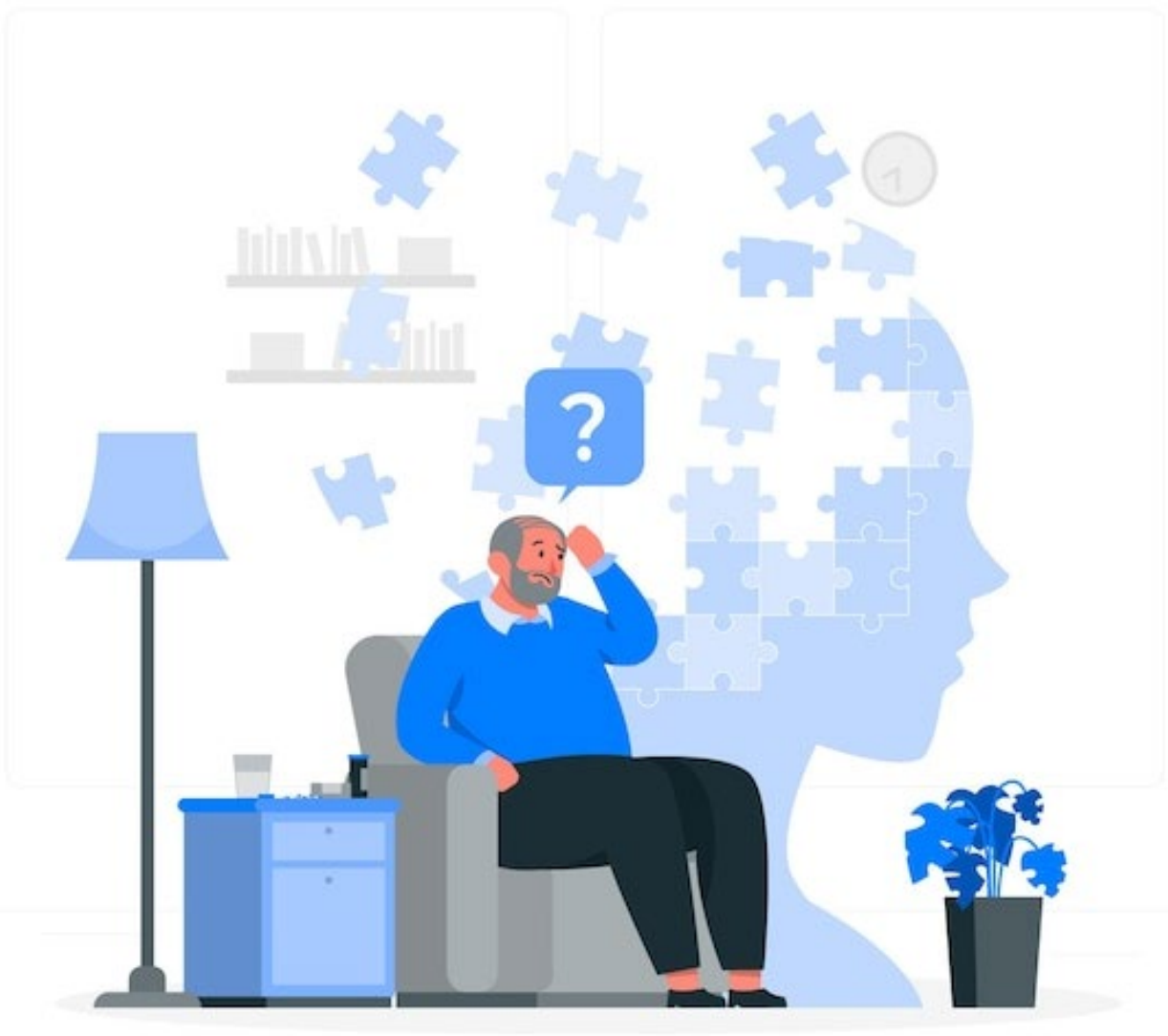


Newer Treatments for Alzheimer's Disease and Dementia

J. Mark Ruscin, Pharm.D., FCCP

Professor, Dept of Pharmacy Practice

SIUE School of Pharmacy

My Background and Perspective

- Faculty member at SIUE School of Pharmacy since 2008
- Previously at Univ of CO School of Pharmacy and Center on Aging (1995 – 2008)
- Teaching, clinical service, and research interests revolve around the care of older adults

John D Ruscin

1927 - 2024

SCIENCE & MEDICINE

FDA OKs Alzheimer's Disease Treatment : Health Officials say drug is not a cure but that it will offer relief from symptoms for some. It is expected to cost about $1,500 a year.

By MARLENE CIMONS
Sept. 10, 1993 12 AM PT

TIMES STAFF WRITER

WASHINGTON — The Food and Drug Administration on Thursday approved the first drug for the treatment of Alzheimer's disease, a debilitating brain ailment that robs millions of elderly people of their memory, independence and dignity.

https://www.latimes.com/archives/la-xpm-1993-09-10-mn-33566-story.html

A brief look at the history of FDA drug approvals for Alzheimer's Disease (AD)

Isoxuprine, cyclandelate, dipyridamole (not FDA approved)

Tacrine - First treatment FDA approved for AD 1993

Donepezil - FDA approved in 12/1996

Rivastigmine - FDA approved in 4/2000

Galantamine - FDA approved in 2/2001

Memantine - FDA approved in 10/2003

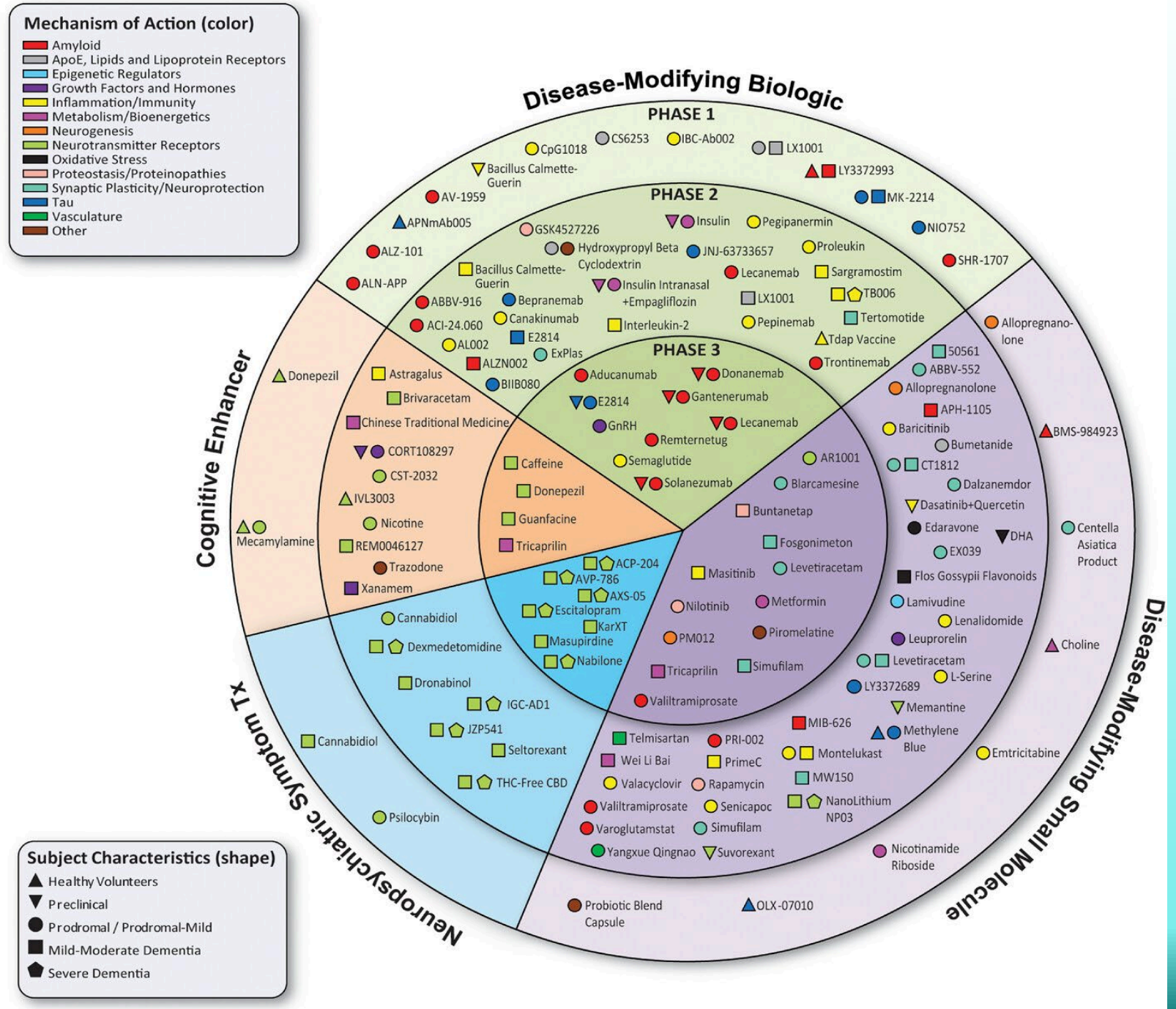
Aducanumab* – accelerated FDA approval Jan 2021
*(Off market as of Jan 2024)

