

# **DUKE DEMENTIA FAMILY SUPPORT PROGRAM**

## **Caregiver Connections**

**An Educational Webinar Series With The Experts**

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

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**919-660-7510**



# Lecanemab

*Anti-amyloid treatment for early Alzheimer's Disease*

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# Disclosures

- No disclosures



# How I got here...

- I'm a geriatrician, memory disorders specialist, and researcher.
- I see patients at the Duke Memory Disorders clinic.
- My research centers on understanding how diet and exercise promote brain resilience and reduce dementia risk.



# Outline

## 1. Definitions & Background

*What is Alzheimer's disease?*

## 2. Anti-Amyloid Treatment

*How does lecanemab work?*

## 3. Potential Benefits

*Does lecanemab slow down Alzheimer's?*

## 4. Potential Risks

*What are the side effects?*

## 5. Putting it All Together

*Is lecanemab right for me?*

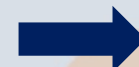


# What do we mean by MCI and dementia?

## Normal Aging



## Mild Cognitive Impairment (MCI)



## Dementia

- You have occasional lapses in memory. You forget someone's name but remember it later.
- You takes more time to learn new information or a new skill but can still do it.
- You occasionally miss a payment or forget to take a medication.

- Significant change in memory and thinking that you and others notice.
- Changes aren't severe enough to keep you from working, doing your taxes, or taking your medications correctly.
- These changes are not caused by another medical or psychiatric problem.

- You have changes in memory and thinking that others notice.
- Changes make it so it's difficult for you to hold down a job and you need assistance to manage your finances and medications.
- Dementia Stages
  - Mild: Need help with finances
  - Moderate: Need help dressing/bathing
  - Severe: Not talking or moving around much

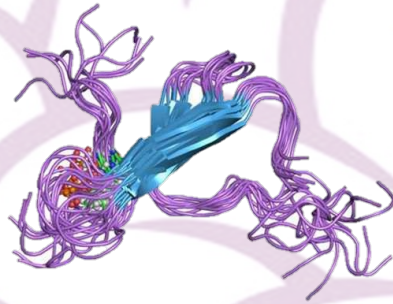
# Alzheimer's Disease

*The most common cause of dementia*

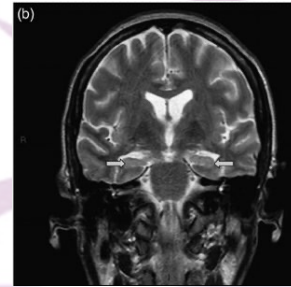
**Amyloid  $\beta$**



**Tau**



**Neurodegeneration**



**Cognitive  
Impairment**

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)

