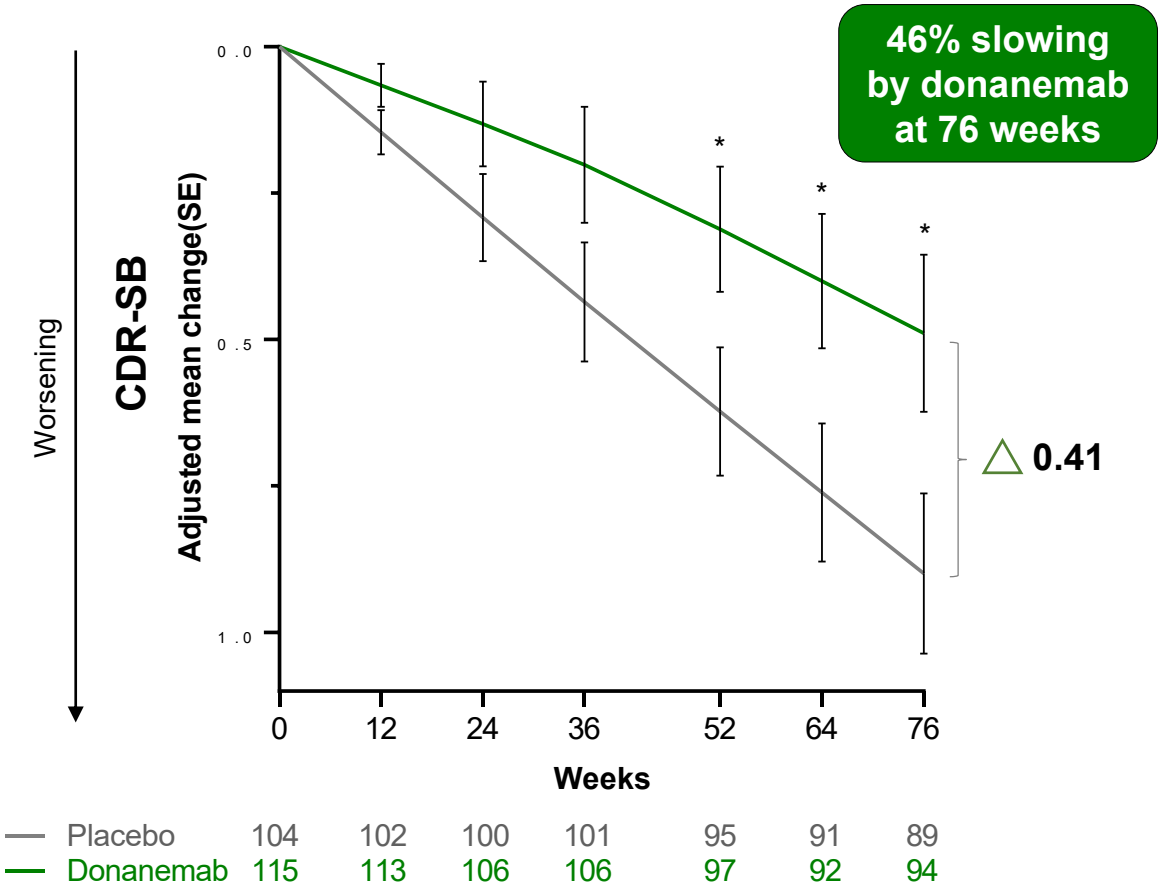
TRAILBLAZER-ALZ 2 primary (iADRS) used the NCS model with 2 degrees of freedom adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, baseline tau level (overall model only), and baseline acetylcholinesterase inhibitor/memantine use. For CDR-SB: adjusted mean change from baseline, SE, 95% CI and p-value are derived using pre-specified mixed model repeated measures methodology with fixed factors for treatment, visit, treatment-by-visit interaction, and covariates for baseline score, baseline score-by-visit interaction, age at baseline, pooled investigator, and baseline acetylcholinesterase inhibitor/memantine use. * P<0.05, ** P<0.01, *** P<0.001, **** P<0.0001. Abbreviations: CDR-SB=Clinical Dementia Rating–Sum of Boxes; iADRS=Integrated Alzheimer's Disease Rating Scale; NCS=natural cubic spline; SE=Standard Error

Pre-specified Subpopulation: MCI Low-medium Tau Population

iADRS



CDR-SB

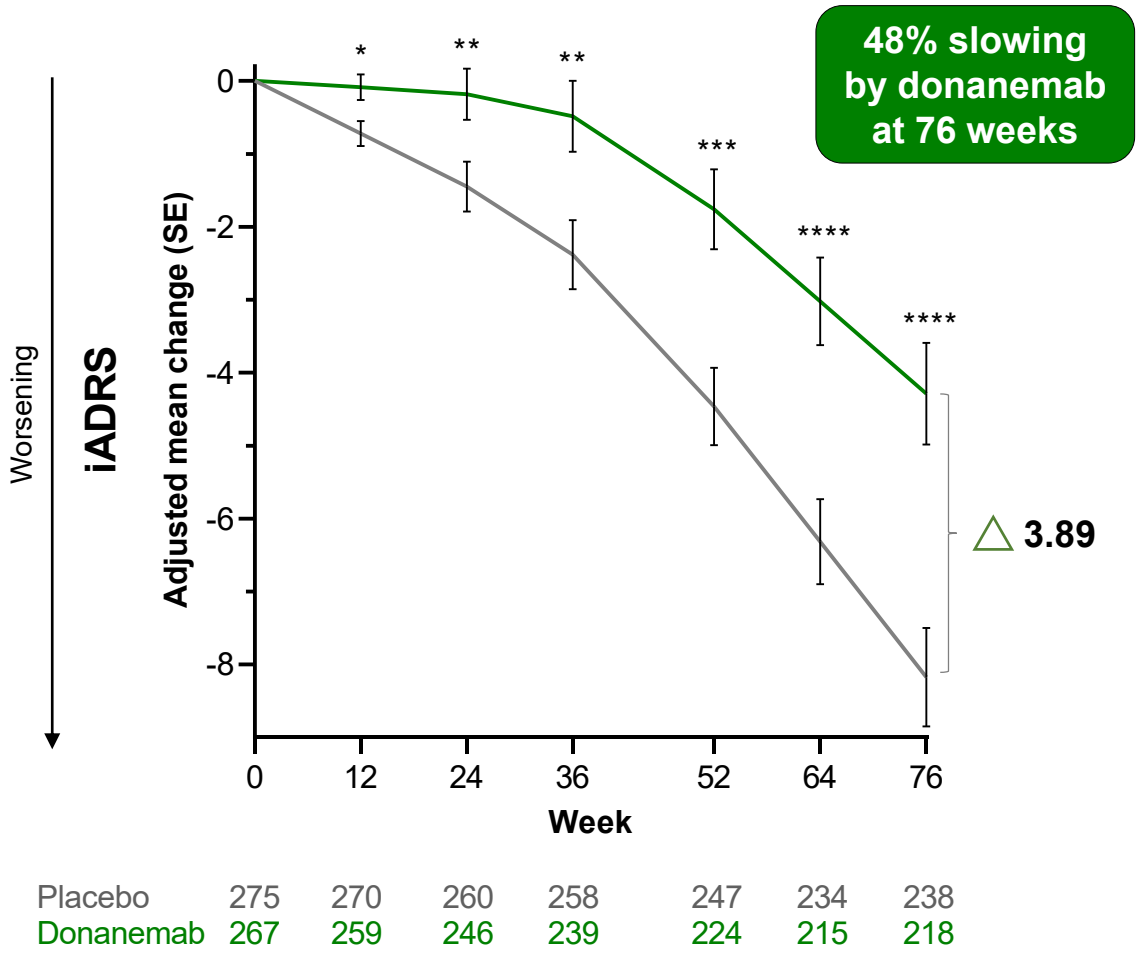


Donanemab showed greater clinical impact in participants at earlier disease stage

MCI=MMSE ≥27 at baseline. SE, 95% CI and p-value are derived using NCS model with 2 degree of freedom. The model was adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction and covariates for age at baseline, pooled investigator, and baseline acetylcholinesterase inhibitor/memantine use. Nominal P-values: * P<0.05, ** P<0.01. Abbreviations: CDR-SB=Clinical Dementia Rating–Sum of Boxes; CI=confidence interval; iADRS=Integrated Alzheimer's Disease Rating Scale; MCI=mild cognitive impairment; MMSE=Mini–Mental State Examination; NCS=natural cubic spline; SE=Standard Error

