

DUKE DEMENTIA FAMILY SUPPORT PROGRAM

Caregiver Connections

An Educational Webinar Series With The Experts

**The presentation will begin shortly.
Thank you for your patience!**

dukefamilysupport.org

919-660-7510



Treatment of Alzheimer's Disease

Daniel Parker, MD
Assistant Professor
Division of Geriatrics
Department of Neurology
Duke School of Medicine



Outline

1. How do we define mild cognitive impairment (MCI), dementia, and Alzheimer's disease?
2. What treatments are currently available for MCI/dementia? What are their limitations?
3. What are anti-amyloid drugs and how do they work?
4. What's next for treatment and prevention of Alzheimer's disease?



What do we mean by SCI, MCI, and dementia?

Normal Cognition



Subjective Cognitive Impairment (SCI)

- I notice subtle changes in my memory and thinking
- Cognitive assessment is normal.
- These changes do not interfere with my day to day activities.



Mild Cognitive Impairment (MCI)

- There are changes in my memory and thinking that I and others notice.
- These changes are picked up on cognitive assessments.
- These changes do not interfere with my day to day activities.
- These changes aren't caused by another medical or psychiatric problem.



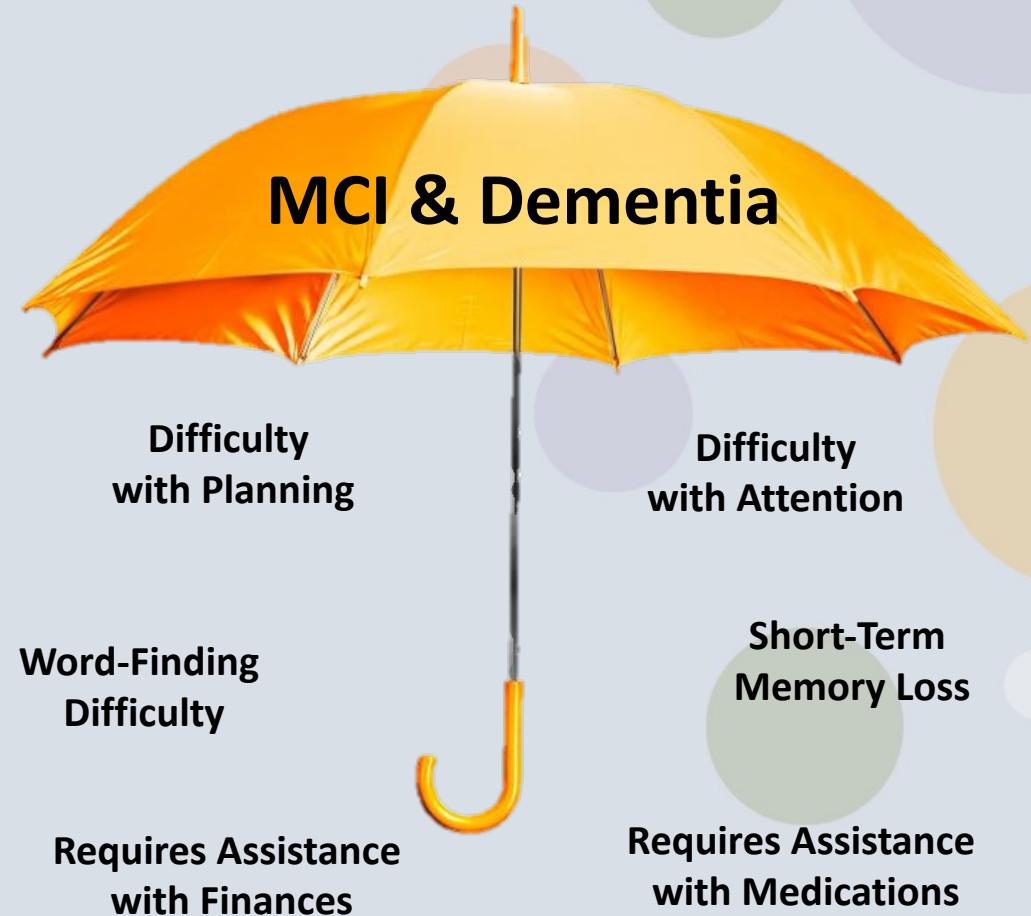
Dementia

- There are changes in my memory and thinking that I and others notice.
- These changes are picked up on cognitive assessments.
- I need extra help with day to day activities.
- These changes aren't caused by another medical or psychiatric problem.