Lecanemab – FDA approved 7/2023

Donanemab – FDA approved 7/2024

Benzgalantamine – FDA approved 7/2024

2024 Alzheimer's Drug Development Pipeline

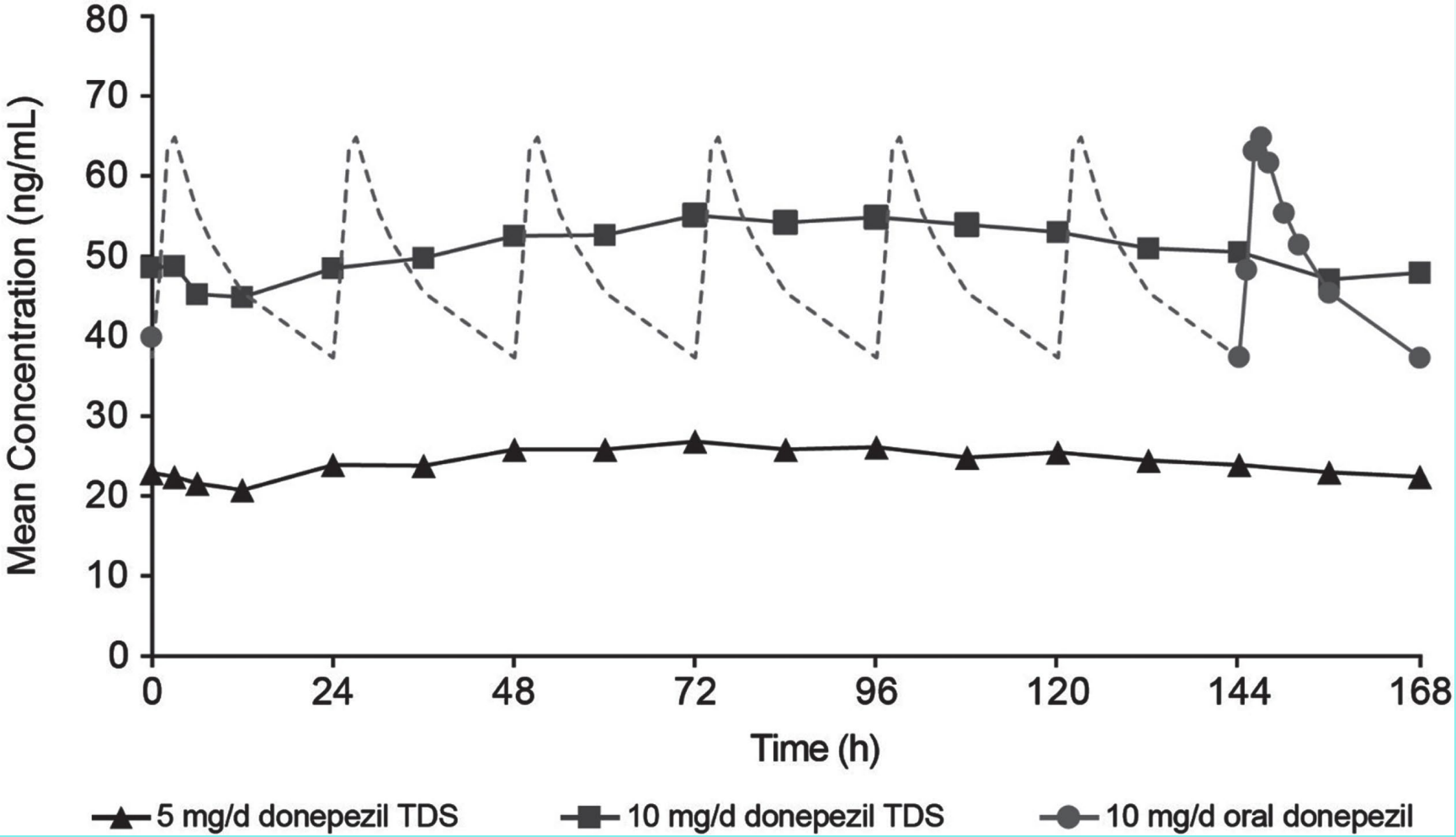


Cummings J, et al. Alzheimer's disease drug development pipeline 2024. *Alzheimer's Dement.* 2024;10:e12465

“New” Medications

- Donepezil patch (Adlarity) 5mg or 10mg systems
  - Transdermal administration – once weekly (apply to upper back)
  - FDA approved 3/22 - acetylcholinesterase inhibitor indicated for the treatment of mild, moderate, and severe dementia of the Alzheimer’s type
  - Must be refrigerated
  - Clinical implications
    - Avoids first pass metabolism
    - Lower risk of GI adverse effects
    - Common AE – skin irritation/rash
    - Once per week dosing vs once per day
  - Cost
    - Cash price around $480/4week supply (4 patches – 5mg or 10mg)
    - Compared to oral generic donepezil ~ $120 ($10-20 with discount cards)

Kinetics of oral vs TDS donepezil



Tariot PN, et al. Comparison of steady-state pharmacokinetics of donepezil transdermal delivery system with oral donepezil. *J Alz Disease* 2022;90(1):161-172.

Adverse effects – oral vs patch

Side effect	Donepezil Oral	Donepezil Patch
Nausea	11%	Undefined
Diarrhea	10%	4%
Headache	10%	15%
Insomnia	9%	7%
Pain	9% (various locations)	6% (abdominal pain)
Dizziness	8%	4%
Application site itching/irritation	Not applicable	6% to 9%
Muscle spasms/cramps	6%	9%
Constipation	Rare	6%
Abnormal dreams	3%	4%

https://www.goodrx.com/conditions/alzheimers-disease/aricept-vs-adlarity-alzheimers