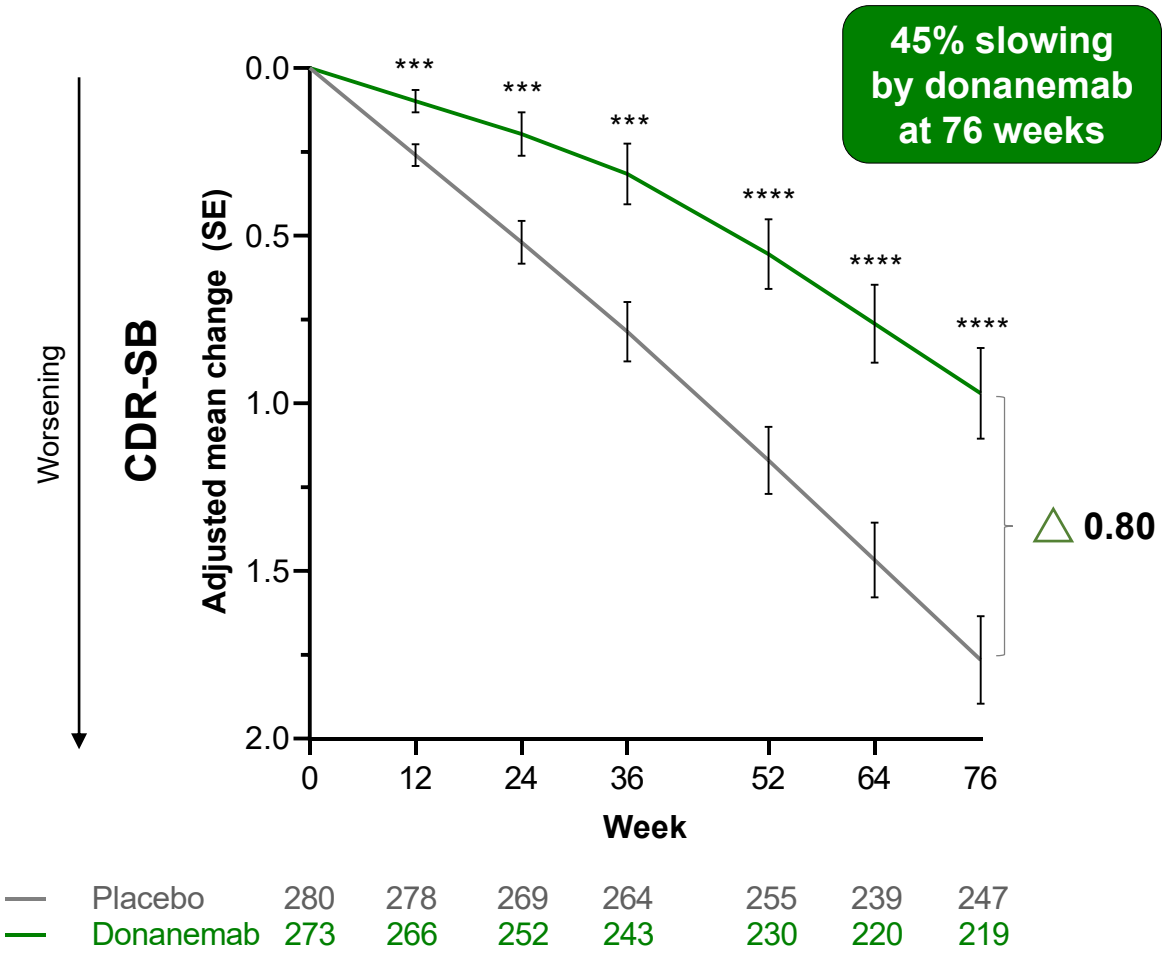
Subgroup: Younger Participants
Low-medium Tau Population

iADRS: Age <75 years



Placebo	275	270	260	258	247	234	238
Donanemab	267	259	246	239	224	215	218

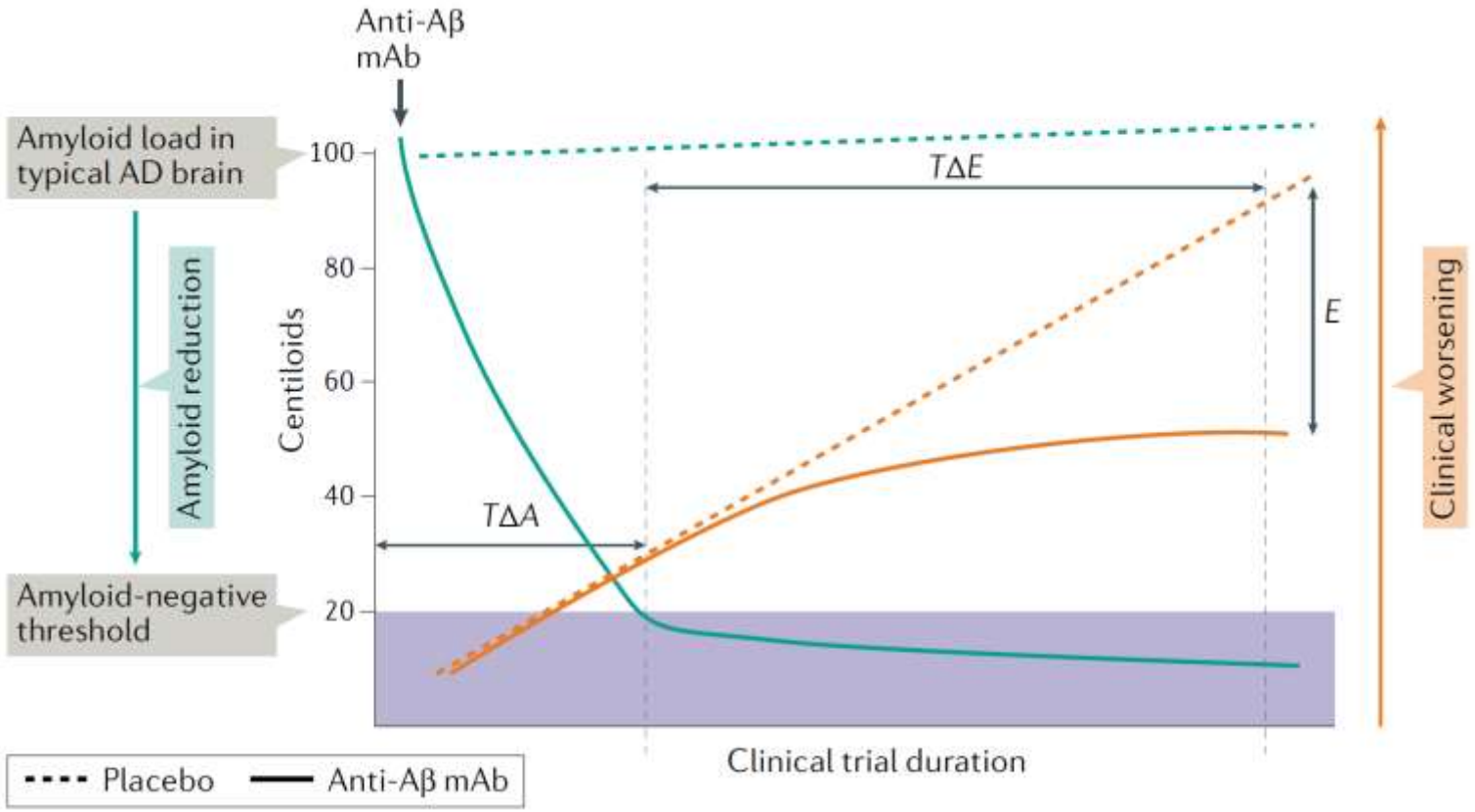
CDR-SB: Age <75 years



Placebo	280	278	269	264	255	239	247
Donanemab	273	266	252	243	230	220	219

NCS model with 2 degrees of freedom adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, baseline tau level and baseline acetylcholinesterase inhibitor/memantine use. Additional fixed terms include subgroup by treatment, subgroup by basis expansion, and subgroup by basis expansion by treatment interactions. Nominal P-values: * P<0.05, ** P<0.01, *** P<0.001, **** P<0.0001. Abbreviations: iADRS=Integrated Alzheimer's Disease Rating Scale; NCS=natural cubic spline; SE=standard error

Pazienti responders e non responders li sappiamo individuare ?