MCI and dementia are “umbrella” terms

Syndromes or “Umbrella” Terms

- MCI and dementia are syndromes or “umbrella” terms which describe a group of symptoms that occur together.
- They describe cognitive symptoms and their impact on function.
- They don’t tell us what’s going on in the brain that is causing the symptoms.
- There are different diseases that can cause MCI and dementia.

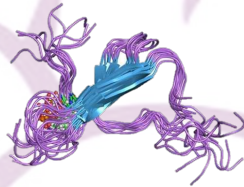


Alzheimer's Disease is the Most Common Cause of Dementia

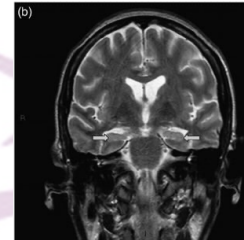
Amyloid β



Tau



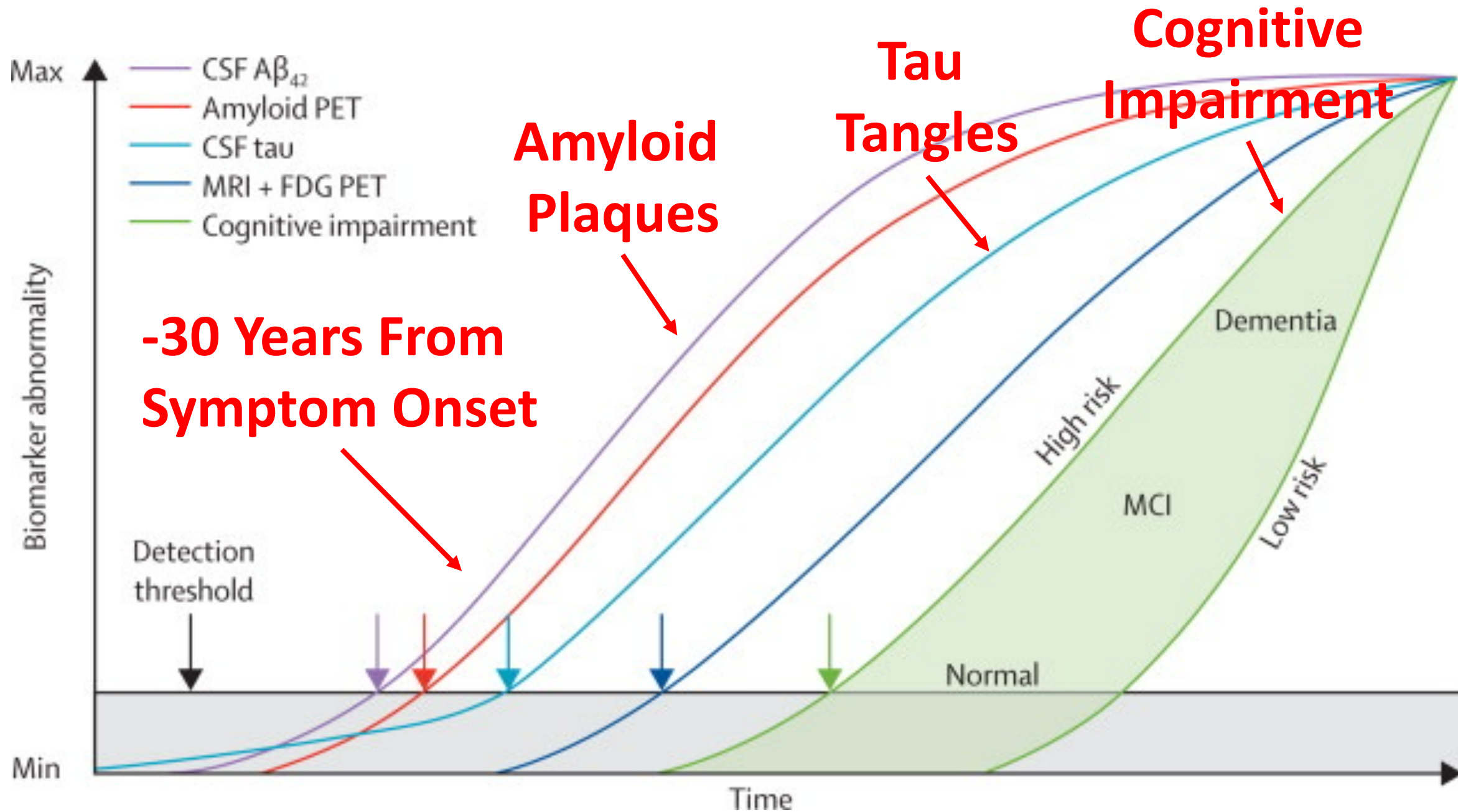
Neurodegeneration



**Cognitive
Impairment**
(SCI, MCI, Dementia)

Amyloid Cascade Hypothesis

*The “Amyloid Cascade Hypothesis” is the leading theory
for the development of Alzheimer’s Disease*