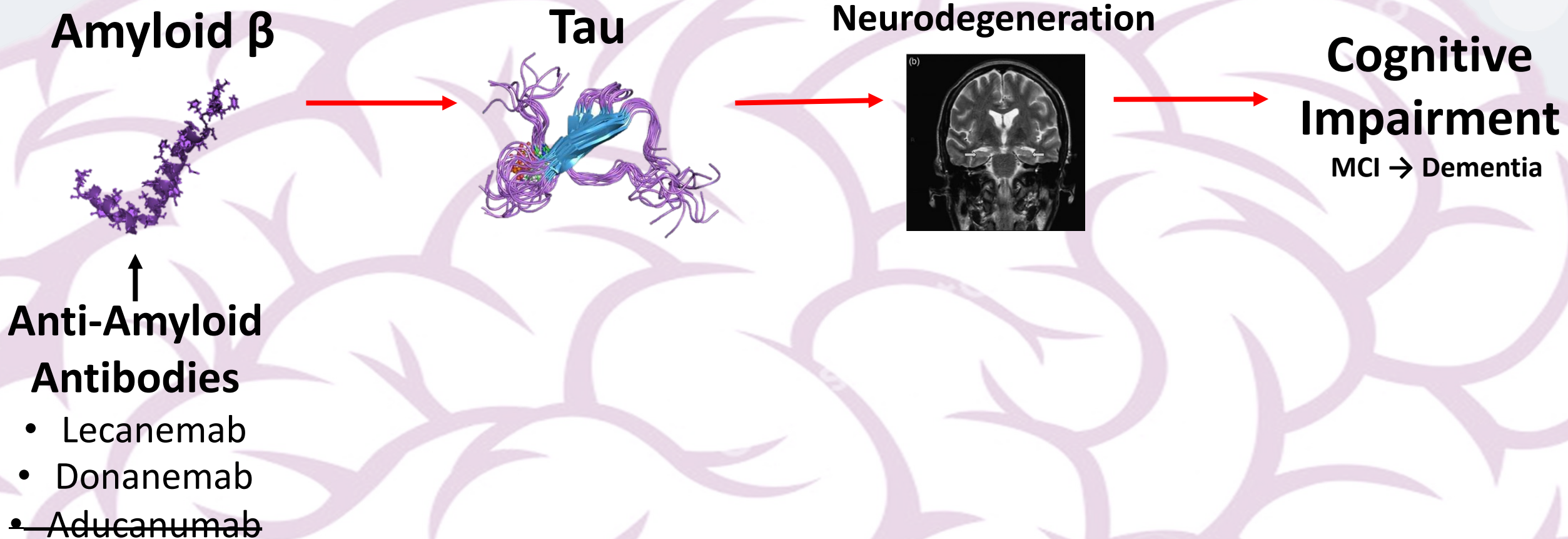
## Disease-Modifying Treatments

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

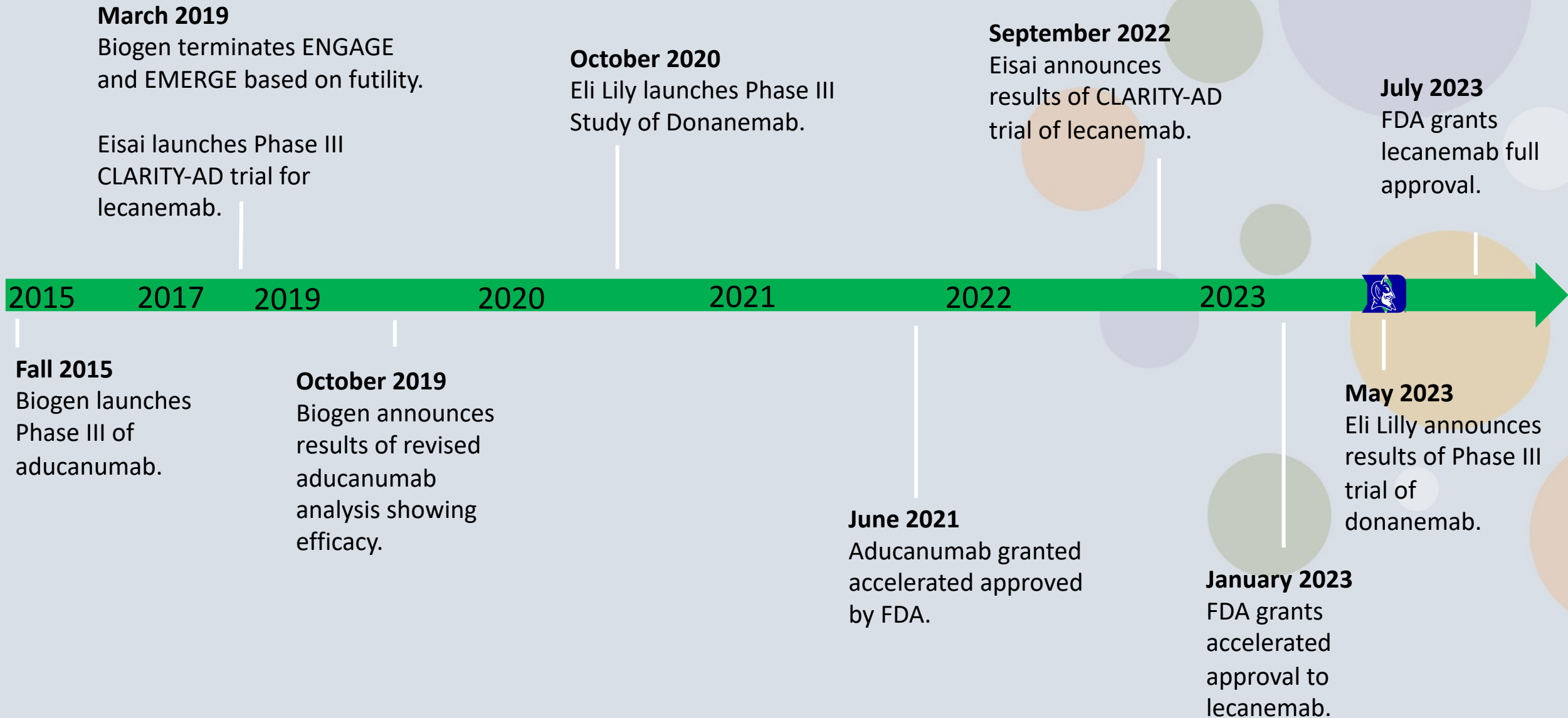


# Alzheimer's Disease

*The most common cause of dementia*



# Timeline of Anti-Amyloid Therapy



# CLARITY-AD Phase III Study of Lecanemab

- A Phase III trial determines if a drug is safe and if it is effective for a disease.
- CLARITY-AD compared lecanemab treatment to placebo (saline infusion) to see if it slowed down changes in memory and thinking due to Alzheimer's disease. 859 participants received lecanemab and 875 received placebo.
- All trial participants had confirmed Alzheimer's disease by lumbar puncture or amyloid PET.
- Around half of participants were taking donepezil or memantine.