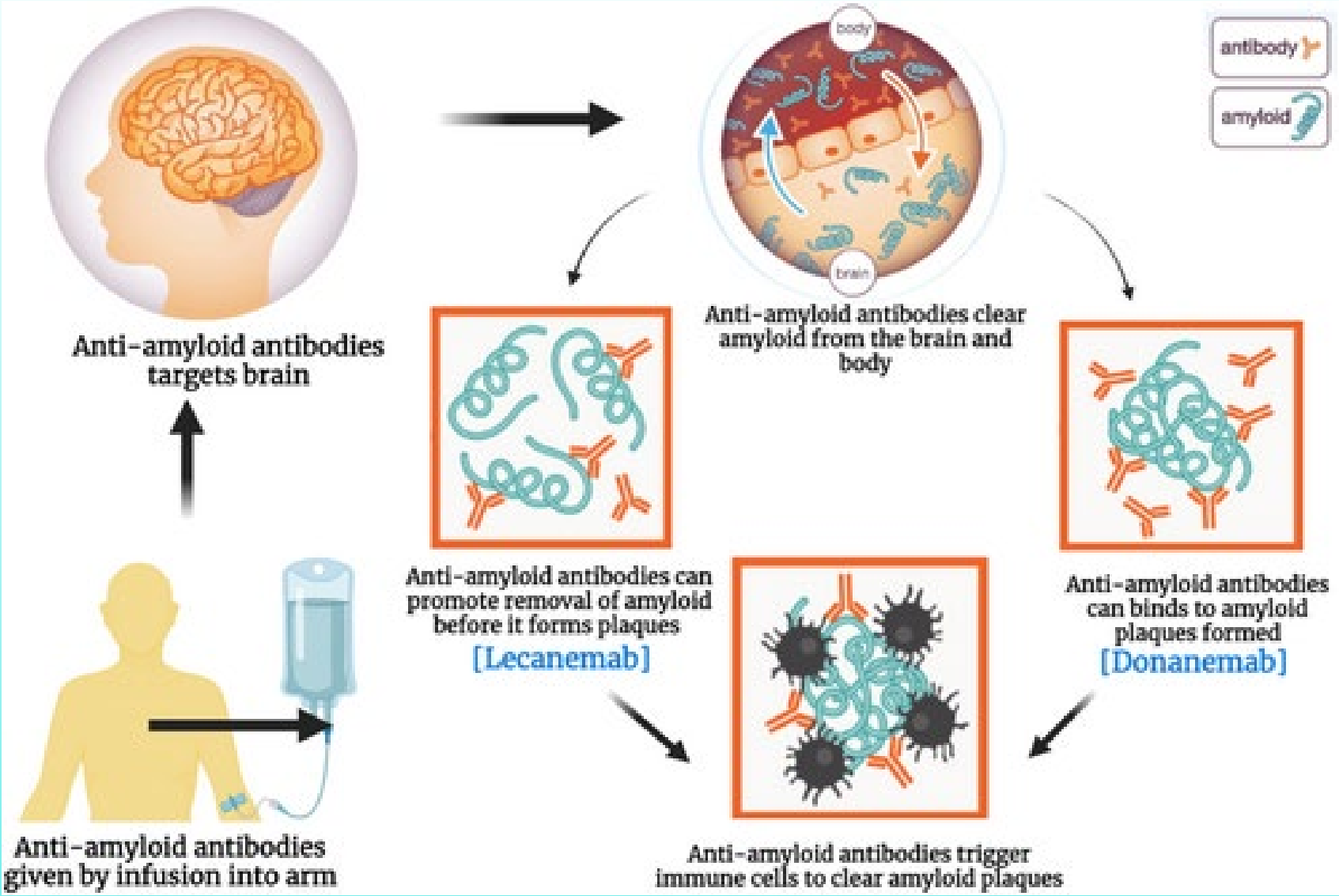
“New” Medications

- Benzgalantamine (Zunveyl)
  - ChEI approved for mild to moderate AD
    - Dosed 5mg BID; after 4 weeks can increase to 10mg BID, up to max 15mg BID
  - Inactive prodrug of galantamine
    - metabolized in the liver to galantamine
  - Reduced enteral binding to gut cholinergic receptors
    - lowering GI adverse effects
  - Bioequivalence studies showed equivalence to galantamine IR and ER
  - Combo formulation with Memantine in the works for treatment of mod-severe AD
  - Cost
    - Cash price ~ $500/mo vs generic galantamine $140 or $20-30 with GoodRx Coupon

Aducanumab (Aduhelm)

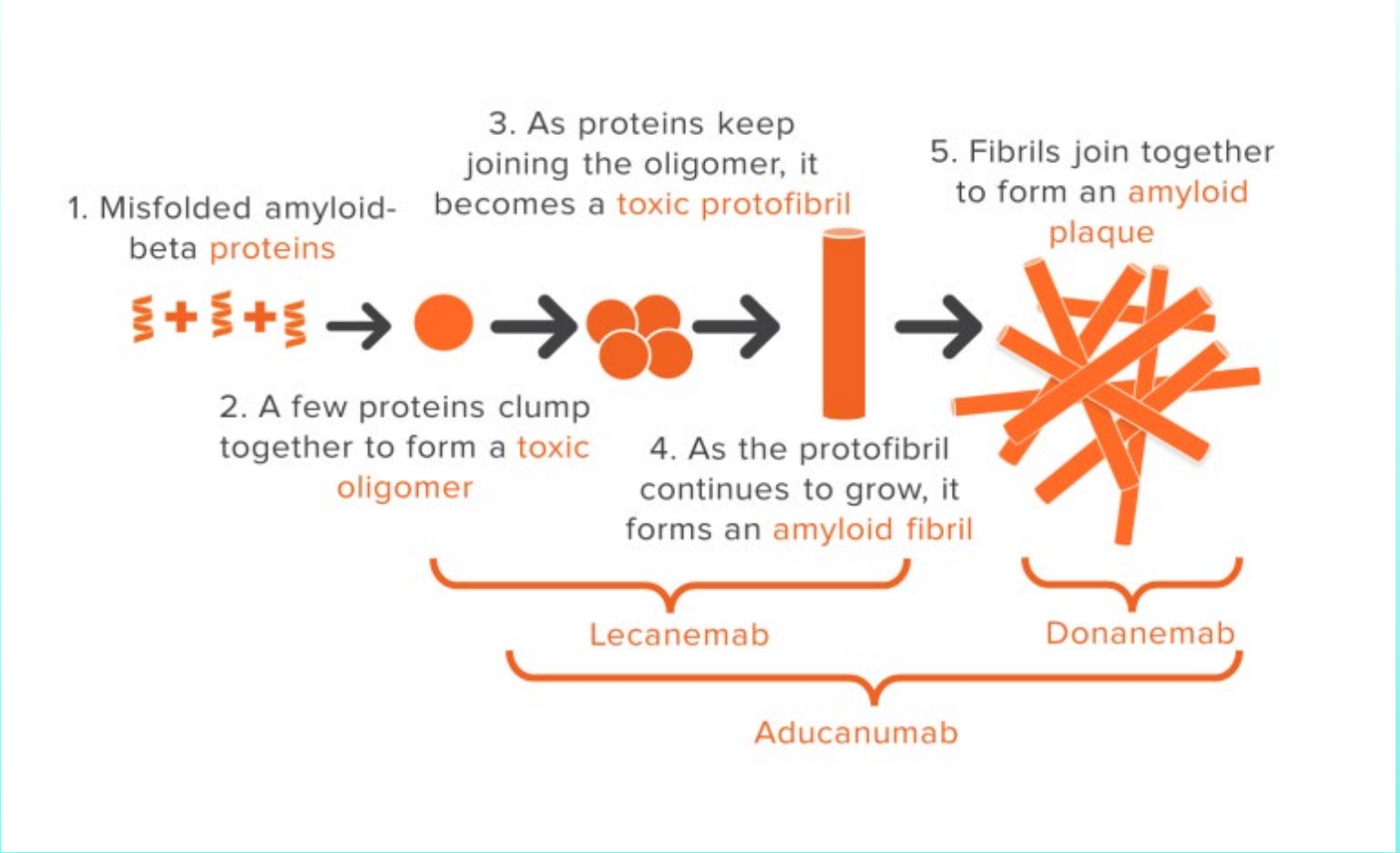
- Human monoclonal antibody directed against aggregated soluble and insoluble forms of amyloid beta
- Started the wave of new approvals for AD
- Approved by FDA in January 2021 – accelerated approval
  - Conditional on a confirmatory clinical trial
- Controversy surrounding the approval
  - 2 studies (EMERGE & ENGAGE) – 1600 patients with MCI/mild dementia
    - Studies were halted based on analysis of pooled data @ 50% enrollment
    - Reanalysis of data showed benefit in EMERGE, but not ENGAGE
    - Both studies showed reduced amyloid
- Company voluntarily removed from market in Jan 2024

Anti-amyloid therapies



https://www.alzheimersresearchuk.org/news/new-alzheimers-drug-donanemab-what-is-it-and-how-does-it-work/

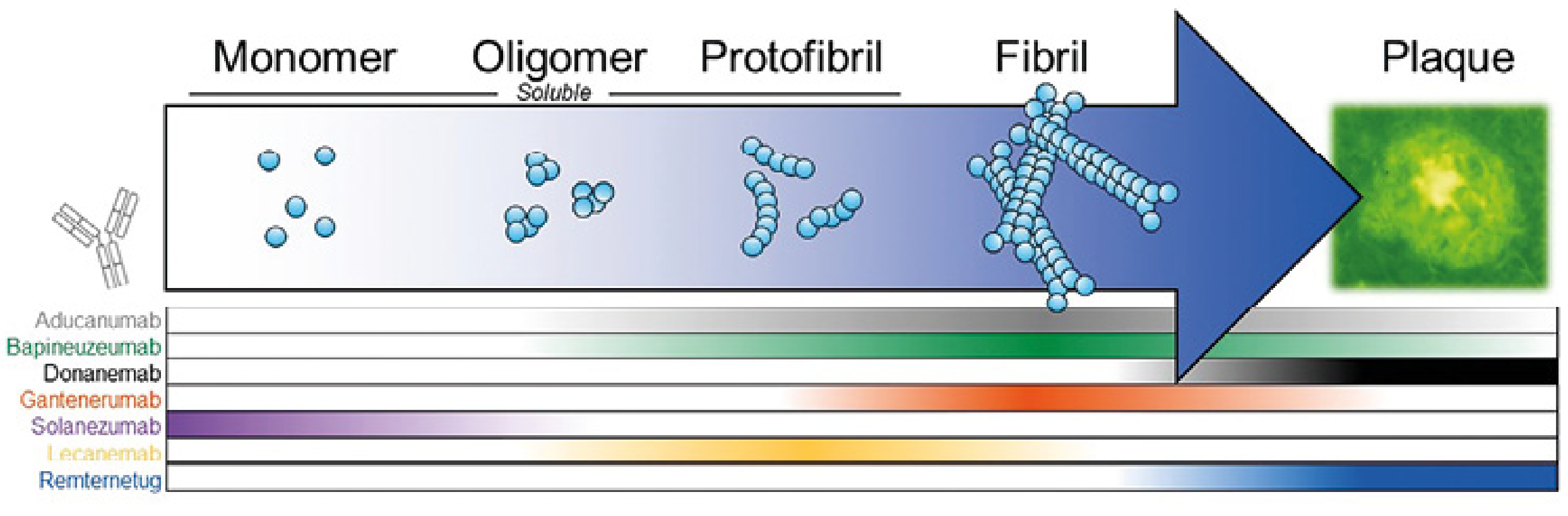
Amyloid therapy



New Medications Approved in 2023: Alzheimer's Disease, Depression, Anxiety and Schizophrenia (Psych Education)