Types of Treatment

Symptomatic Treatments

- Improve symptoms of disease, but do not affect the disease process or address underlying issue that caused the disease
- Donepezil (Aricept) or Memantine (Namenda)

Disease-Modifying Treatments

- Addresses the underlying problem causing the disease, which slows down or preventing disease progression
- Lecanemab (Leqembi)

Cholinesterase Inhibitors

- Donepezil (Aricept), rivastigmine (Exelon), and galantamine (Razadyne) are symptomatic treatments for dementia.
- Increase concentrations of the neurotransmitter acetylcholine in the brain.
- Modest improvement in cognition, behaviors, and function. Response is highly individual.
- Side effects include nausea, diarrhea, decreased appetite, insomnia, and decreased heart rate.

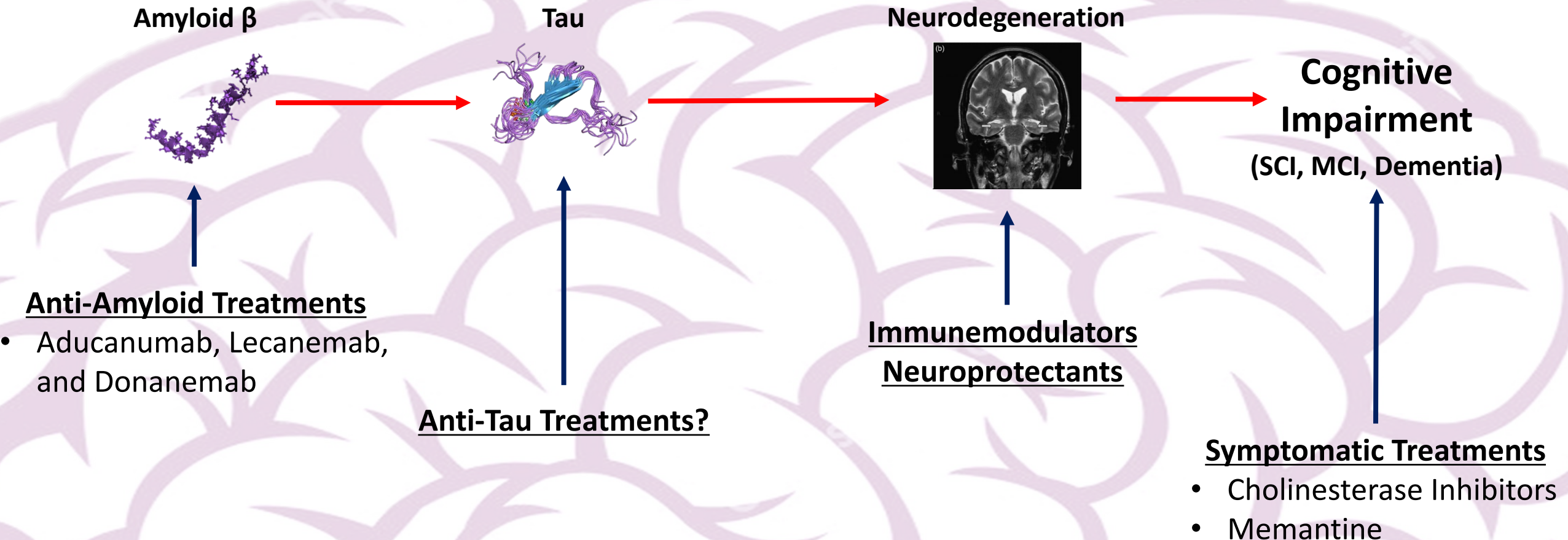


Memantine

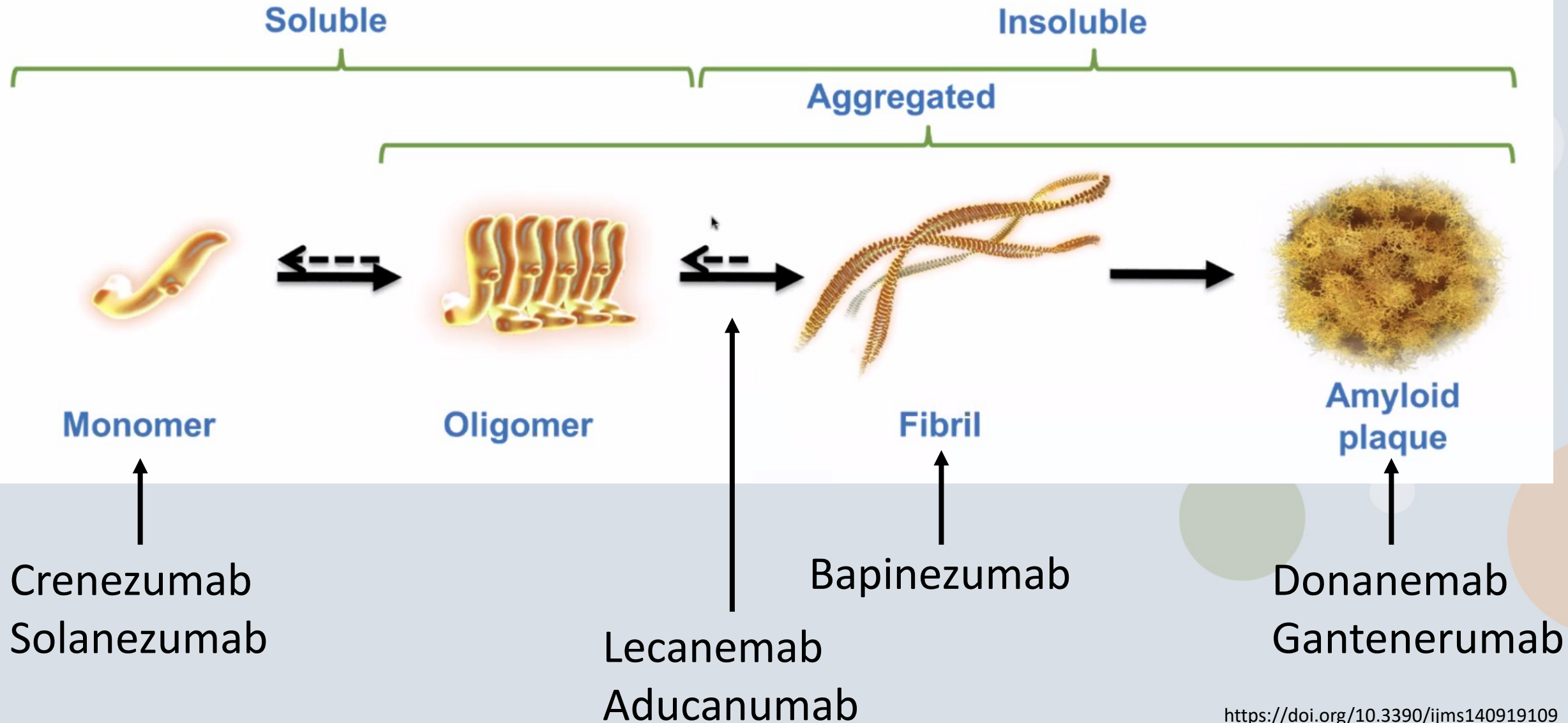
- Memantine (Namenda) is a symptomatic dementia.
- Blocks overactive glutamate signaling in the brain.
- Small beneficial effects in cognition and function.
- Often used in combination with cholinesterase inhibitor.
- Most common side effect is dizziness.