**Average Age = 71**

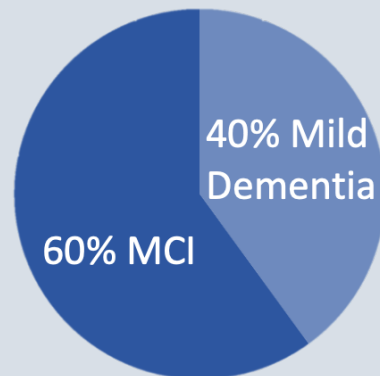
Age Range 50-90

**MMSE Score:**

Average = 25

Range 22-30

## Clinical Diagnosis



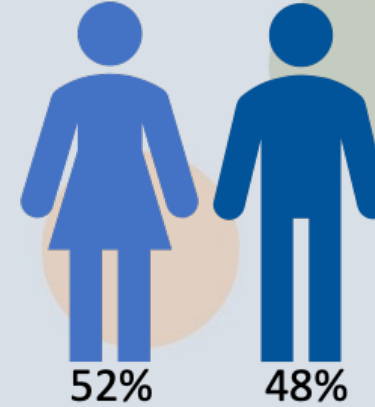
**Onset of symptoms:**

~4 years

**Time since diagnosis:**

~1.5 years

Women Men



## Race & Ethnicity

76% White

13% Hispanic

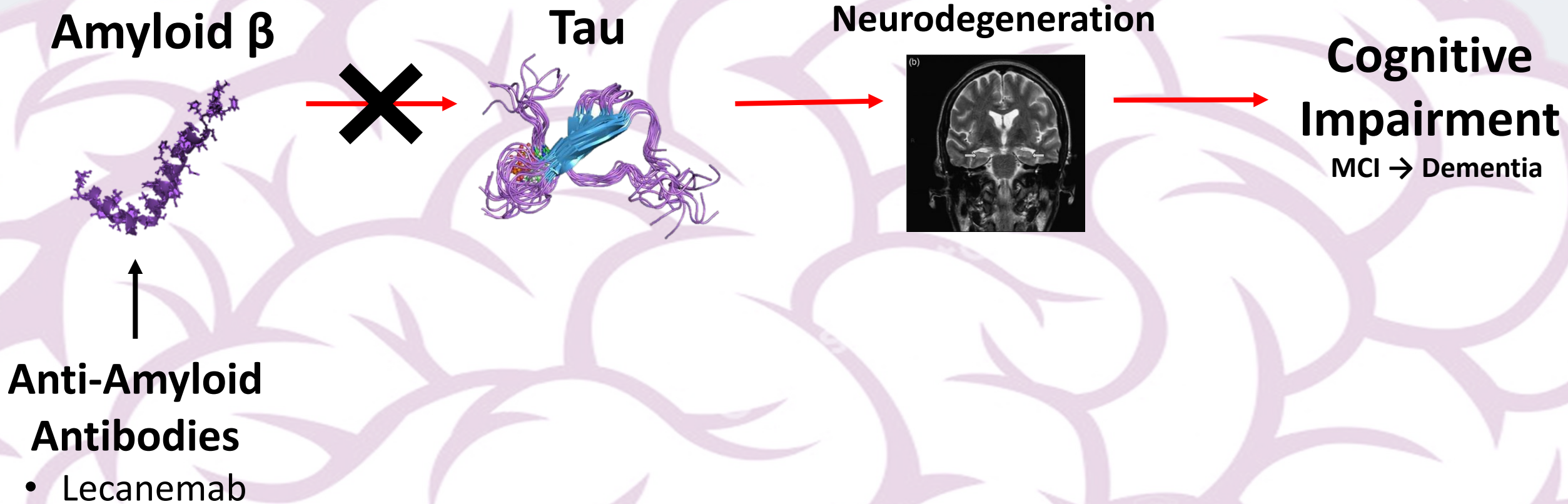
17% Asian

2% Black

## Excluded Participants with:

- Unstable medical conditions
- Depression
- BMI >35 or <17
- Stroke, TIA, bleeding disorder, or seizure in the past 12 months