- By Flavio Guzman, M.D.
- Last updated 16 Jan, 2024 (https://psycheducation.org/new-medications-approved-in-2023-alzheimers-disease-and-depression-2/)

Monoclonal antibody affinity for amyloid β plaque development stages



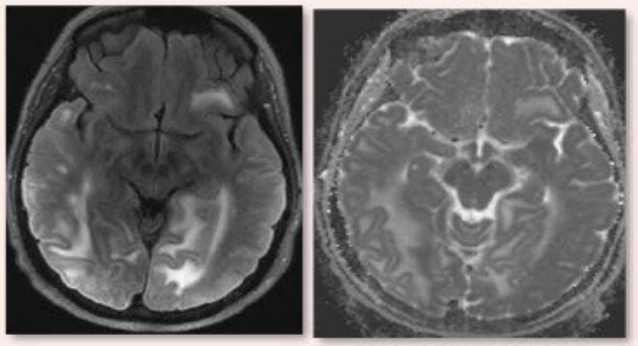
Updates on pharmacological treatment for Alzheimer's disease
Philip W. Tipton
DOI: 10.5603/pjnns.96286
Pubmed: 37606550
Neurol Neurochir Pol 2024;58(2):150-160.

Amyloid-Related Imaging Abnormalities (ARIA)

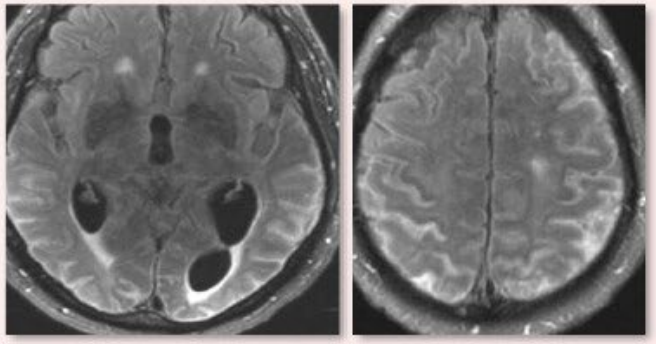
- **ARIA** is thought to be associated with the clearance of amyloid plaques, potentially leading to increased vascular permeability and disruption of the blood-brain barrier.
  - **Types of ARIA:**
    - **ARIA-E:** Characterized by edema (fluid accumulation) and/or effusion (fluid leakage) in the brain.
    - **ARIA-H:** Characterized by microhemorrhages (small bleeds) and/or superficial siderosis (iron deposition).
  - **Clinical Significance:**
    - ARIA often asymptomatic/self-resolving, it can lead to symptoms like headache, confusion, nausea, dizziness, and in rare cases, seizures and even death.
  - **Monitoring and Management:**
    - ARIA monitoring is crucial during anti-amyloid therapy, and management strategies include temporary suspension or discontinuation of treatment, depending on the severity and type of ARIA.
  - **Risk Factors:**
    - Certain factors, such as Apoε4 carrier status and a history of prior strokes, can increase the risk of developing ARIA

Amyloid-related Imaging Abnormalities in Alzheimer Disease Treated with Anti-amyloid-β Therapy

Amyloid-related imaging abnormalities (ARIA)

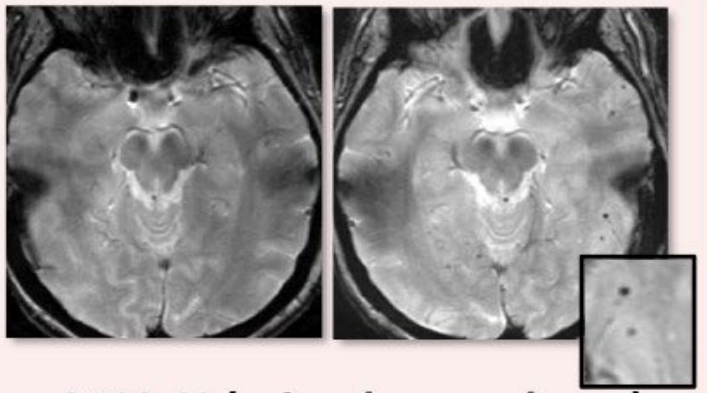


ARIA-E (edema)



ARIA-E (effusion)

ARIA-E is characterized by parenchymal edema and/or sulcal effusion. This is the most common side effect of monoclonal antibodies.



ARIA-H (microhemorrhage)

ARIA-H is characterized by parenchymal microhemorrhages and/or superficial siderosis.

Increased vascular permeability forms the basis of both ARIA-E and ARIA-H. Therefore, both entities can occur **concurrently**.

Agarwal A et al. Published online: August 31, 2023
https://doi.org/10.1148/rg.230009

RadioGraphics

Agarwal A. Published Online: August 31, 2023
https://doi.org/10.1148/rg.230009

RadioGraphics

Amyloid Therapy – FDA Black Box Warning

WARNING: AMYLOID RELATED IMAGING ABNORMALITIES

Monoclonal antibodies directed against aggregated forms of beta amyloid can cause amyloid related imaging abnormalities (ARIA), characterized as ARIA with edema (ARIA-E) and ARIA with hemosiderin deposition (ARIA-H). Incidence and timing of ARIA vary among treatments. ARIA usually occurs early in treatment and is usually asymptomatic, although serious and life-threatening events rarely can occur. Serious intracerebral hemorrhages >1 cm, some of which have been fatal, have been observed in patients treated with this class of medications. Because ARIA-E can cause focal neurologic deficits that can mimic an ischemic stroke, treating clinicians should consider whether such symptoms could be due to ARIA-E before giving thrombolytic therapy in a patient being treated with Lecanemab/Donanemab

<u>ApoE ε4 Homozygotes</u>
Patients who are apolipoprotein E ε4 (ApoE ε4) homozygotes (approximately 15% of Alzheimer's disease patients) treated with this class of medications have a higher incidence of ARIA, including symptomatic, serious, and severe radiographic ARIA, compared to heterozygotes and noncarriers. Testing for ApoE ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. Prior to testing, prescribers should discuss with patients the risk of ARIA across genotypes and the implications of genetic testing results. Prescribers should inform patients that if genotype testing is not performed, they can still be treated; however, it cannot be determined if they are ApoE ε4 homozygotes and at higher risk for ARIA

Consider the benefits of treatment of Alzheimer's disease and potential risk of serious adverse events associated with ARIA when deciding to initiate treatment.

Apolipoprotein E4

- ApoE gene (chromosome 19) role in the transport of cholesterol and other lipids between peripheral tissues and the liver
- ApoE gene has 3 major alleles (variants) – E2, E3, E4
  - E3 is the ‘normal’ variant
  - E4 one copy or two copies is associated with increased risk of AD
- How do you know? -testing can be done with various home testing genetic kits - cheek swab or blood draw
- ApoE4 carrier status is also associated with increased risk of ARIA
  - Heterozygotes < Homozygotes

Lecanemab (Leqembi)

- Traditional FDA approval 7/6/2023
- humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble and insoluble forms of amyloid beta.
- Approved for early symptomatic AD, which includes mild cognitive impairment (MCI) or mild dementia stage
  - MMSE 22-29/CDR Global score of 0.5 to 1.0 = CDR-SB 0.5 – 6.0)
- Confirm the presence of Amyloid beta pathology (PET scan or CSF analysis)
- Administered by IV-infusion 10mg/kg over 60min every 2 weeks
  - Recent FDA approval (Jan 25) allows for Q4 week maintenance dosing (after initial 18mo tx)
- Baseline MRI – and prior to 5^{th}, 7^{th}, and 14^{th} infusions
  - ARIA safety measures

Lecanemab Pivotal Study (CLARITY AD)

Van Dyck CH. *NEJM* 2023:388:9-21

- 1795 patients with MCI or mild dementia due to AD
- Age 50 – 90
- Evidence of Amyloid on PET or CSF
- Randomized to Lecanemab 10mg/kg infusion Q 2 weeks, or placebo
  - Stratified by:
    - MCI vs Mild AD
    - Concomitant use of approved meds, AChEI/Mentantine (present vs absent)
    - APOe4 carrier vs noncarrier
    - Geographic region
- Primary outcome – Clinical Dementia Rating-Sum of Boxes (CDR-SB)

Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology* 1993;43:2412-14.