Emerging Treatment Approaches for Alzheimer's Disease

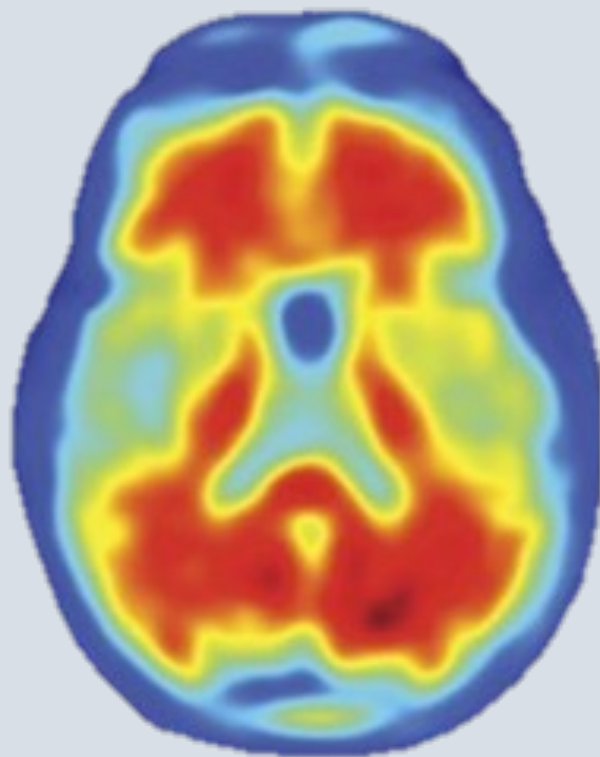


Amyloid Biology is Complex

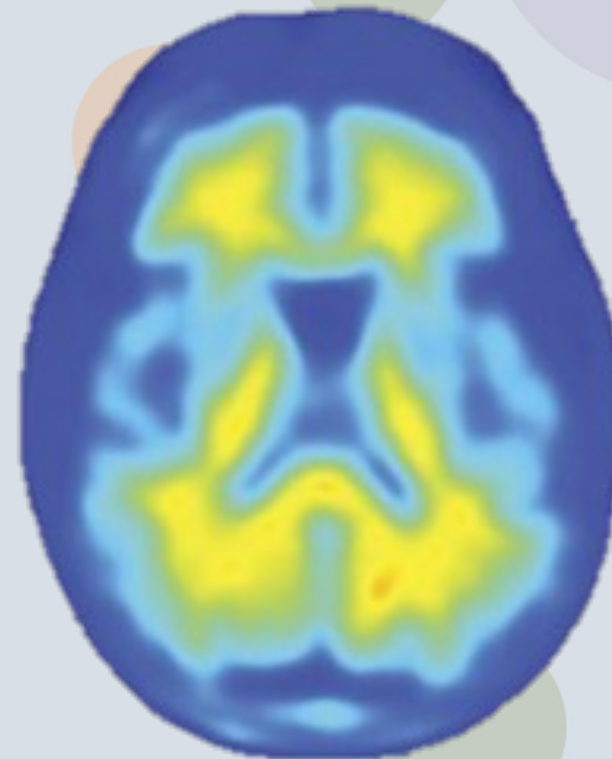


Anti-Amyloid Therapy

Before Treatment



After Treatment



One Year

Does getting rid of amyloid help memory and thinking?

Anti-Amyloid Therapy

- Anti-amyloid antibodies get rid of amyloid, but do they help memory, thinking, and day to day function?
- Treatment with aducanumab, lecanemab, or donanemab slow down decline in memory, thinking, and day to day function.
- These drugs do not stop or reverse cognitive decline.
- These drugs can have serious side effects.



CLARITY-AD

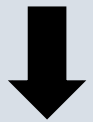
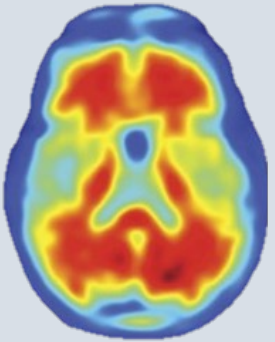
- Anti-amyloid therapy is not effective in moderate or severe Alzheimer’s disease dementia.
- Anti-amyloid therapy has shown efficacy in patients with mild cognitive impairment or mild dementia due to Alzheimer’s disease.
- All trial participants had confirmed Alzheimer’s disease by lumbar puncture or amyloid PET.

Table 1. Characteristics of the Participants at Baseline (Modified Intention-to-Treat Population).*		
Characteristic	Lecanemab (N = 859)	Placebo (N = 875)
Age — yr	71.4±7.9	71.0±7.8
Sex — no. (%)		
Female	443 (51.6)	464 (53.0)
Male	416 (48.4)	411 (47.0)
Race — no. (%)†		
White	655 (76.3)	677 (77.4)
Black	20 (2.3)	24 (2.7)
Asian	147 (17.1)	148 (16.9)
Other or missing	37 (4.3)	26 (3.0)
Hispanic ethnic group — no. (%)‡	107 (12.5)	108 (12.3)
Time since diagnosis — yr	1.41±1.51	1.34±1.54
Time since onset of symptoms — yr	4.13±2.35	4.15±2.53
Global CDR score — no. (%)‡		
0.5	694 (80.8)	706 (80.7)
1	165 (19.2)	169 (19.3)
Clinical subgroup — no. (%)		
Mild dementia due to Alzheimer’s disease	331 (38.5)	331 (37.8)
Mild cognitive impairment due to Alzheimer’s disease	528 (61.5)	544 (62.2)
ApoE ε4 status — no. (%)		
Noncarrier	267 (31.1)	275 (31.4)
Carrier	592 (68.9)	600 (68.6)
Heterozygotes	456 (53.1)	468 (53.5)
Homozygotes	136 (15.8)	132 (15.1)
Current use of medication for symptoms of Alzheimer’s disease — no. (%)	447 (52.0)	468 (53.5)