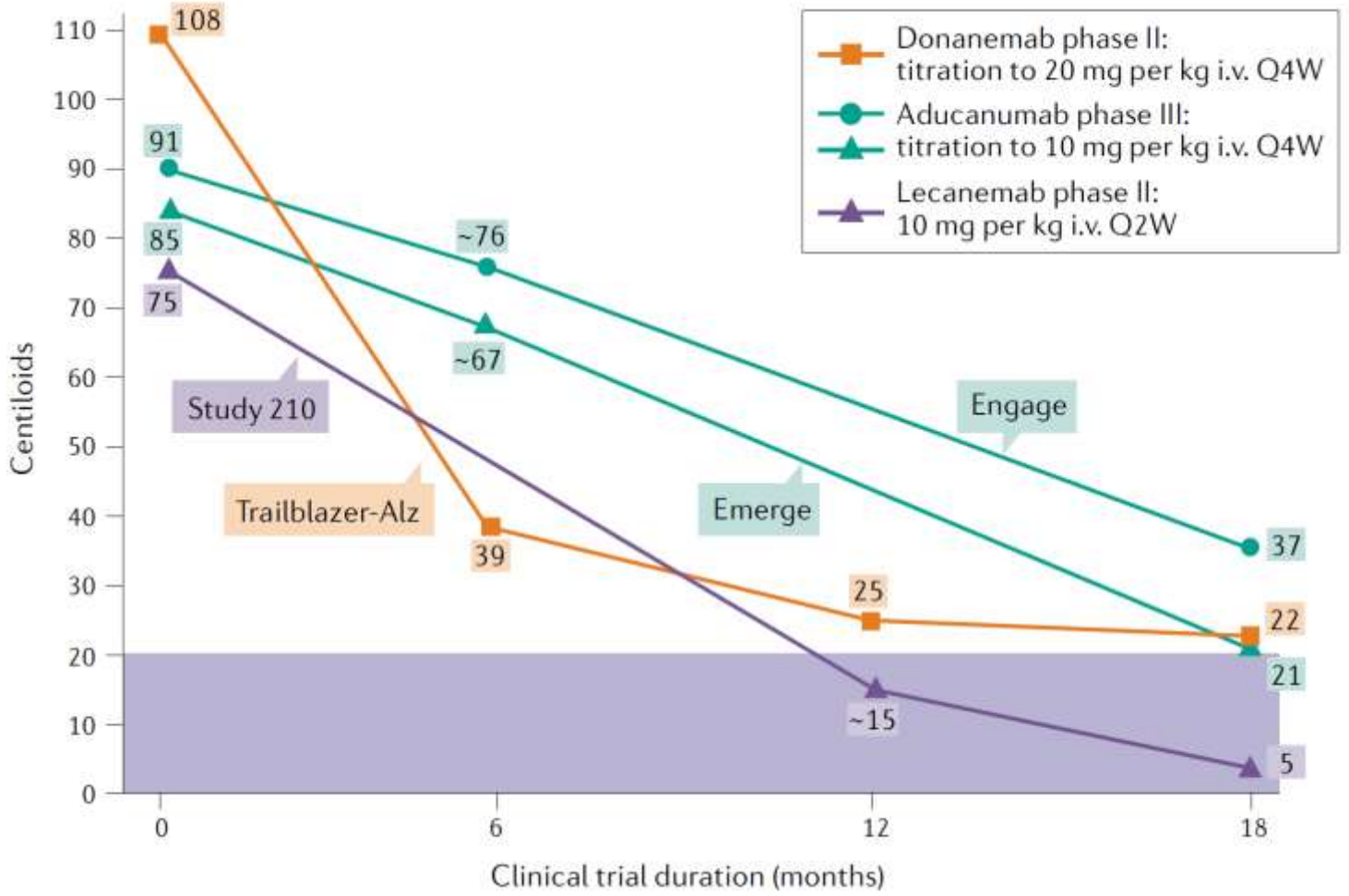
La soglia di Centiloids di amiloide presenti determina la risposta
Maggiore sarà la distanza percorsa per portare il livello di amiloide alla normalità e maggiore sarà il tempo necessario per evidenziare una risposta alla terapia in quanto questo sarà distribuito nel tempo

L'attuale valutazione quantitativa della presenza di amiloide non è praticabile prima di un trattamento con Aducanumab

Difficoltà a identificare i soggetti responders

Quale il migliore anticorpo monoclonale ?

- Dipendenza dalla fase di malattia
- Dipendenza dal carico amiloideo del soggetto



Eventi avversi emergenti dal trattamento

Treatment-Emergent AE ≥5%#

Preferred Term, n (%)	Placebo (N=874)	Donanemab (N=853)
Participants with ≥1 TEAE	718 (82.2)	759 (89.0)
ARIA-E	**17 (1.9)**	**205 (24.0)**
ARIA-H	**65 (7.4)**	**168 (19.7)**
COVID-19	154 (17.6)	136 (15.9)
Headache	**86 (9.8)**	**119 (14.0)**
Fall	110 (12.6)	114 (13.4)
Infusion-related reaction	**4 (0.5)**	**74 (8.7)**
Superficial siderosis of CNS	**10 (1.1)**	**58 (6.8)**
Dizziness	48 (5.5)	53 (6.2)
Arthralgia	42 (4.8)	49 (5.7)
Urinary tract infection	59 (6.8)	45 (5.3)
Diarrhea	50 (5.7)	43 (5.0)
Fatigue	45 (5.1)	42 (4.9)

in donanemab group after rounding

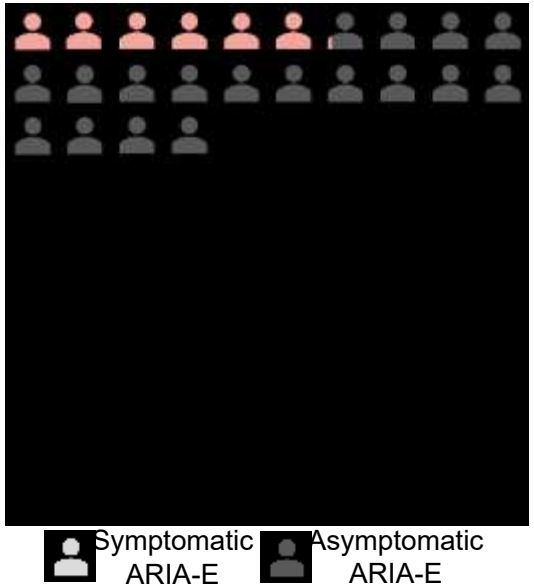
Abbreviations: AE=adverse event; ARIA-E=amyloid-related imaging abnormalities-edema/effusions; ARIA-H=amyloid-related imaging abnormalities-hemorrhage/hemosiderin deposition; CNS=central nervous system; N, n=number of participants; TEAE=treatment-emergent adverse event

Riassunto di ARIA e macroemorragia

Event[a], n (%)	Placebo (N=874)	Donanemab (N=853)
Any ARIA (-E or -H)	130 (14.9)	314 (36.8)
Any SAE of ARIA	0 (0)	14 (1.6)
ARIA-E	18 (2.1)	205 (24.0)
Asymptomatic	17 (1.9)	153 (17.9)
Symptomatic	1 (0.1)[b]	52 (6.1)
SAE of ARIA-E	0 (0)	13 (1.5)
ARIA-H	119 (13.6)	268 (31.4)
SAE of ARIA-H	0 (0)	4 (0.5)
Isolated ARIA-H	108 (12.4)	108 (12.7)
Macrohemorrhage	2 (0.2)	3 (0.4)
SAE of Macrohemorrhage	1 (0.1)	1 (0.1)

[a] ARIA and macrohemorrhage events based on MRI or TEAE cluster
[b] One placebo-treated participant had ARIA-E during the placebo-controlled period; however, the participant developed symptoms during the long-term extension period

Il 24% dei partecipanti trattati con donanemab ha manifestato ARIA-E



- Gli eventi ARIA-E sono stati in gran parte radiografici da lievi a moderati (94%)
- I sintomi comunemente riportati dell'ARIA-E sintomatica erano cefalea e confusione

Abbreviations: ARIA-E=amyloid-related imaging abnormalities-edema/effusions; ARIA-H=amyloid-related imaging abnormalities-hemorrhage/hemosiderin deposition; MRI=magnetic resonance imaging; N, n=number of participants; SAE=serious adverse event; TEAE=treatment-emergent adverse event

ARIA e APOE

ARIA by *APOE* ε4 Carrier Status

No./Total No. (%)[a,b]	Placebo (N=870)	Donanemab (N=850)
ARIA-E		
Non-carrier	2/250 (0.8)	40/255 (15.7)
Heterozygous carrier	9/474 (1.9)	103/452 (22.8)
Homozygous carrier	5/146 (3.4)	58/143 (40.6)
ARIA-H[c]		
Non-carrier	28/250 (11.2)	48/255 (18.8)
Heterozygous carrier	57/474 (12.0)	146/452 (32.3)
Homozygous carrier	30/146 (20.5)	72/143 (50.3)

[a] Based on MRI.
[b] Participants with missing *APOE* ε4 carrier status are excluded.
[c] Treatment-emergent microhemorrhage is based on new incidents of microhemorrhages. Treatment-emergent superficial siderosis is based on new or worsening superficial siderosis.