CLINICAL DEMENTIA RATING (CDR)

CLINICAL DEMENTIA RATING (CDR):	0	0.5	1	2	3

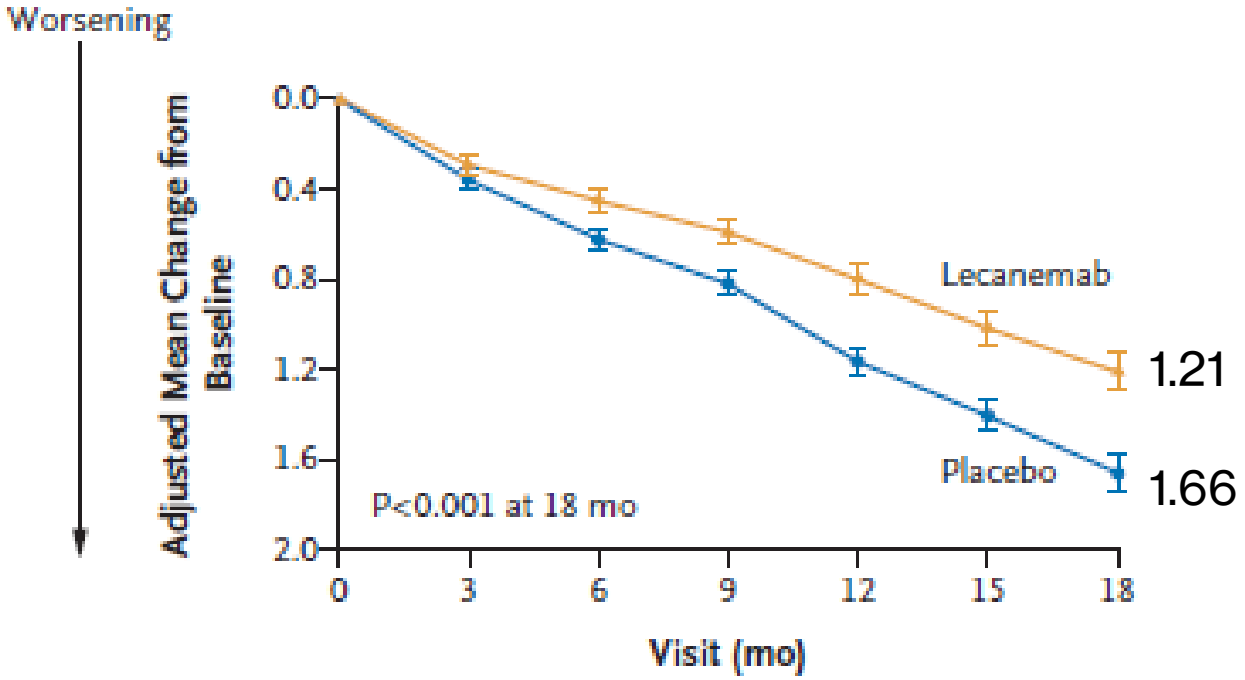
	Impairment				
	None 0	Questionable 0.5	Mild 1	Moderate 2	Severe 3
Memory	No memory loss or slight inconsistent forgetfulness	Consistent slight forgetfulness; partial recollection of events; "benign" forgetfulness	Moderate memory loss; more marked for recent events; defect interferes with everyday activities	Severe memory loss; only highly learned material retained; new material rapidly lost	Severe memory loss; only fragments remain
Orientation	Fully oriented	Fully oriented except for slight difficulty with time relationships	Moderate difficulty with time relationships; oriented for place at examination; may have geographic disorientation elsewhere	Severe difficulty with time relationships; usually disoriented to time, often to place	Oriented to person only
Judgment & Problem Solving	Solves everyday problems & handles business & financial affairs well; judgment good in relation to past performance	Slight impairment in solving problems, similarities, and differences	Moderate difficulty in handling problems, similarities, and differences; social judgment usually maintained	Severely impaired in handling problems, similarities, and differences; social judgment usually impaired	Unable to make judgments or solve problems
Community Affairs	Independent function at usual level in job, shopping, volunteer and social groups	Slight impairment in these activities	Unable to function independently at these activities although may still be engaged in some; appears normal to casual inspection	No pretense of independent function outside home Appears well enough to be taken to functions outside a family home	Appears too ill to be taken to functions outside a family home
Home and Hobbies	Life at home, hobbies, and intellectual interests well maintained	Life at home, hobbies, and intellectual interests slightly impaired	Mild but definite impairment of function at home; more difficult chores abandoned; more complicated hobbies and interests abandoned	Only simple chores preserved; very restricted interests, poorly maintained	No significant function in home
Personal Care	Fully capable of self-care		Needs prompting	Requires assistance in dressing, hygiene, keeping of personal effects	Requires much help with personal care; frequent incontinence

Score only as decline from previous usual level due to cognitive loss, not impairment due to other factors.

Lecanemab Outcomes

- Pivotal clinical trial (CHvanDyck. *NEJM* 2023:388:9-21)
  - Allowed use of approved AD medications (AChEI and Memantine)

A CDR-SB Score

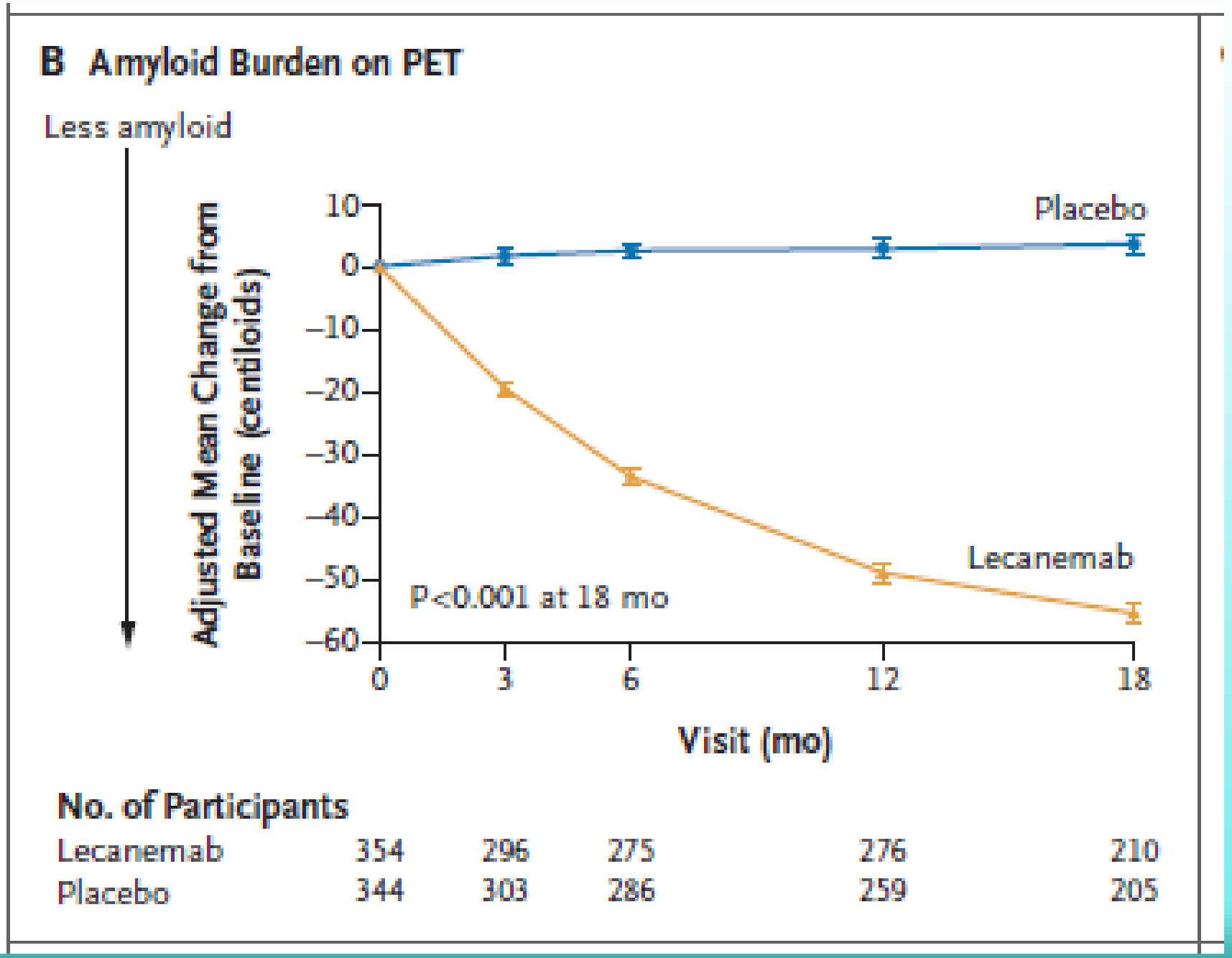


Diff = -0.45

No. of Participants

Lecanemab	859	824	798	779	765	738	714
Placebo	875	849	828	813	779	767	757

Change in Amyloid burden



CHvanDyck. *NEJM* 2023:388:9-21

Lecanemab – Adverse Effects

- Non-ARIA AEs
  - Infusion reactions (26% vs 7%)
  - Headache (11% vs 8%)
- AEs leading to study drug discontinuation (7% vs 3%)
- ARIA (26.6% vs 9.4%)
  - ARIA-E (12.6% vs 1.7%)
    - Symptomatic ARIA-E (2.8% vs 0%)
    - By APOE4 status: noncarrier - 5.4%; ApoE4 heterozygote - 10.9%; ApoE4 homozygote – 32.6%
  - ARIA-H (17.3% vs 9.0%)
    - Microhemorrhage (14.0% vs 7.6%); superficial siderosis (5.6% vs 2.3%)
- Deaths: 6 (0.7%) vs 7 (0.8%) – none considered related to Lecanemab or ARIA