# Why are these drugs more effective in early Alzheimer's disease?

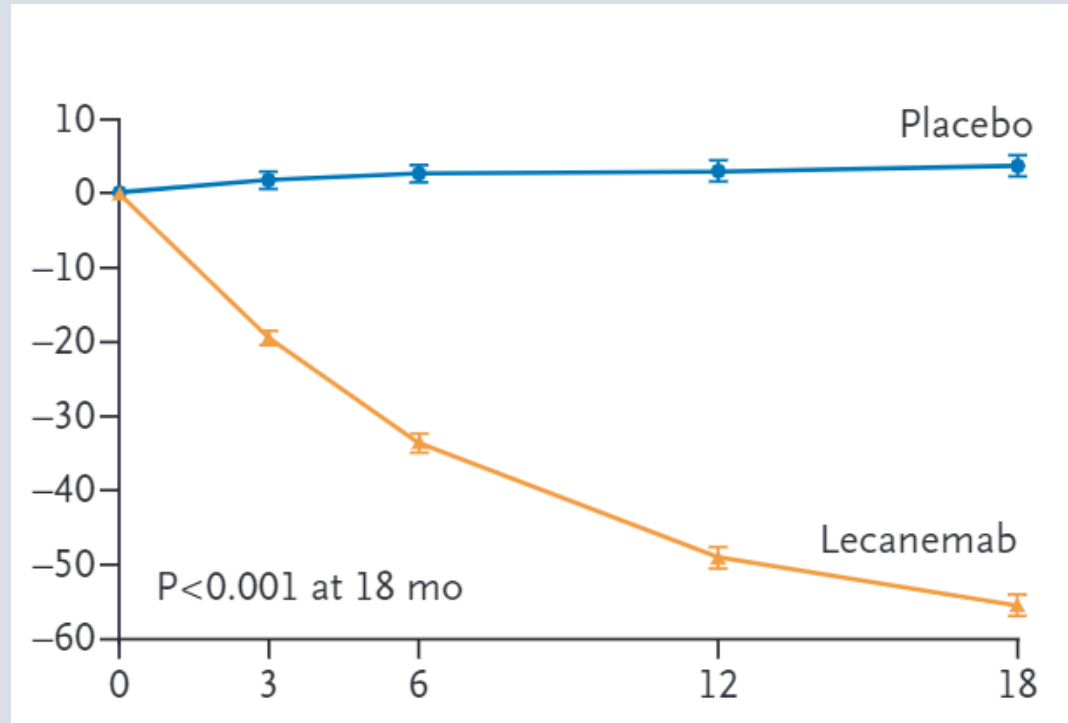
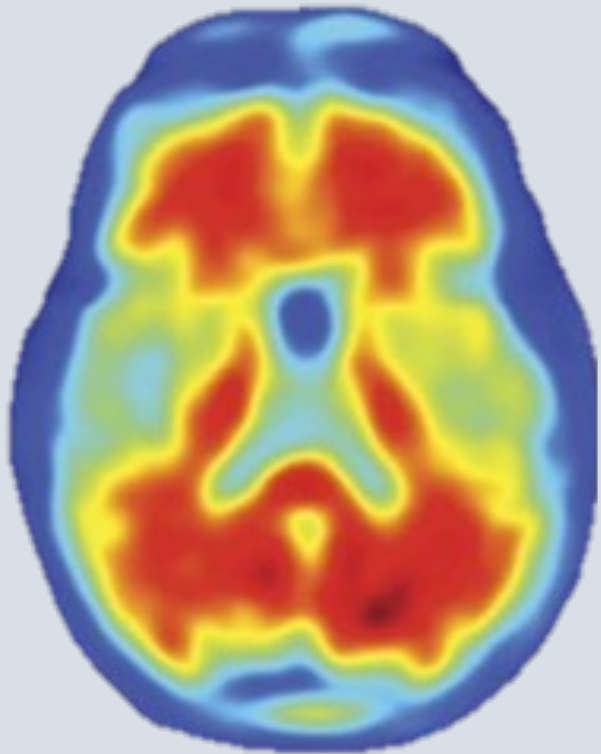


# Lecanemab CLARITY-AD Trial

Before Treatment



After Treatment



18 Months



*Does getting rid of amyloid help memory and thinking?*

# CLINICAL DEMENTIA RATING (CDR)

CLINICAL DEMENTIA RATING (CDR):	0	0.5	1	2	3
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	Impairment				
	None 0	Questionable 0.5	Mild 1	Moderate 2	Severe 3
Memory	No memory loss or slight inconsistent forgetfulness	Consistent slight	Moderate memory loss;	Severe memory loss; only highly learned material	Severe memory loss; only fragments remain
Orientation	Oriented to person only		elsewhere		
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 maintained	Severely impaired in handling problems, similarities, and differences; social	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 independent activities still be engaged appears inspection		
Home and Hobbies	Life at home, hobbies, and interests	Life at home, hobbies, and intellectual interests slightly impaired	Mild but noticeable impairment home; minor chores and complicated interests		
Personal Care	able of self-care		Needs pr		

Scores range from 0-3 for each domain and can be summed to obtain the Sum of Boxes Score

Cognitive Domains

Functional Domains

Meaningful Clinical Difference = 1 Point

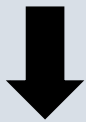
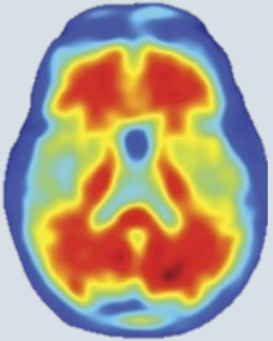
CDR-SB	Staging
0	No Cognitive Impairment
0.5-4.0	Questionable Cognitive Impairment
0.5-2.0	Questionable Impairment
2.5-4.0	Very Mild Dementia
4.5-9.0	Mild Dementia
9.5-15.5	Moderate Dementia
16.0-18.0	Severe Dementia