- Participants with at least 1 serious ARIA event[d]
  - ARIA-E: 12 *APOE* ε4 carriers and 1 non-carrier
  - ARIA-H: 3 *APOE* ε4 carriers and 1 non-carrier

[d] SAEs are by AE reporting

Abbreviations: *APOE*=apolipoprotein E; ARIA-E=amyloid-related imaging abnormalities-edema/effusions; ARIA-H=amyloid-related imaging abnormalities-hemorrhage/hemosiderin deposition; MRI=magnetic resonance imaging; N, n=number of participants

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Special Article

Aducanumab: Appropriate Use Recommendations

J. Cummings[1], P. Aisen[2], J.G. Apostolova[3], A. Atri[4], S. Salloway[5], M. Weiner[6]

Department of Brain Health, School of Integrated Health Sciences, University of Nevada Las Vegas
ch Institute, University of Southern California, San Diego, CA, USA; 3. Departments of Neurology,
y School of Medicine, Indianapolis, Indiana, USA; 4. Banner Sun Health Research Institute, Banner
d Medical School, Boston, MA, USA; 5. Butler Hospital and Warren Alpert Medical School of Brown
ad Biomedical Imaging, Medicine, Psychiatry and Neurology, University of California San Francisco,

Age	50-85	Younger or older patients meeting all other criteria for treatment could be considered candidates for aducanumab
Diagnosis	Clinical criteria for MCI due to AD or mild AD dementia	Clinical criteria for MCI due to AD or mild AD dementia
Scale scores at baseline	CDR Global Score 0.5; MMSE 24-30; RBANS Delayed Memory Score of 85 or less	MMSE 21-30 or equivalent such as MoCA 17-30
Amyloid status	Amyloid positive PET (visual read)	Amyloid positive PET (visual read) or CSF findings consistent with AD
Genetic testing	Consent for APOE genotyping	Genotyping should be discussed with the patient/care partner. ARIA risk should be described, and the patient's preferences assessed.
Neurological examination	Non-AD neurological disorders, stroke, and TIA excluded	Non-AD neurological disorders excluded
Cardiovascular history	Angina; myocardial infarction; congestive heart failure excluded	Stable cardiovascular conditions required; clinical decision can be exercised on the ability of the patient to participate safely with the therapeutic regimen
Medical history	Excluded: clinically significant systemic illness; diabetes than cannot be managed; uncontrolled hypertension (systolic > 165; diastolic > 100); history of cancer unless in remission for 5 years or localized to skin or prostate; impaired liver function; hepatitis; HIV infection	Stable medical conditions required; clinical decision can be exercised on the ability of the patient to participate safely with the therapeutic regimen
Psychiatric history	Unstable psychiatric illness in the past 6 months; alcohol or substance abuse in the past year; use of cannabinoids; positive urine tests for excluded substances	Must be stable psychiatrically; clinical decision can be exercised on the ability of the patient to participate safely with the therapeutic regimen
Reproductive status	Female subjects who are pregnant or breast feeding excluded; female subjects who are of childbearing age must be practicing contraception	Female subjects who are pregnant or breast feeding excluded; female subjects who are of childbearing age must be practicing contraception
Clotting status	Bleeding disorders, anticoagulants excluded	Patients on anticoagulants are excluded
Concomitant medications	Cholinesterase inhibitors and memantine allowed	Patients can be on standard of care with cholinesterase inhibitors and memantine
Baseline MRI	Baseline MRI finding that excluded participation: acute or subacute hemorrhage, macrohemorrhage, greater than 4 microhemorrhages, cortical infarction (>1.5 cm), 1 lacunar infarction (>1.5 cm), superficial siderosis, or diffuse white matter disease	Patients should be excluded if there is evidence of acute or subacute hemorrhage, macrohemorrhage, greater than 4 microhemorrhages, cortical infarction (>1.5 cm), 1 lacunar infarction (>1.5 cm), > 1 area of superficial siderosis, or diffuse white matter disease
Care support	Reliable informant or care partner	May be living independently or with a care partner
Informed consent	Must be signed by participant and care partner	Patient and care partner must understand the nature and requirements of therapy (e.g, monthly infusions to be performed indefinitely) and the expected outcome of therapy (slowing of decline of clinical features)

La FDA non ha indicato nel documento finale:

- lo stadio di malattia a cui iniziare Aducanumab
- la necessità di testare la presenza di beta amiloide
- Non ha indicato la durata del trattamento
- Non ha indicato le controindicazioni all'uso del farmaco.

Pazienti candidabili

Table 1 – Synthetic description of eligible patients for high-clearance anti-amyloid immunotherapies in a real-life setting in case of putative approval in France. Minimum requirements. See text for detail.	
AD diagnosis established by	1) Clinical phenotype: amnestic syndrome of the hippocampal type, posterior cortical atrophy, logopenic variant primary progressive aphasia (and uncommon AD phenotypes) 2) Positive biomarkers of AD pathology: A+ (and T+)
Disease stage	Early symptomatic AD with no or low impact on activities of daily living
Age and comorbid conditions	Life expectancy ≥ 5 years
Strict contraindications	CAA MRI risk factors of ARIA (i.e., non-CAA comorbid cerebrovascular disease, including ≥ 4–5 microbleeds) Antithrombotic drugs* MRI contraindication
Relative contraindications (possible factors increasing the risk of ARIA and/or its severity)	History of ischemic stroke, TIA, high and/or imbalanced cerebrovascular risk factors, autoimmune or inflammatory conditions, seizures, or other disorders associated with extensive white matter pathology
APOE genetic testing	Strongly recommended (for ARIA risk assessment)

A+: positive biomarker of amyloid pathology (low CSF Aβ42, or high CSF Aβ40/42 ratio, or positive amyloid-PET); T+: positive biomarker of tau pathology (high CSF pTau, or positive tau-PET); ARIA: amyloid-related imaging abnormality; TIA: transient ischemic attack; CAA: cerebral amyloid angiopathy. *Whether antithrombotic drugs should be considered as a strict or relative contraindication to high-clearance anti-amyloid immunotherapies will depend on the safety results of the phase III lecanemab and donanemab trials where antithrombotic drugs are allowed.

Quanti potrebbero essere?