CHvanDyck. *NEJM* 2023:388:9-21

Donanemab (Kisunla)

- FDA approval 7/2/2024
- Humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against insoluble N-truncated pyroglutamate amyloid beta
- Approved for early symptomatic AD, which includes mild cognitive impairment (MCI) or mild dementia stage
- Confirm the presence of Amyloid beta pathology (PET scan or CSF analysis)
- Administered by IV-infusion (30-60min) Q 4 weeks
  - Dose 1, 2, 3 – 700mg (diluted in 0.9% NaCl solution)
  - Dose 4 and beyond - 1400mg (diluted in 0.9% NaCl soln)
- Baseline MRI – and prior to 2nd, 3rd, 4th, and 7th infusions
  - ARIA safety measures

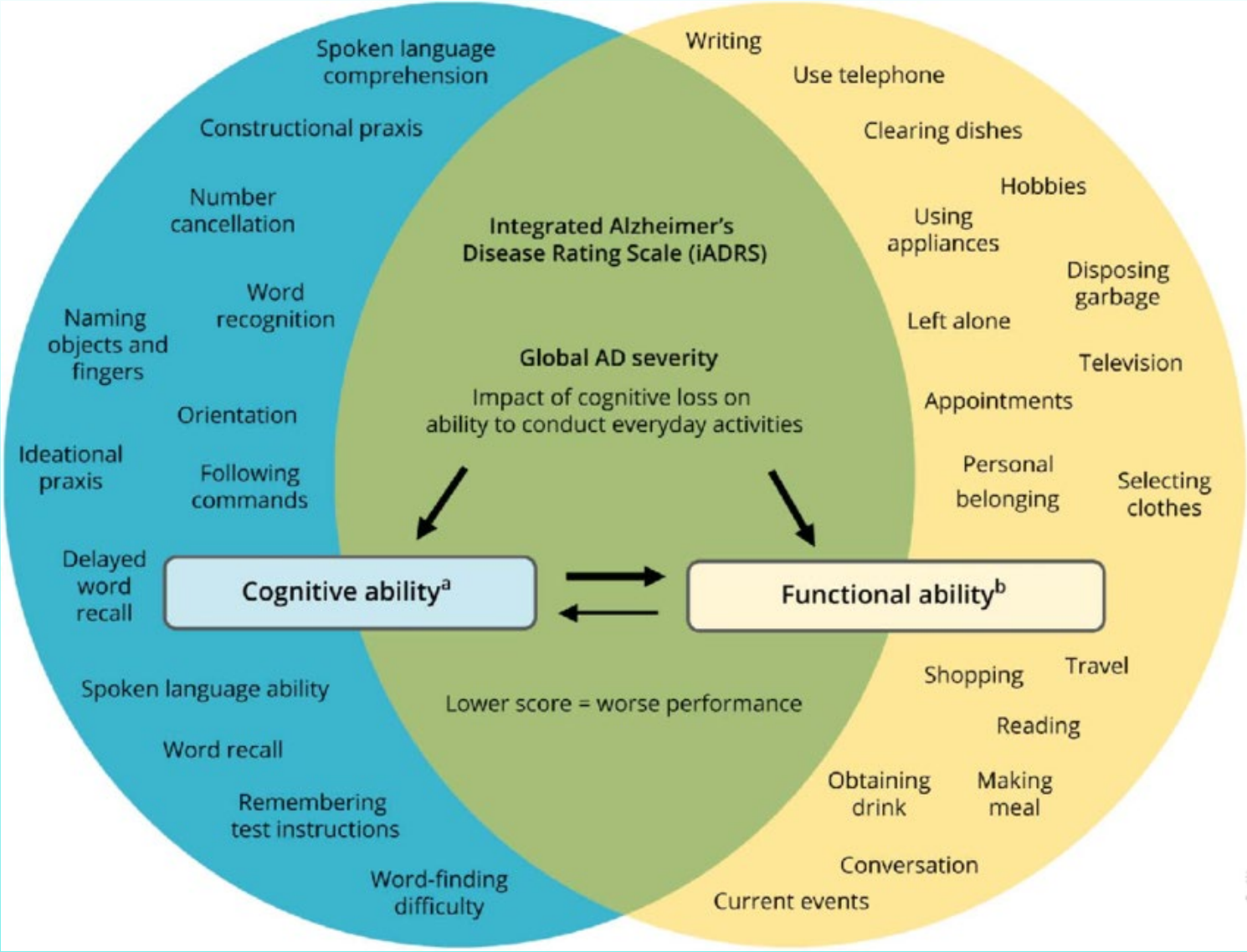
Donanemab Pivotal Study (TRAILBLAZER-ALZ 2)

Sims JR. *JAMA* 2023;330(6):512-527

- 1736 patients with MCI or early symptomatic AD (mild dementia)
- Age 60 – 85
- Screening MMSE of 20-28
- Presence of Amyloid pathology and Tau pathology by PET
  - Low/med Tau pathology and combined group low/med plus high Tau
- Randomized to Donanemab Q4 weeks or placebo x 72 weeks
  - Donanemab dosed at 700mg x 3 doses; then 1400mg thereafter
  - Donanemab switched to placebo if Amyloid lowered to specific thresholds (week 24, 52)
  - Stratified by Tau category and enrolling site
- Primary outcome – change in integrated Alzheimer Disease Rating Scale (iADRS)

Donanemab Outcomes

iADRS Score
0 - 144



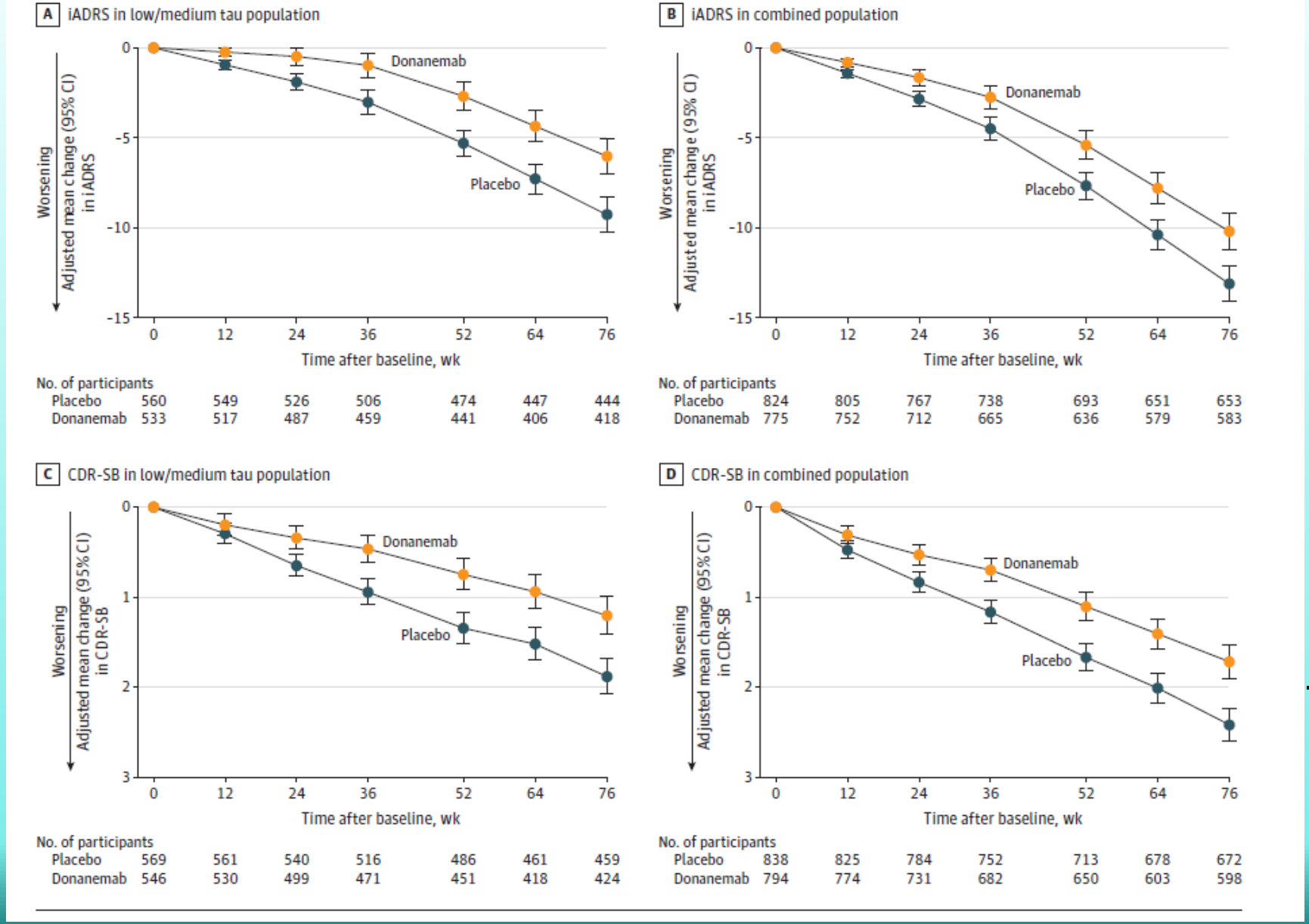
Wessels AM, et al.. A Combined Measure of Cognition and Function for Clinical Trials: The Integrated Alzheimer's Disease Rating Scale (iADRS). J Prev Alzheimers Dis. 2015 Dec 1;2(4):227-241. doi: 10.14283/jpad.2015.82. PMID: 27019841; PMCID: PMC4806404.