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

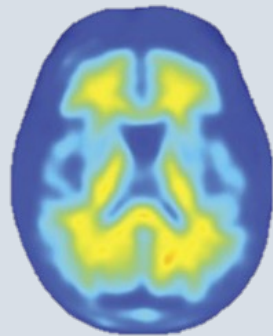
# Lecanemab – CDR Sum of Boxes

## Amyloid PET Scan

Before Treatment



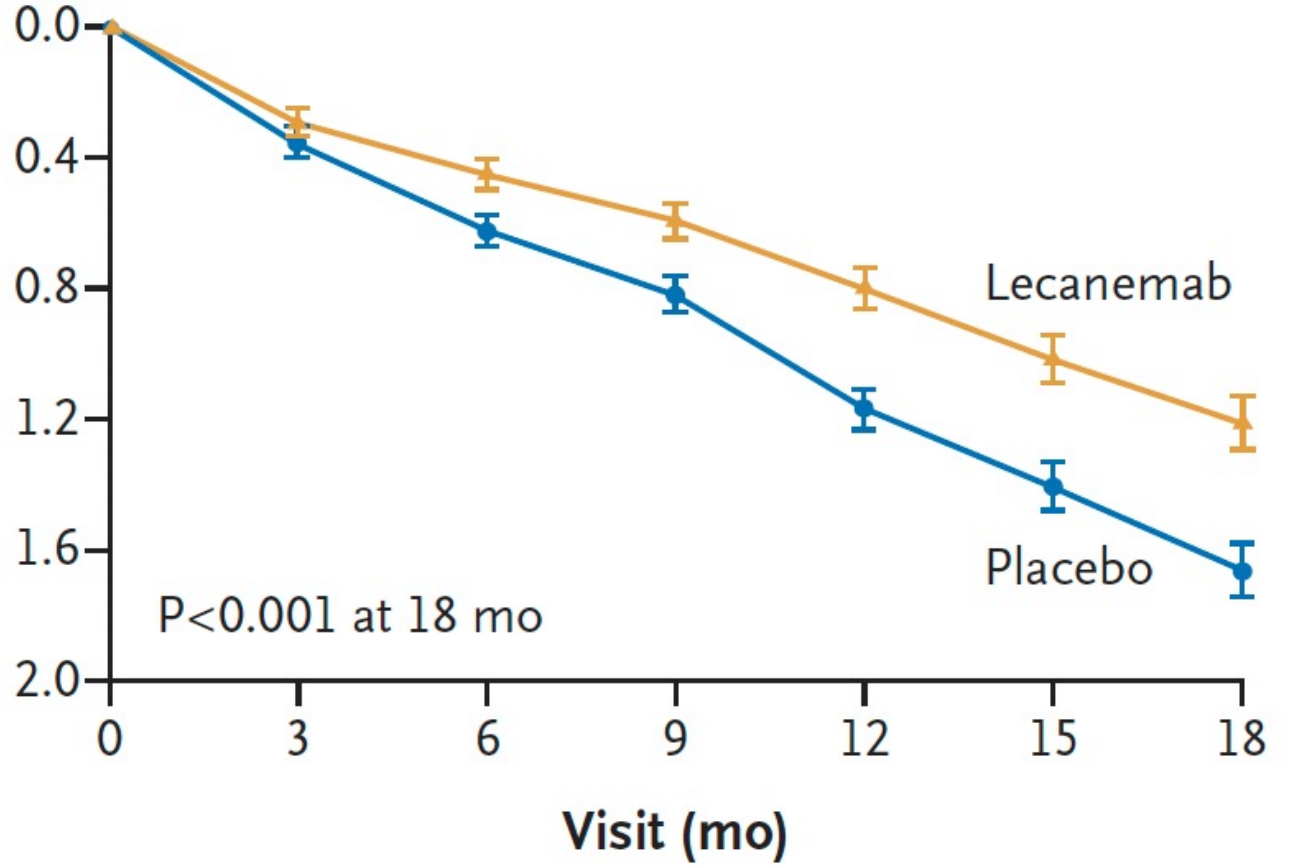
After Treatment



Worsening



Adjusted Mean Change from Baseline



CLINICAL DEMENTIA RATING (CDR)

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

Trial	Phase	Drug	Baseline		18 Month Δ	
			Placebo	Treatment	Placebo	Treatment
CLARITY-AD	III	Lecanemab	3.22 (1.34)	3.17 (1.34)	1.66	1.21
TRAILBLAZER-ALZ 2	III	Donanemab	3.9 (2.1)	4.0 (2.1)	2.33	1.66