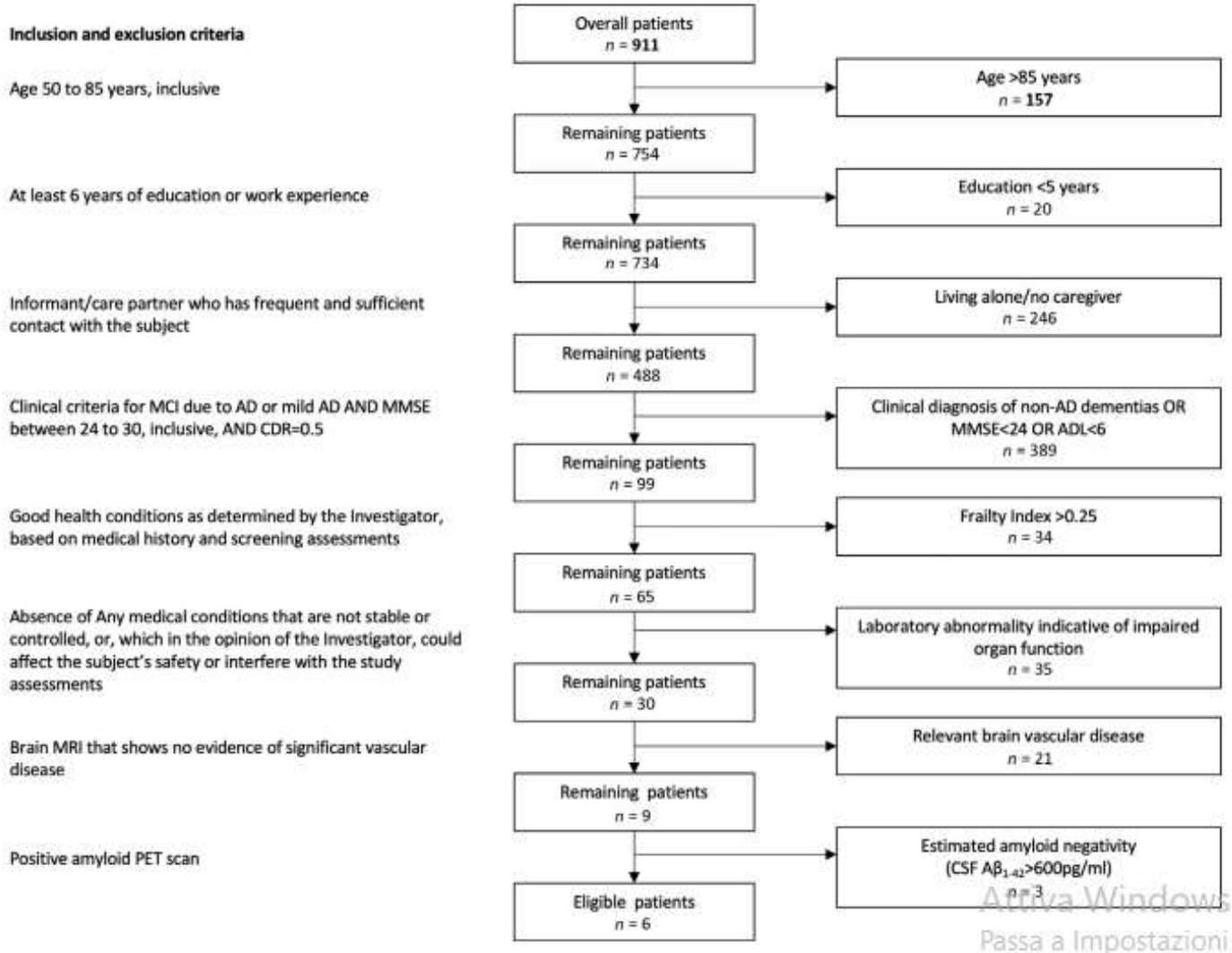
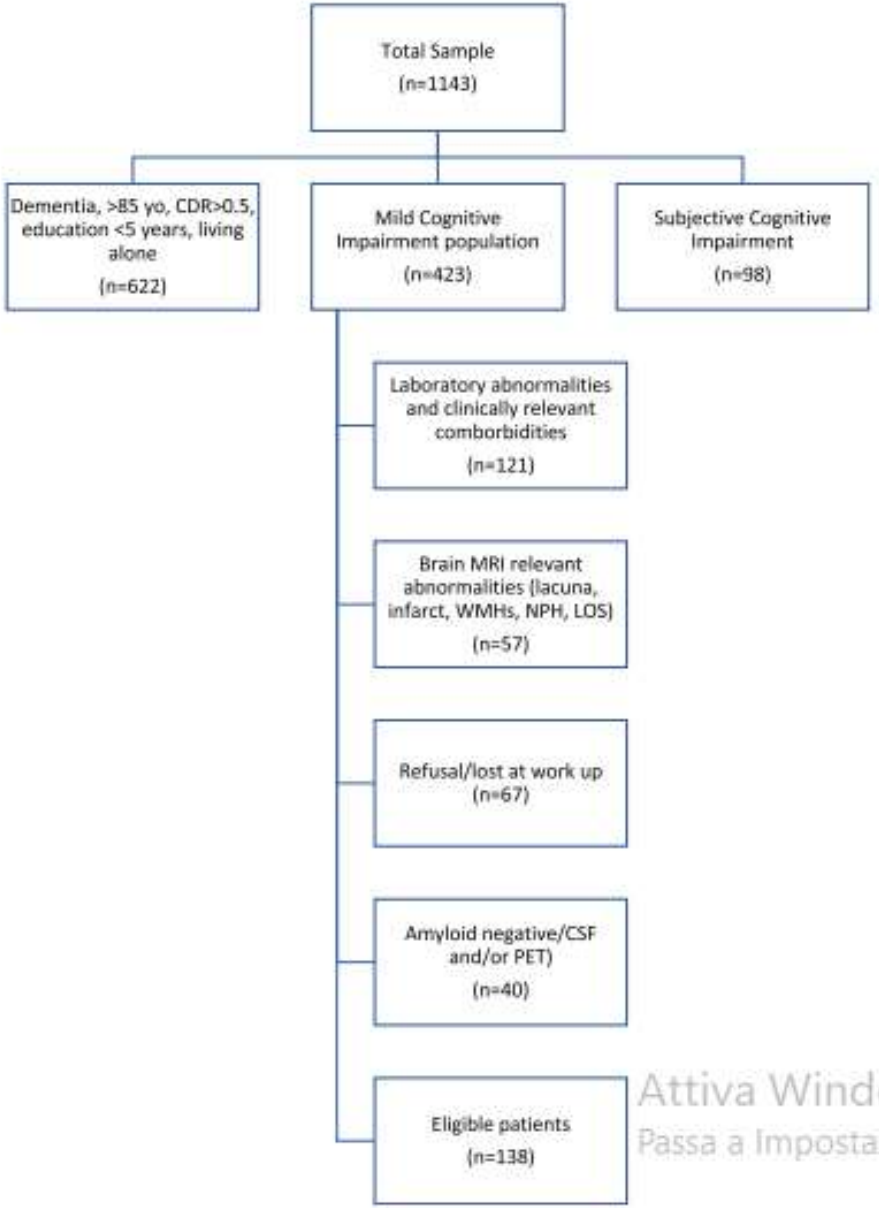


FIGURE 1 Application of the EMERGE and ENGAGE eligibility criteria to real-world patients attending a university memory clinic

Canevelli M, et al J Am Geriatr Soc 2021;69:2995–8. http://dx.doi.org/10.1111/ jgs.17390

Con criteri di esclusione Aducanumab
0.6% di un ambulatorio CDCD geriatrico di pazienti con MCI due to AD



Con criteri di esclusione Aducanumab
1141 (mean ± SD age = 74.0 ± 8.6) CDCD neurologico

12% potenzialmente trattabili

Padovani A, et al J Am Geriatr Soc 2021;8–10. http://dx.doi.org/10.1111/jgs.17530

How prevention and diagnostic for dementia are implemented in Italy ?

J Prev Alz Dis 2024;
Published online July 11, 2024, https://doi.org/10.14283/jpad.2024.144

Original Research

Universal Prevention of Dementia in Italy: A Document Analysis of the 21 Italian Regional Prevention Plans

S. Salemme[1,2], D. Marconi[3], S.M. Pani[4], G. Zamboni[1,5], C. Sardu[4], G. Lazzeri[5,6], M. Corbo[7], E. Lacorte[8], N. Locuratolo[9], A. Ancidoni[10], N. Vanacore[3], G. Bellomo[9]

	Low education	Hypertension	Hearing loss	Smoking	Alcohol	Obesity	Depression	Physical inactivity	Diabetes	Social isolation	TBI	Air pollution
Abruzzo								3				
Basilicata								4				
Calabria								4				
Campania				2	1	1		7		6		1
Emilia-Romagna				1		2		6				
Friuli Venezia Giulia		1		1	2	3		9	2			
Lazio		1		1	1	1		8				
Liguria								4				
Lombardia		1		1	1	1		16	2			
Marche				1	1			6	1			1
Molise				1				6				
PA Trento		2						2	2	1		
Piemonte								6		2		
Puglia				1				3				
Sardegna								4				
Sicilia		1		1	1	1		5	1			
Toscana				1	1			6		4	1	
Umbria								4				
Valle d'Aosta								7		1		
Veneto				3	2			7				
PA Bolzano	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Total	0	6	0	14	10	9	0	117	8	14	1	2

Journal of Alzheimer's Disease xx (20xx) x–xx
DOI 10.3233/JAD-240594
IOS Press
CORRECTED PROOF

The Profile of the Italian Centers for Cognitive Disorders and Dementia in the Context of New Drugs in Alzheimer's Disease