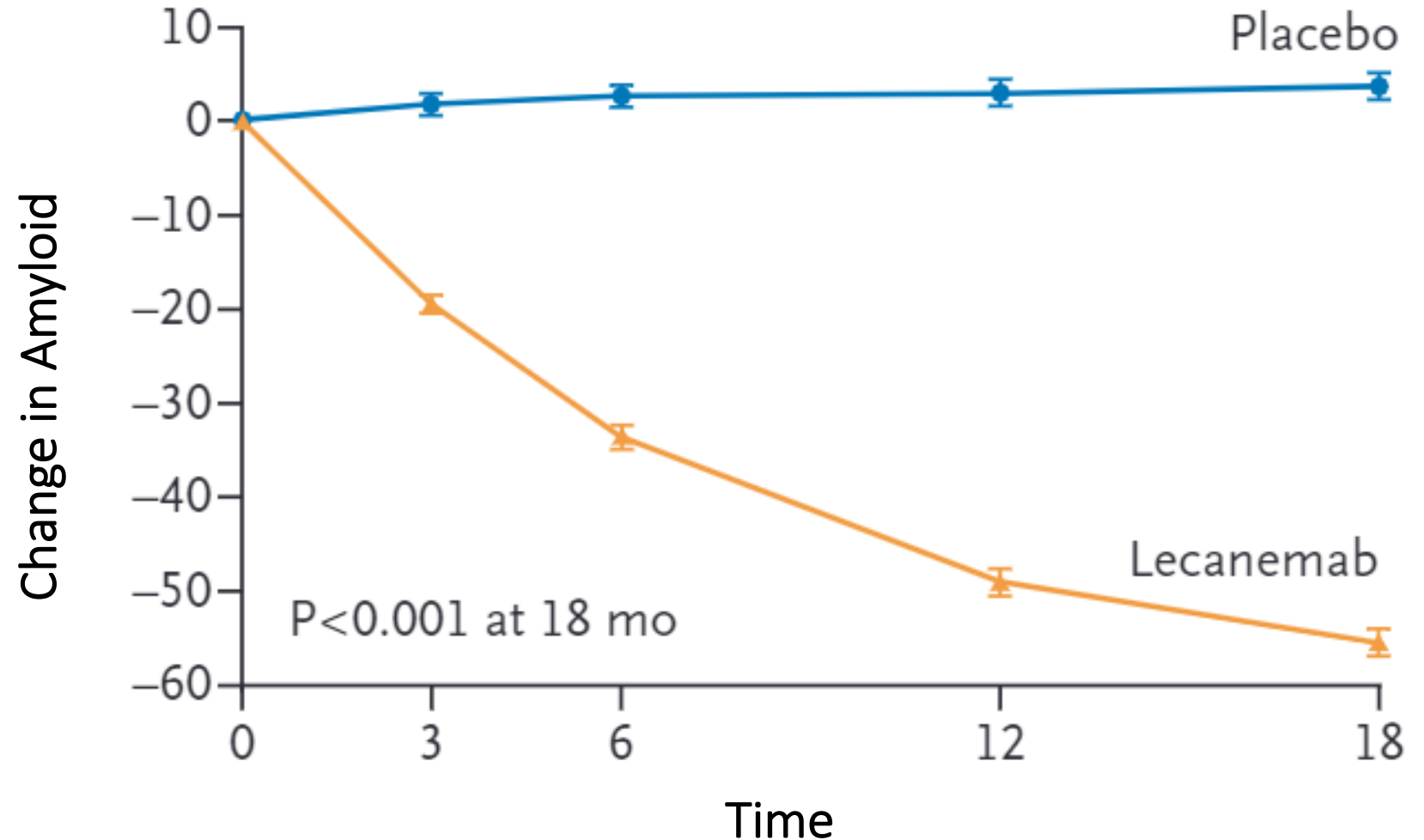
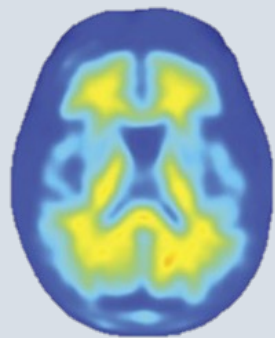
Lecanemab (Leqembi)

Amyloid PET Scan

Before Treatment



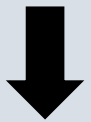
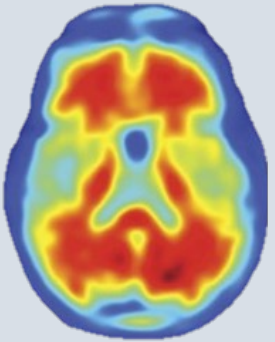
After Treatment