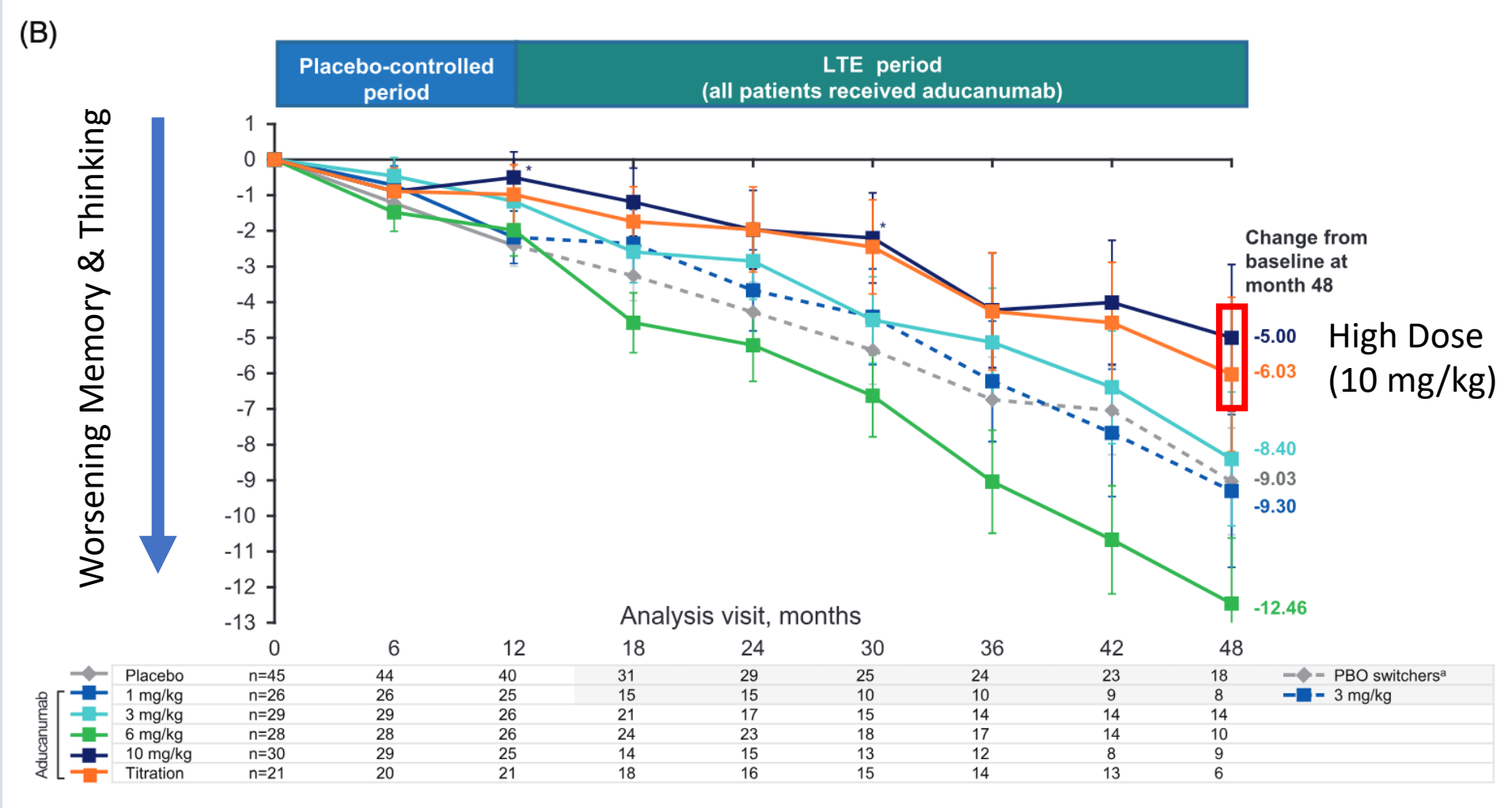


# Understanding Potential Benefits

- Based on a modeling study, in people with MCI or mild dementia due to Alzheimer's disease, lecanemab may delay progression to the next stage by around 2-3 years.
- Study participants receiving lecanemab and their care partners reported higher quality of life and less caregiver stress.
- Over one year, people on donanemab had a 1/2 chance of maintaining stable cognition and function. People who received placebo had a 1/3 chance.