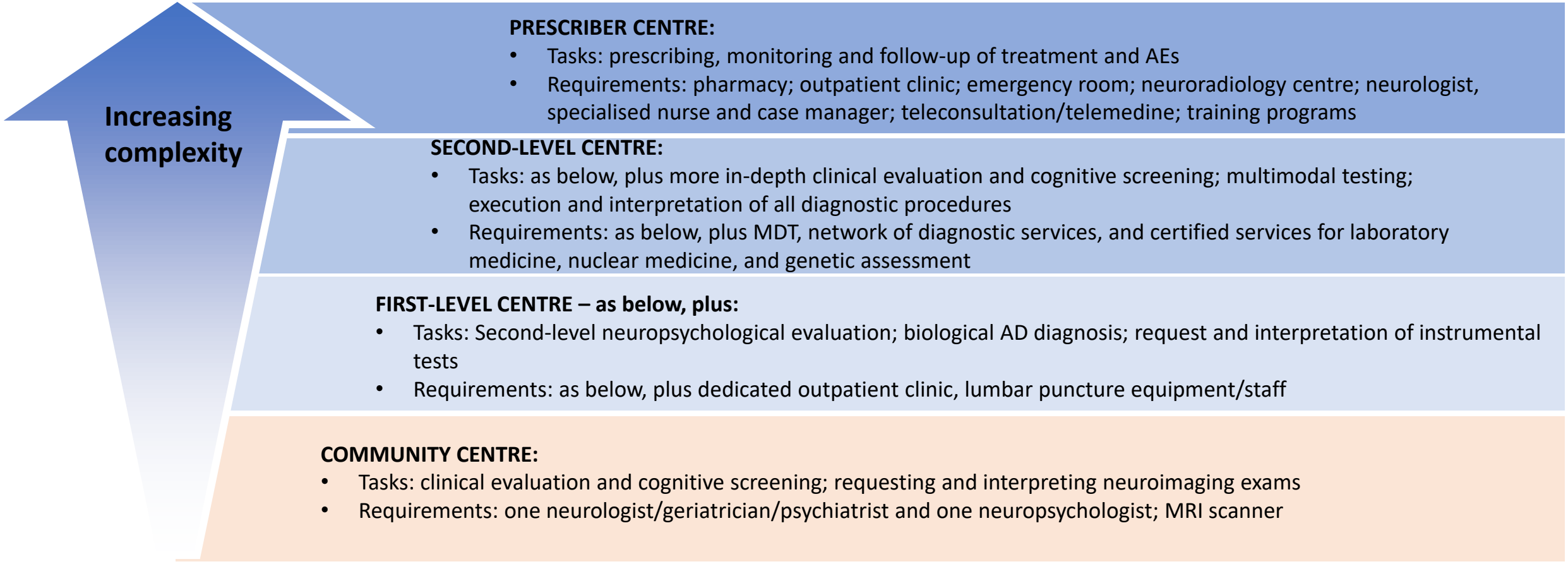
Francesco Giaquinto[a], Patrizia Lorenzini[b,*], Emanuela Salvi[c], Giulia Carnevale[d], Roberta Vaccaro[d,e], Fabio Matascioli[d,f], Massimo Corbo[g], Nicoletta Locuratolo[h], Nicola Vanacore[b], Ilaria Bacigalupo[b] and the Permanent Table of the National Dementia Plan Study Group and the CCDDs Study Group

1) Multidisciplinary team;
2) Minimum Core Test for the neuropsychological assessment;
3) PET, CSF, and Brain MRI assessments.
4) Continuing Professional Development and Counselling Services

I dati del CDCD derivano da un'indagine nazionale, che ha raggiunto un tasso di risposta dell'84%.

Come progettare la migliore organizzazione dei servizi in uno scenario di diagnosi biologica e possibili terapie modificanti la malattia?

Expert Opinion leader proposal on future organisation of dementia care in Italy



The high risk/benefit ratio of disease-modifying therapies needs a highly specialised diagnostic work-up and a thorough exclusion criteria assessment, which should be provided by expert centres

- AD, Alzheimer's disease; MDT, multidisciplinary team; MRI, magnetic resonance imaging.
Filippi M, et al. *JOON* 2023;270(6):3159–70.

Courtesy Filippi M.

Delphi Sindem

TOPIC 1 L'organizzazione dei servizi dal case finding alla gestione delle fasi avanzate

TOPIC 2 Accesso alla diagnosi biologica della malattia di Alzheimer

TOPIC 3 Requisiti per la somministrazione di farmaci modificanti la malattia

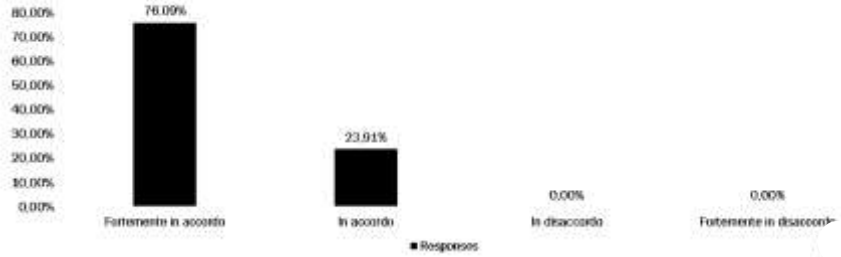
TOPIC 4 La gestione, il case manager e il monitoraggio del paziente con disturbi cognitivi

Towards a New Scenario for the Management of Dementia in Italy: a SINDEM Delphi Consensus study submitted , 2024 JOON

L'organizzazione dei servizi assistenziali dalla diagnosi precoce alla gestione delle fasi avanzate

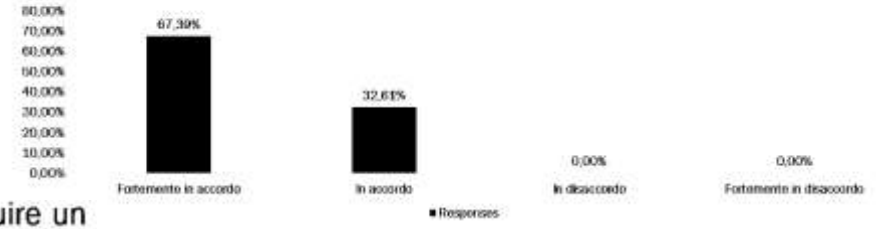
Ogni Regione deve avere un Percorso Diagnostico Terapeutico Assistenziale (PDTA) sulle demenze conforme alle indicazioni del Tavolo Nazionale Demenze

Accordo: 100%



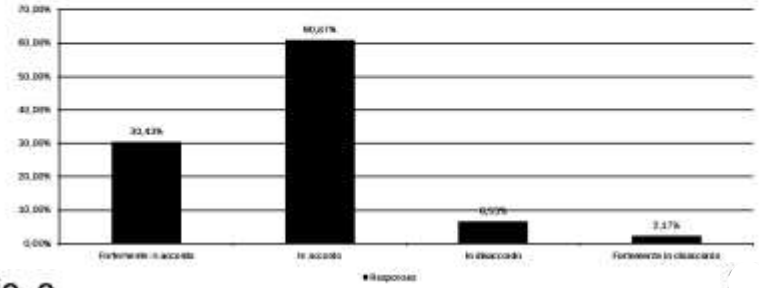
E' auspicabile che il MMG applichi carte del rischio per attuare politiche di prevenzione e intercettare pazienti sospetti.

Accordo: 100%



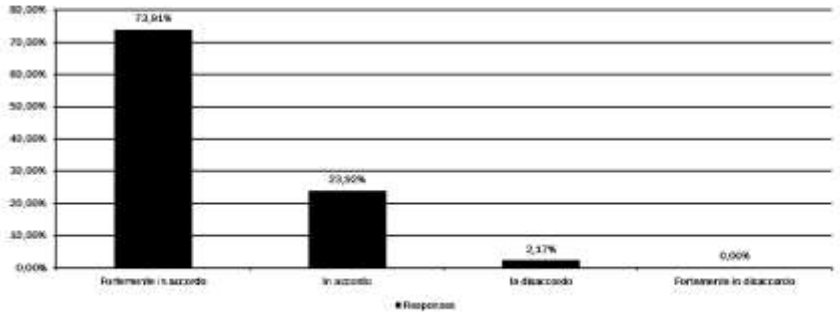
Nel sospetto di deficit cognitivi il MMG deve eseguire un test di screening (es GP-Cog) prima di selezionare i pazienti da inviare al Centro Disturbi Cognitivi e Demenza CDCD.

Accordo: 91,30%



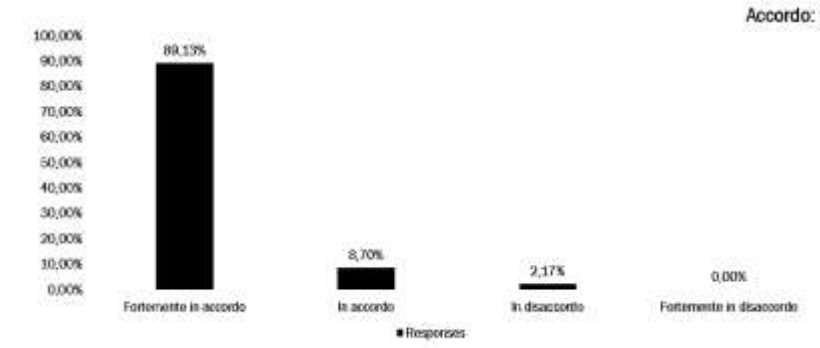
. E' necessario integrare in rete i CDCD del territorio e quelli dell'ospedale in modo da rispondere ad esigenze e fasi diverse della demenza in base alle proprie specificità.

Accordo: 97,83%



E' necessario integrare in una rete di servizi integrati (specialisti territoriali, centri diurni, ADI, servizi socio-sanitari) le fasi assistenziali extra CDCD per quanto riguarda soprattutto le fasi avanzate e o complesse di malattia sulla base di quanto descritto nei PDTA regionali.