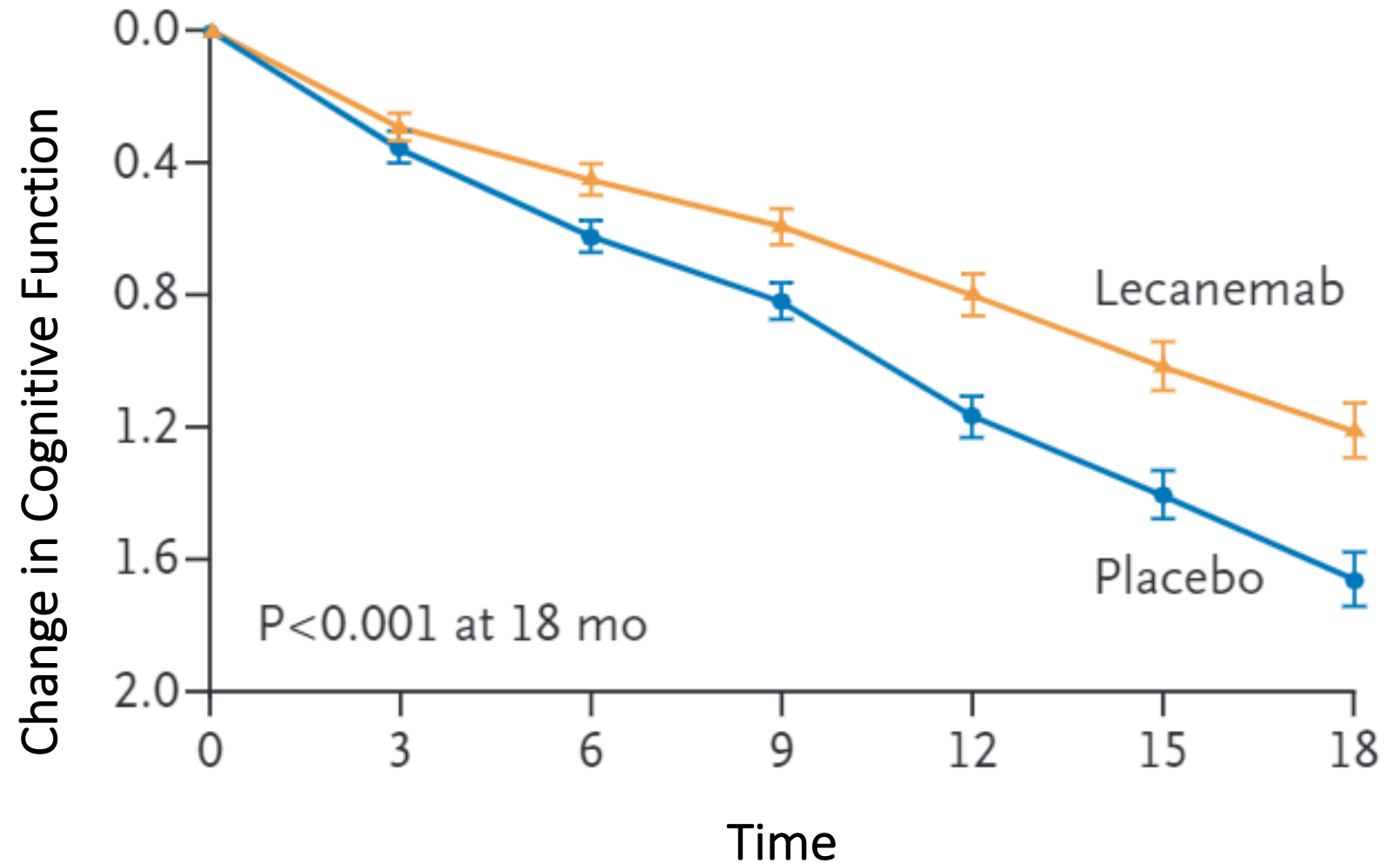
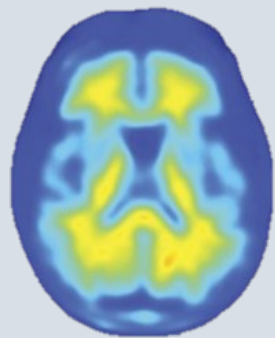
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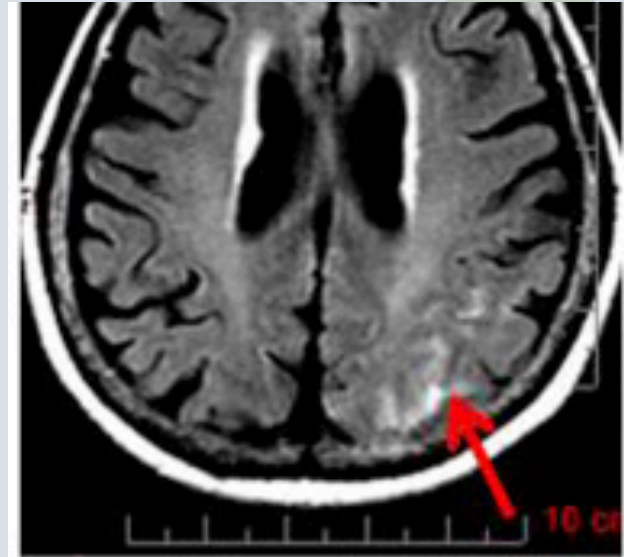