# Sustained Benefit Over Time?

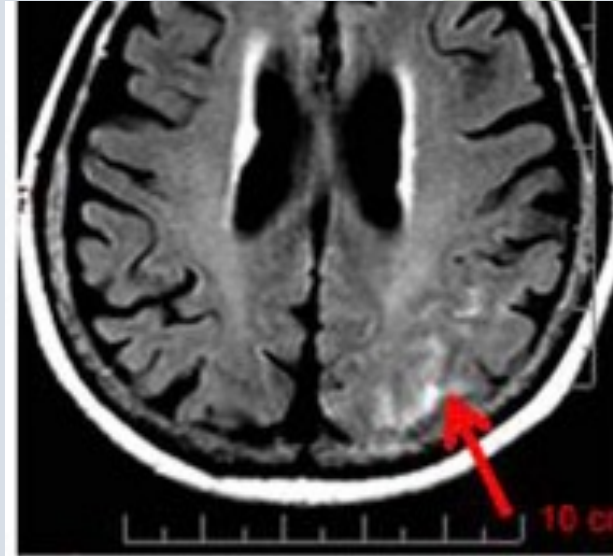


*Participants receiving the highest doses of aducanumab maintained memory and thinking better than those on the lowest dose over 4 years.*

Chen, T. et al. Results from the long-term extension of PRIME: A randomized Phase 1b trial of aducanumab. *Alzheimer's Dement.* (2024) doi:10.1002/alz.13755.

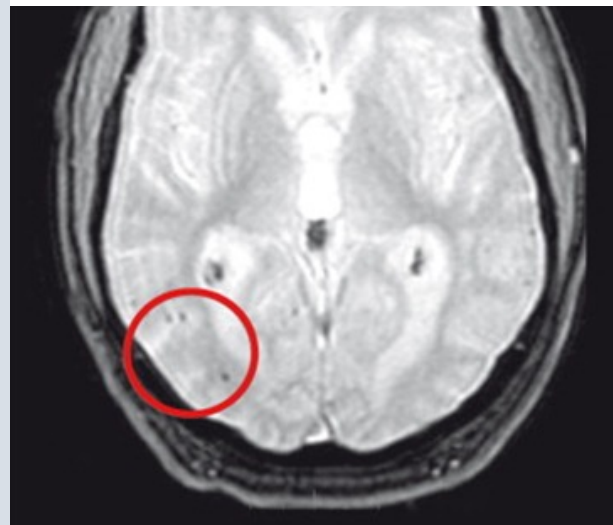
# Side Effects

- Anti-amyloid antibodies can cause brain swelling (edema) or small areas of bleeding (hemorrhage).
- These side effects are referred to as *Amyloid Related Imaging Abnormality (ARIA)*.
- Most cases of ARIA are asymptomatic.
  - Common ARIA-related symptoms include: headache, confusion, visual changes, dizziness, nausea, gait difficulty
  - Serious ARIA-related symptoms include: seizures, status epilepticus, encephalopathy, stupor, focal neurological deficits.
- There have been 4 deaths in patients receiving lecanemab.
- There were 3 deaths with donanemab due to severe ARIA unrelated to anticoagulants.



## ARIA-E

Edema or  
Swelling



## ARIA-H

Hemorrhage  
or  
Bleeding

# APOE-ε4 is a Major Risk Factor for ARIA

	ARIA-E				ARIA-H			
	All	No ε4	One ε4	Two ε4	All	No ε4	One ε4	Two ε4
Lecanemab	12.6%	5.4%	10.9%	32.6%	17.3%	11.3%	14%	34%
Aducanumab	35%	20%	36%	64%	19%	12%	17%	41%
Donanemab	24%	16%	23%	41%	31%	19%	32%	50%

*APOE-ε4 is the **strongest genetic risk factor** for Alzheimer's disease that develops after age 65 and the greatest risk factor for side effects with lecanemab.*

# Who is eligible for lecanemab?

- ✓ Diagnosis of MCI or mild AD dementia.
- ✓ Amyloid PET or CSF studies indicative of AD.
- ✓ MMSE 22-30 or other cognitive screening instrument with a score compatible with MCI or mild dementia.
- ✓ Symptomatic treatments (donepezil, rivastigmine, memantine) are OK.
- ✓ Adequate support. Patient and care partners understand the requirements and the potential benefits and harms.

# Not Eligible for Treatment

- X Other diseases or conditions that are contributing to the cognitive symptoms.
- X Inability to undergo MRI.
- X History of stroke or TIA within the last 12 months or any history of seizure.
- X Significant psychiatric/behavioral symptoms
- X Significant autoimmune disease or treatment with immunosuppressives or other antibody-based drugs.
- X Anticoagulants, poorly controlled bleeding disorder, platelet count <50,000, or INR>1.5.
- X Presence of unstable medical conditions.
- X MRI Findings Suggestive of Increased Risk
  - X >4 microhemorrhages.
  - X Evidence of brain bleeding or brain swelling.
  - X >2 lacunar infarcts or stroke involving a major vascular territory.
  - X Severe subcortical white matter hyperintensities consistent with Fazekas score of 3.
  - X Evidence of a non-AD cause of the cognitive symptoms.