Donanemab Outcomes

Sims JR. *JAMA* 2023;330(6):512-527

3.25

2.92

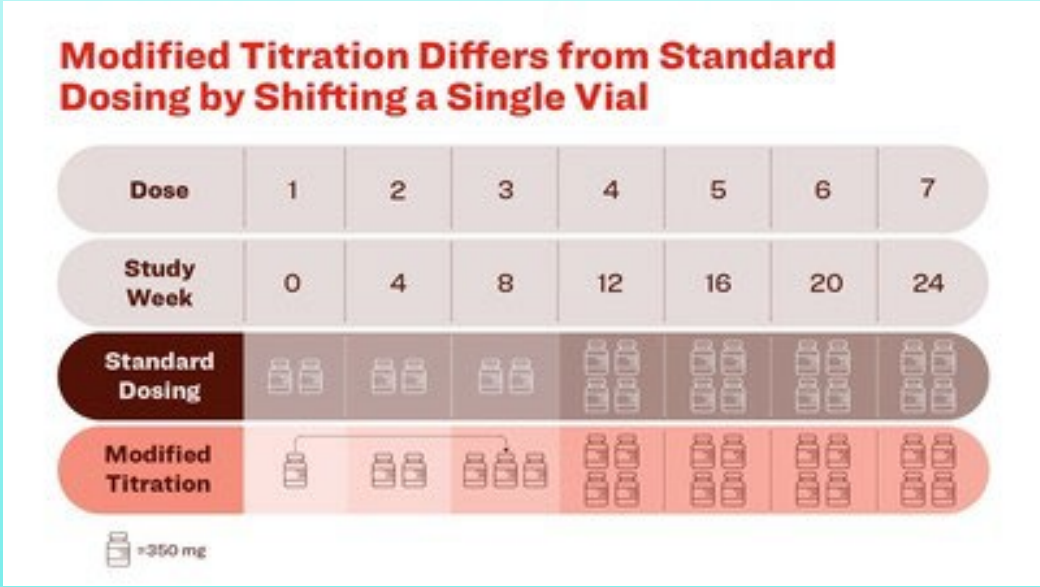


-0.67

-0.7

Donanemab - Adverse Effects

- Non-ARIA AEs
  - Infusion reactions (8.7% vs 0.5%)
  - Headache (14% vs 9.8%)
- ARIA (36.8% vs 14.9%)
  - ARIA-E (24.0% vs 2.1%)
    - Symptomatic ARIA-E (6.1% vs 0.1%)
    - APOE4 status: noncarrier: 15.7% E4 heterozygote: 22.8% E4 homozygote: 40.6%
  - ARIA-H (31.4% vs 13.6%)
    - Microhemorrhage (26.8% vs 12.5%)
    - Superficial Siderosis (15.7% vs 3.0%)
- Deaths: 16 (1.9%) vs 10 (1.1%)
  - Treatment related: 3 (0.4%) vs 1 (0.1%)
    - 3 with serious ARIA died (2 ApoE4 carriers; 1 noncarrier)



Sims JR. *JAMA* 2023;330(6):512-527

ddhttps://investor.lilly.com/news-releases/news-release-details/modified-titration-donanemab-demonstrated-reduction-aria-e-early

Lecanemab or Donanemab-related ARIA-E

Dosing Recommendations for Patients With ARIA-E			
Clinical Symptom Severity[a]	**ARIA-E Severity on MRI**		
	Mild	**Moderate**	**Severe**
Asymptomatic	May continue dosing at current dose and schedule	Suspend dosing[b]	Suspend dosing[b]
Mild	May continue dosing based on clinical judgment	Suspend dosing[b]	
Moderate or Severe	Suspend dosing[b]		

[a] Mild: discomfort noticed, but no disruption of normal daily activity.
Moderate: discomfort sufficient to reduce or affect normal daily activity.
Severe: incapacitating, with inability to work or to perform normal daily activity.

[b] Suspend until MRI demonstrates radiographic resolution and symptoms, if present, resolve; consider a follow-up MRI to assess for resolution 2 to 4 months after initial identification. Resumption of dosing should be guided by clinical judgment.

Lecanemab or Donanemab-related ARIA-H

Dosing Recommendations for Patients With ARIA-H			
Clinical Symptom Severity	**ARIA-H Severity on MRI**		
	Mild	**Moderate**	**Severe**
Asymptomatic	May continue dosing at current dose and schedule	Suspend dosing[a]	Suspend dosing[b]
Symptomatic	Suspend dosing[a]	Suspend dosing[a]	

[a] Suspend until MRI demonstrates radiographic stabilization and symptoms, if present, resolve; resumption of dosing should be guided by clinical judgment; consider a follow-up MRI to assess for stabilization 2 to 4 months after initial identification.

[b] Suspend until MRI demonstrates radiographic stabilization and symptoms, if present, resolve. Use clinical judgment when considering whether to continue treatment or permanently discontinue treatment.

In patients who develop intracerebral hemorrhage greater than 1 cm in diameter during treatment, suspend dosing until MRI demonstrates radiographic stabilization and symptom resolution, if present, resolve. Consideration to resume dosing should be guided by clinical judgment.

Infusion Reactions to Lecanemab/Donanemab

- **Infusion-related reactions:**
  - fever
  - flu-like symptoms (chills, body aches, feeling shaky, joint pain)
  - nausea and/or vomiting
  - dizziness or lightheadedness
  - fast or slow heart rate, or feeling like your chest is pounding
  - difficulty breathing or shortness of breath
- If experience infusion-related reaction, can consider standard infusion-reaction type medications
  - NSAIDs, antihistamines, acetaminophen, steroids

Anticoagulants/Antiplatelet with Amyloid Tx

- Lecanemab Phase 3 Clarity AD Trial: ARIA With the Use of Antiplatelets or Anticoagulants in Early Alzheimer's Disease
  - ARIA rates on lecanemab
    - no antiplatelet or anticoagulation: 21.8%, antiplatelet: 17.9%, anticoagulation: 13.3%
  - ARIA-E was 13.1% in the lecanemab group and 1.5% in the placebo group when no antiplatelet or anticoagulant medication was used
    - 10.4% in the lecanemab group and 0.84% in the placebo group when antiplatelet medication was used
    - 4.8% in the lecanemab group and 2.7% in the placebo group when anticoagulant medication was used.
  - ARIA did not occur more frequently in lecanemab-treated participants on antiplatelet or anticoagulant drugs compared to lecanemab-treated participants that were not on either.