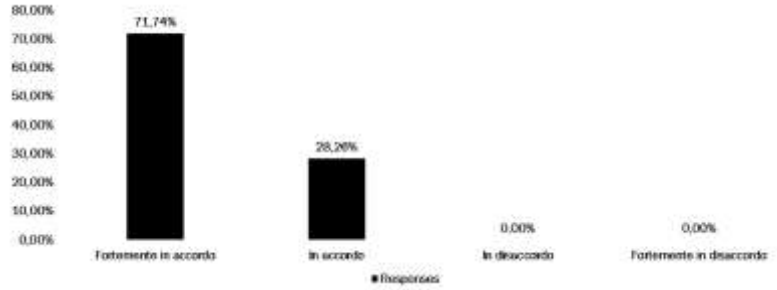
Accordo: 97,83%



La presa in carico, gli attori e la gestione del paziente con disturbi cognitivi

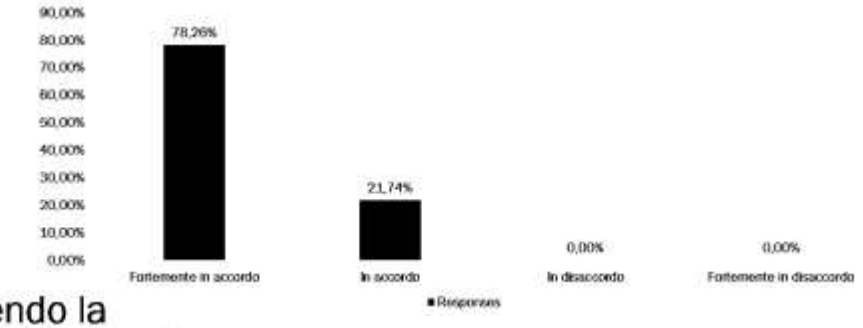
. I PDTA sono fondamentali per l'organizzazione dell'assistenza sanitaria e sociale alle persone con disturbo neurocognitivo e per una corretta presa in carico.

Accordo: 100%



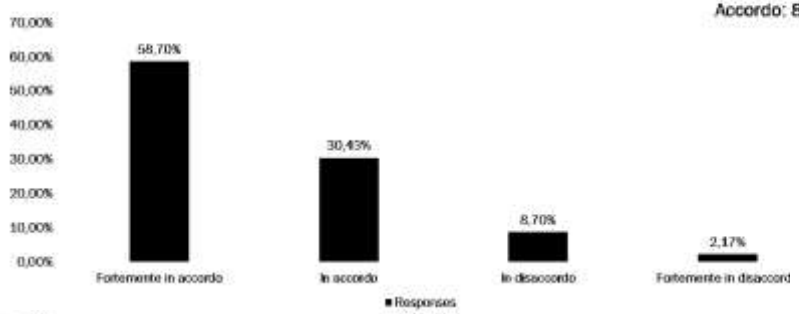
. La presa in carico del paziente non può essere legata solo al CDCD ma deve essere organizzata a livello territoriale coinvolgendo MMG, neurologia e geriatria territoriale, centri diurni, reti dei caffè Alzheimer, Ospedali di Comunità e RSA.

Accordo: 100%



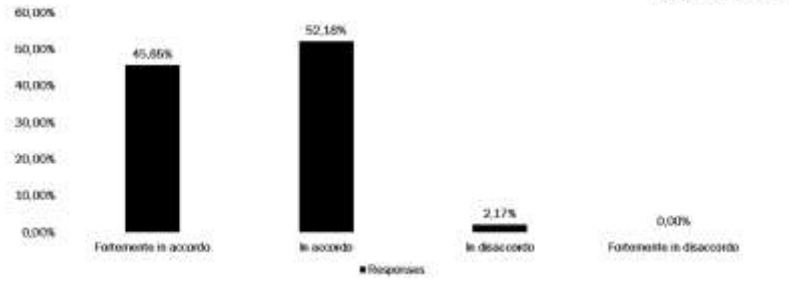
. La nota 85 può essere abolita garantendo la presa in carico dei pazienti da parte dei CDCD per gli appropriati percorsi diagnostico assistenziali.

Accordo: 89.13%



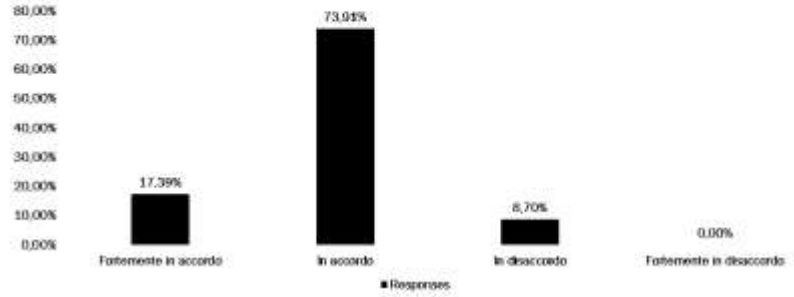
. Le associazioni dei familiari svolgono un ruolo di supporto importante nel percorso socio-assistenziale.

Accordo: 97.83%



. La telemedicina deve essere usata nei CDCD nelle visite di controllo, valutazioni cognitive di follow-up, per aggiustamenti terapeutici e per riabilitazione/stimolazione logopedica e cognitiva.

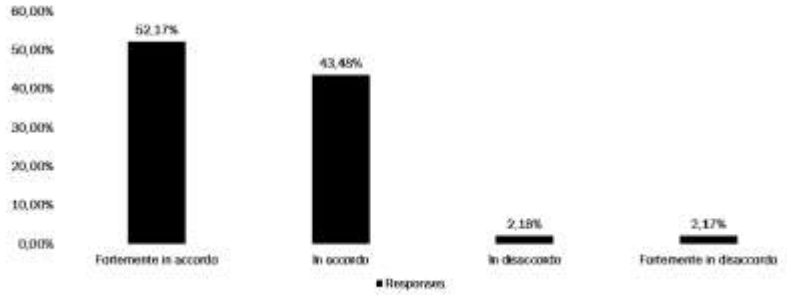
Accordo: 91.30%



L'accesso alla diagnosi Biologica di Malattia di Alzheimer

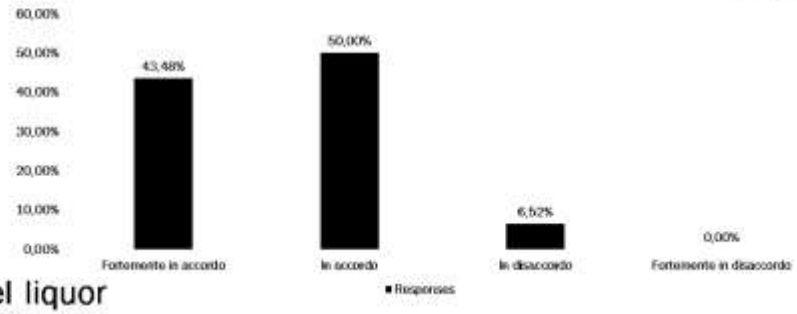
L'attuale organizzazione dei CDCD non permette di effettuare la diagnosi biologica di malattia di Alzheimer in modo uniforme in tutto il territorio nazionale.

Accordo: 95,65%



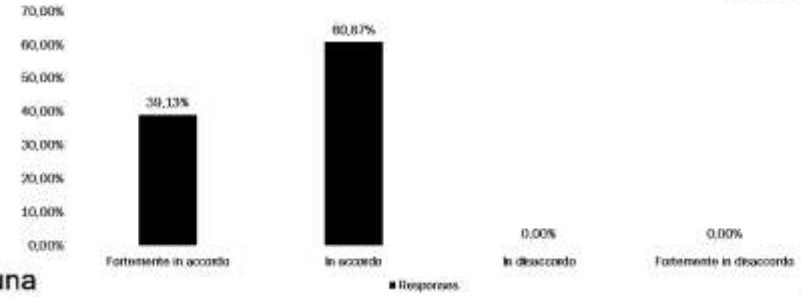
Per permettere a tutti i pazienti di accedere alla diagnosi biologica la rete dei CDCD, sulla base delle loro diverse funzioni, deve essere organizzata a livello distrettuale (modello hub and spoke).

Accordo: 93,48%



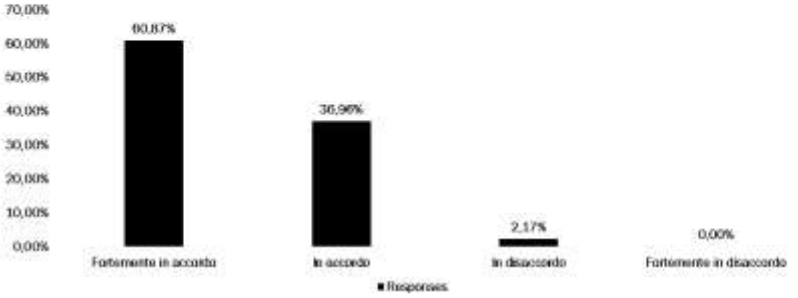
Per ottenere una diagnosi biologica l'esame del liquor fornisce informazioni di patologia più specifiche rispetto alla PET con tracciante per amiloide.