After Treatment



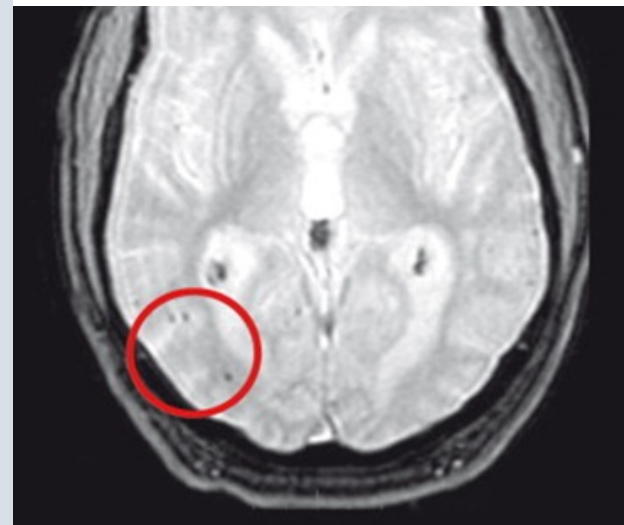
Anti-Amyloid Side Effects

- Most concerning side effect of anti-amyloid antibodies is *Amyloid Related Imaging Abnormality* (ARIA).
- Anti-amyloid antibodies can cause brain swelling (edema) or small areas of bleeding (hemorrhage).
- Most cases of ARIA are asymptomatic. Common ARIA-related symptoms can include dizziness, headache, confusion, fatigue.
- There have been some deaths related to ARIA.



ARIA-E

Edema or
Swelling



ARIA-H

Hemorrhage
or
Bleeding

Summary

- In people with MCI or mild dementia due to Alzheimer's disease, lecanemab treatment decreases amyloid and slows down cognitively decline by ~30%.
- Lecanemab is generally safe and well-tolerated, but some individuals develop brain swelling or bleeding (ARIA), which can be life-threatening.
- The risk of ARIA is higher in people who are APOE- ϵ 4 carriers or taking blood thinners.
- The ideal duration of treatment is unknown.



Next Steps

- Can treatment with anti-amyloid therapy prevent the development of cognitive impairment due to Alzheimer's disease?
- What is the role of combination therapy? Lecanemab + Anti-Tau or Lecanemab + Immune Modulator?
- Still no disease-modifying therapies for other causes of dementia.



What about....

Bredsen Protocol

- Popularized by a book called, “The End of Alzheimers.”
- Based on a trial with 10 patients
- Personalized medicine approach that involves diet changes, exercise, hormones, supplements.

Prevagen

- Jelly fish protein
- Huge marketing campaign
- One company-run study without a placebo control group

Young Plasma

- Based on experiments in mice
- FDA shut down “young blood” clinics in February 2019
- Potential risks include transmission of disease, immune reactions

Stem Cell Therapy

- No evidence of benefit and potentially harmful
- Very expensive

Hyperbaric Oxygen

- Some small studies have shown beneficial effects
- Requires frequent treatments and how long the beneficial effects last is unclear

Summary

- ✓ Address modifiable risk factors
 - Blood pressure, diabetes, hearing/vision loss, depression/social isolation
- ✓ Increase cognitive resilience
 - Cognitive stimulation and social isolation
- ✓ Promote overall health and well-being
 - Regular physical exercise, healthy diet, vaccinations
- ✓ Symptomatic treatment of cognitive symptoms
 - Cholinesterase inhibitor or memantine
- ✓ Anti-amyloid therapy
 - Lecanemab



Take Home Message

- If you or someone you know is concerned about changes in memory and thinking, schedule an appointment with a memory specialist. Early intervention is key!!
- We plan to begin treating patients at Duke with lecanemab in the coming months.
- Consider participating in research to help us identify effective preventions and treatments for dementia.

Questions?

Daniel.Parker@Duke.edu



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