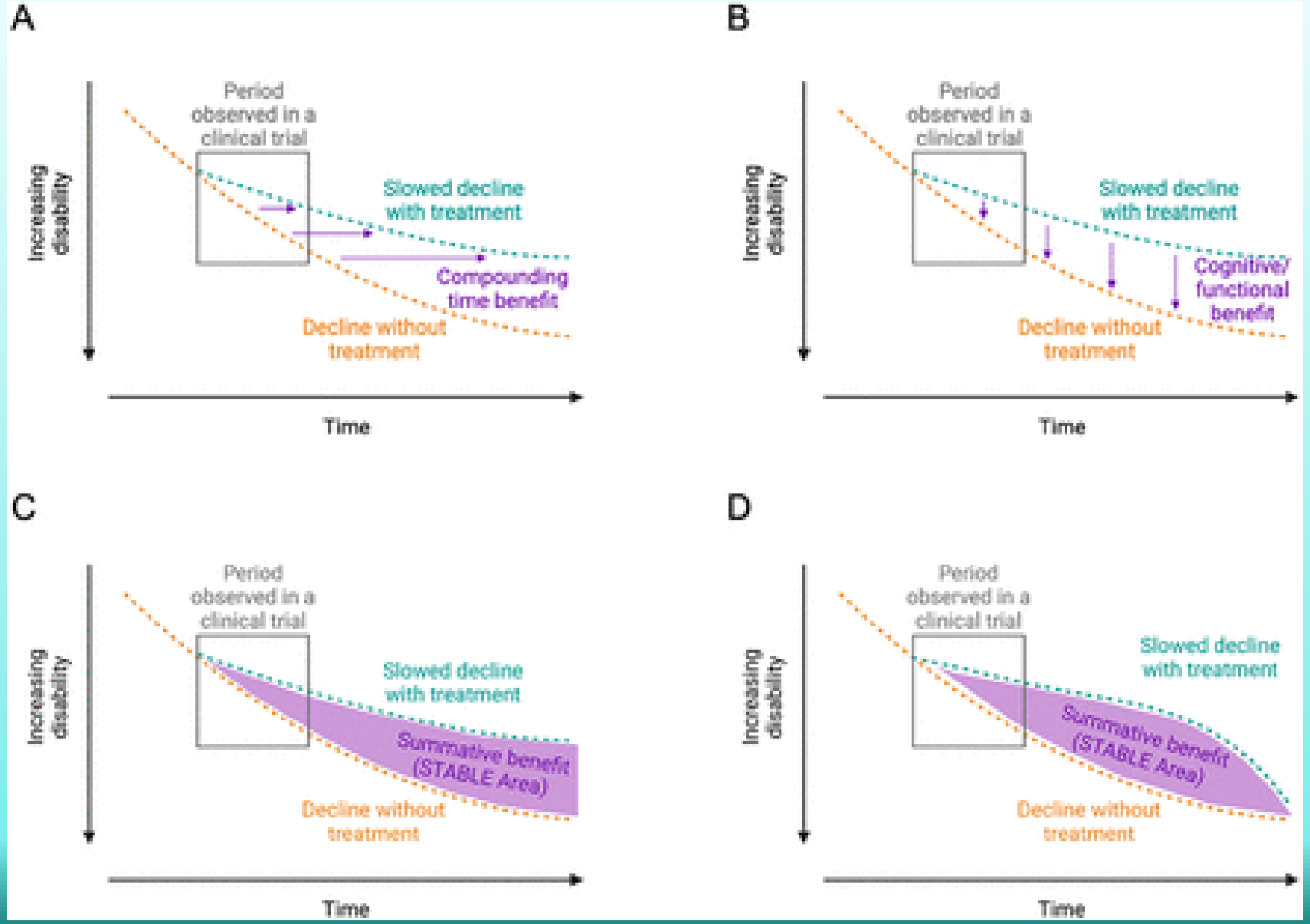
Van Dyck CH. *NEJM* 2023:388:9-21

Paying for Anti-Amyloid Treatment

- Cost of the medication
  - ~ $26,500/yr for Lecanemab
  - ~ $32,000/yr for Donanemab
- When considering all costs (infusions, MRI, PET, labs, medical visits, other services)
  - Some estimates run as high as $75 – 90,000/yr
- Treatment is covered by CMS
  - Medicare part B covers 80% of costs (20% to patient/family)
    - Pt must meet criteria (similar to study enrollment requirements, MMSE, MoCA scores, registry enrollment)
    - Supplemental insurance may cover some/all of remaining costs
- Commercial insurance may cover costs (depending on the insurance) – may require PA
  - Meeting criteria for CMS and similar to clinical trials – including ARIA monitoring
- Drug company assistance programs
  - Lecanemab: https://www.eisaipatientsupport.com/patient/leqembi
  - Donanemab: https://www.lillycares.com/assets/pdf/lilly_cares_application.pdf

Time-cognitive benefit

What's in It for Me? Contextualizing the Potential Clinical Impacts of Lecanemab, Donanemab, and Other Anti-β-amyloid Monoclonal Antibodies in Early Alzheimer's Disease
Michelle Jin and James M. Noble
eNeuro 27 September 2024, 11 (9) ENEURO.0088-24.2024; https://doi.org/10.1523/ENEURO.0088-24.2024



Anti-Amyloid Tx and Unanswered Questions

- What do we do for our more severe AD patients - or patients that do not qualify?
- Does treatment delay the need for Nursing Home placement down the road?
- Does treatment have an effect on neurospsychiatric symptoms as the disease progresses into later stages?
- Will these drugs be studied in patients with more advanced stages of disease?
- Will study extensions answer any of these questions?

Remternetug (LY3372993)

- Monoclonal antibody targeting pyroglutamated forms of Aβ
- Studies ongoing:
  - Phase III – TRAILRUNNER-ALZ 1 – initiated August 2022
    - Blinded crossover study to evaluate Amyloid clearance
    - Additional safety cohort
    - IV infusion and subcutaneous injection
    - Scheduled to end late 2025/early 2026
  - Phase III – TRAILRUNNER-ALZ 3 – initiated October 2024
    - 1200 patients with no or minimal cognitive impairment (pTau217)
    - 18 mo treatment with home treatment admin subcutaneously (CDR-G; CDR-SB)
    - Scheduled to complete 2029
- Subcutaneous injection (at home administration)
- ARIA-E and ARIA-H seen in Phase I studies (most in APOE4 carriers)

Semaglutide

- GLP-1 RA currently FDA approved for T2DM and Obesity
- 2 similar Phase III trials (EVOKE and EVOKE+)
  - Oral daily Semaglutide vs Placebo
  - Age 55-85 with MCI or Mild AD
    - Confirmed Amyloid pathology (PET/CSF)
  - 2-year main treatment phase + 1 year extension
- Enrolled ~ 1800 pts in each trial (between 5/2021 – 9/2023)
- Completion of 2-year main treatment phase expected 9/2025, with ext. to fall 2026
- Primary outcome is change from baseline to 104 weeks in CDR-SB
  - Also evaluating AD biomarkers and neuroinflammation

Cummings JL, Evoke and Evoke+: design of two large-scale, double-blind, placebo-controlled, phase 3 studies evaluating efficacy, safety, and tolerability of semaglutide in early-stage symptomatic Alzheimer's disease. *Alz Res Therapy* **17**, 14 (2025). https://doi.org/10.1186/s13195-024-01666-7

Tau Targeting Therapies

- **Tau Aggregation Inhibitors:**
  - These drugs aim to prevent tau proteins from forming tangles.
  - Examples include methylene blue derivatives and Hydromethylthionine mesylate (HMTM).
  - TRx0237, a new form of a tau aggregation inhibitor, is being tested in Phase III trials for Alzheimer's and frontotemporal dementia.
- **Antisense Oligonucleotides:**
  - These drugs target the gene that produces tau protein, reducing its production.
  - BIIB080 is an example of an antisense oligonucleotide being tested in a phase 1 trial for Alzheimer's.
- **Immunotherapies:**
  - These therapies use antibodies to target and remove pathological tau proteins.
  - Posdinemab and JNJ2056 are investigational monoclonal antibody that targets phosphorylated tau.

Hydromethylthionine Mesylate (HMTM)

- Anti-malarial drug Methylene Blue derivative
- LUCIDITY Trial - TauRx completed a Phase III trial of HMTM – failed to meet co-primary endpoints
- Subgroup analysis of patients with MCI – reduced levels of NfL (neurofilament light chain)
  - **Predicting Cognitive Decline -** higher NfL levels correlate with worse cognitive performance and faster cognitive decline.
  - **Tracking Neurodegeneration -** track the status of neurodegeneration and assess the effect of treatment on neurodegeneration.

Alzheimer's Tau Platform (ATP) Trial

Part of the NIA/NIH funded Alzheimer's Clinical Trials Consortium

The goal of the Alzheimer's Tau Platform (ATP) trial is to conduct a randomized, placebo controlled, Phase 2 trial in preclinical-prodromal AD that will simultaneously test at least two different tau-directed therapies, alone or in combination with an anti-amyloid therapy, to determine safety and tolerability

https://www.actcinfo.org/trials/

What QUESTIONS do you have?