Accordo: 100%



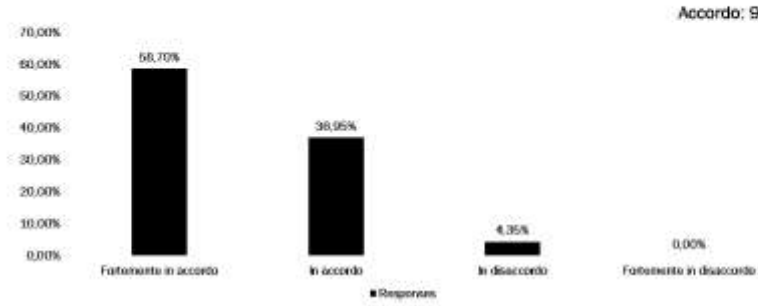
E' opportuno sottoporre prioritariamente alle indagini per una diagnosi biologica di Malattia di Alzheimer quelle persone per cui sarà proponibile, sulla base dei limiti prescrittivi previsti dall'authority, una terapia disease modifying.

Accordo: 97,83%



L'utilizzo di biomarkers plasmatici è implementabile come indagine preliminare per attuare screening indirizzati a selezionare i soggetti da sottoporre a indagini più invasive o costose per il SSN.

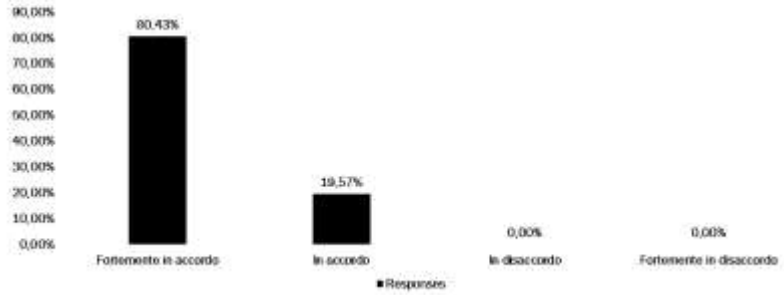
Accordo: 95,65%



I requisiti per la somministrazione dei farmaci disease modifying

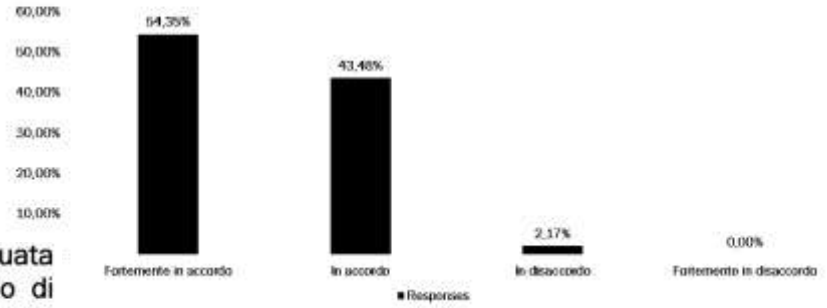
Per potere procedere a un corretta prescrizione, somministrazione e monitoraggio delle terapie DM è necessaria una riorganizzazione e potenziamento dei servizi di Day Hospital/service, di radiologia e una specifica formazione di tutti gli operatori coinvolti.

Accordo: 100%



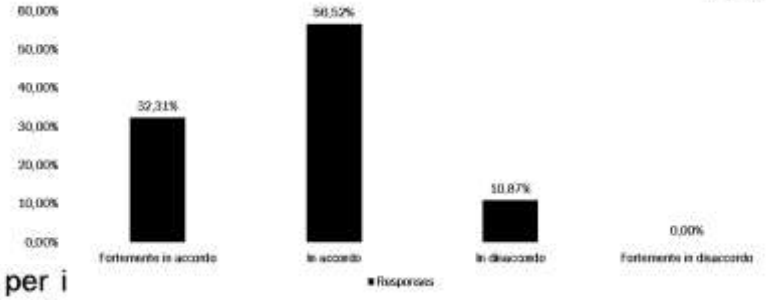
. La prescrizione dei farmaci disease modifying deve essere in carico ai CDCD

Accordo: 97,83%



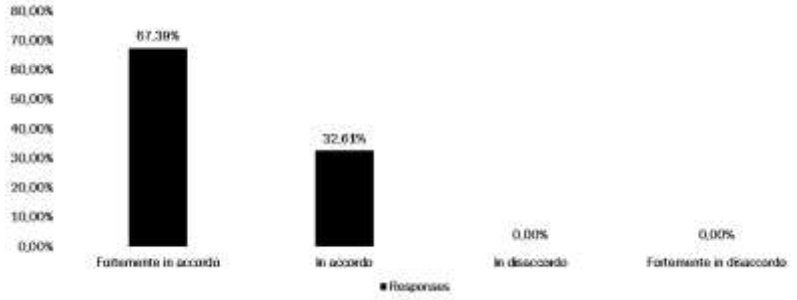
. La somministrazione dei farmaci DM può essere effettuata anche da strutture ospedaliere specializzate purchè in grado di garantire la sicurezza nella somministrazione e il monitoraggio clinico- radiologico.

Accordo: 89.13%



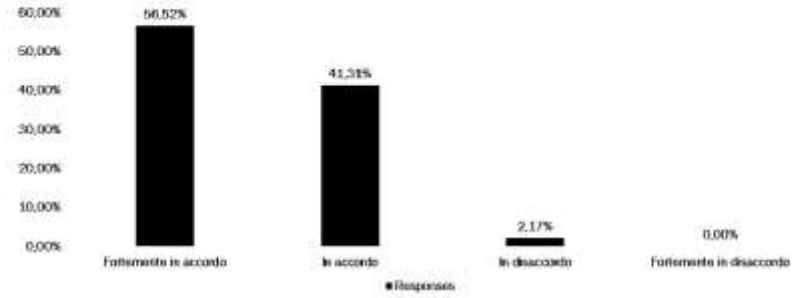
E' necessario che i CDCD che sono centri di infusione per i farmaci DM siano in grado di eseguire anche il monitoraggio clinico-radiologico.

Accordo: 100%



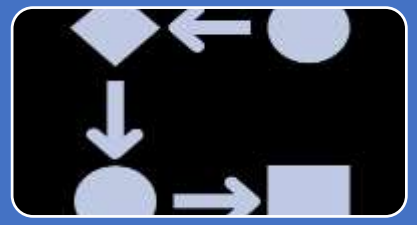
. I CDCD che sono centri di infusione devono avere caratteristiche specifiche (possibilità di accesso a PS h 24, agevolato contatto con lo specialista di riferimento).

Accordo: 97.83%



Management

- PDTA e organizzazione in network dei servizi
- Formazione dei MMG al case finding ed allo screening



Attori e gestione

- Presa in carico e ruolo dei CDCD
- Ruolo dell'associazionismo
- Territorio e medicina di prossimità

La Diagnosi Biologica

Organizzazione hub and spoke

Implementazione risorse e criteri di priorità delle analisi

Ruolo di screening dei biomarcatori plasmatici

Requisiti strutturali centri per la somministrazione DMT

- Ruolo centrale dei CDCD con necessità di orario esteso
- Monitoraggio radiologico nel centro infusionale
- Disponibilità di PS e/o continuità assistenziale

CONSIDERAZIONI CONCLUSIVE

Sebbene le terapie anti-Aβ siano promettenti per intervenire sulla cascata degenerativa, l'importanza della tau e di altre target di neurodegenerazione che possono svolgere un ruolo significativo è solo parzialmente preso in considerazione.

Mancanza al momento di criteri operativi per definire le modalità di intervento e il corretto percorso per la corretta definizione biologica dei pazienti e dello stadio di malattia.

Diversa qualità delle terapie anti-Aβ suggeriscono che siamo lontani dalla possibilità di definire il profilying dei pazienti più adeguati a un determinato tipo di farmaco

Mancanza di una organizzazione dei servizi in rete che permetta l'accesso dei pazienti a terapie DM indipendentemente da localizzazione geografica e disponibilità economica

Necessità di una organizzazione in rete di tutti i servizi per l'Alzheimer per facilitare il 'case finding', l'intervento DM e il monitoraggio senza dimenticare coloro che non accedono a queste cure e che necessitano di una presa in carico convenzionale.

Prospettiva futura di intervento multicomponenziale con differenti target di attacco in modo da incidere in modo complessivo e diacronico nella storia di malattia.

Acknowledgments

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Dr. Noemi Martellacci

Dr. Tommaso G Morganti

Dr. Alessandra M. Rosati

Dr. Alessandro Scalese

Dr. M Gabriella Vita

AI-Mind

PROGETTO INTERCEPTOR

COMFORTAGE