# Is Lecanemab right for me?

## Logistical/Financial Burden

- Do I want to spend ~3 hours at an infusion clinic every other week for 18 months?
- Am I willing to undergo three MRI scans within the first 6 months of treatment?
- Do I have a care partner to help me navigate this process, accompany me to infusions, monitor for side effects, etc.?
- Does my insurance plan cover treatment?
- What are my out-of-pocket costs of treatment?

## Potential Benefit

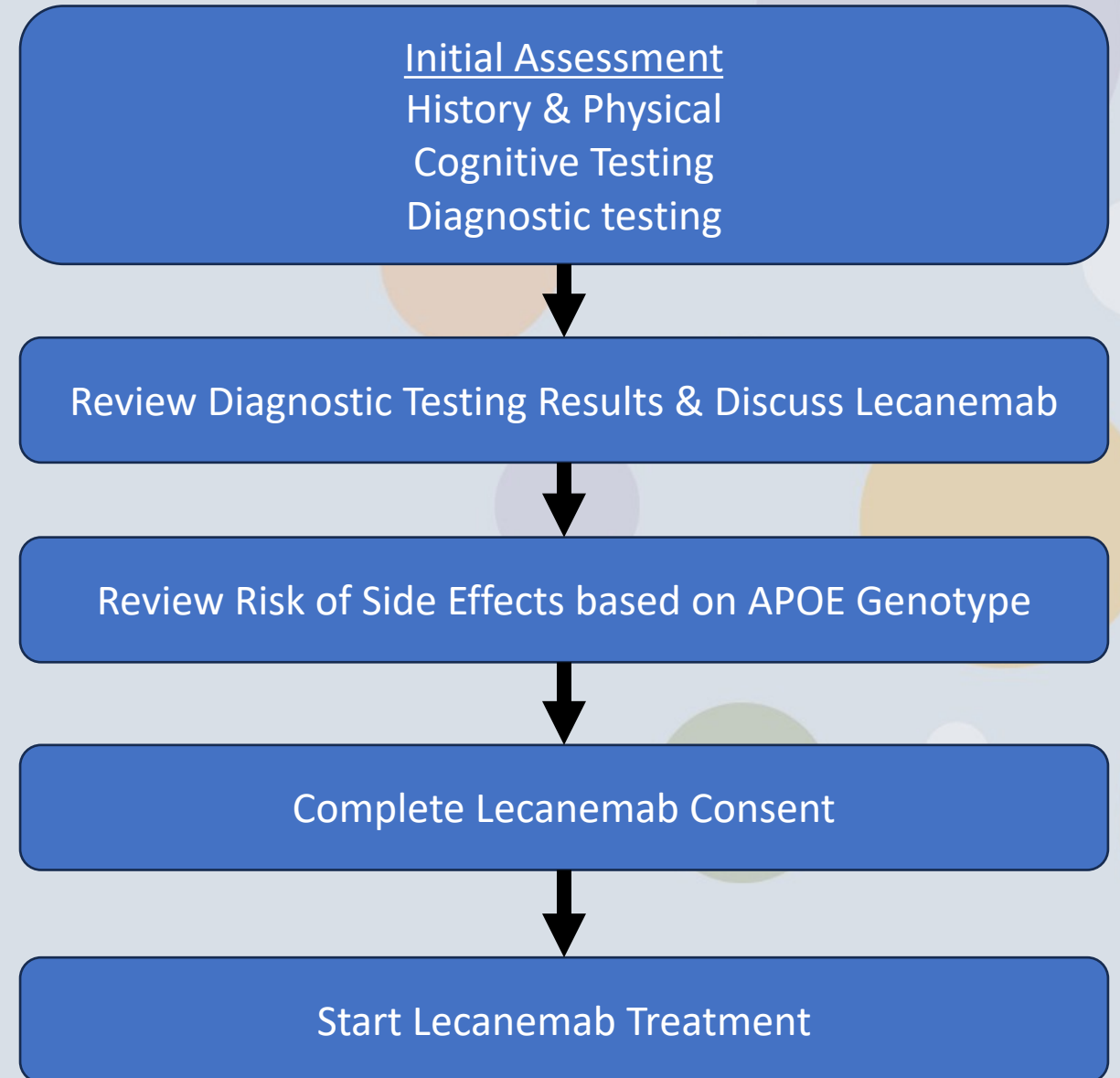
- Am I comfortable with the uncertainty with respect to potential benefits of this drug?
- Benefits likely greater in MCI compared to mild dementia.
- Benefits may be greater in men compared to women and younger compared to older people.
- People with better overall health and fewer medical problems are likely to benefit more.

## Risk of Side Effects

- Am I comfortable with the risk of brain swelling, brain bleeding, and death?
- People with 1 or 2 copies of the APOE-ε4 variant are at higher risk of side effects.
- People who are receiving a blood thinner are at higher risk of side effects.
- High blood pressure also appears to increase the risk of side effects.

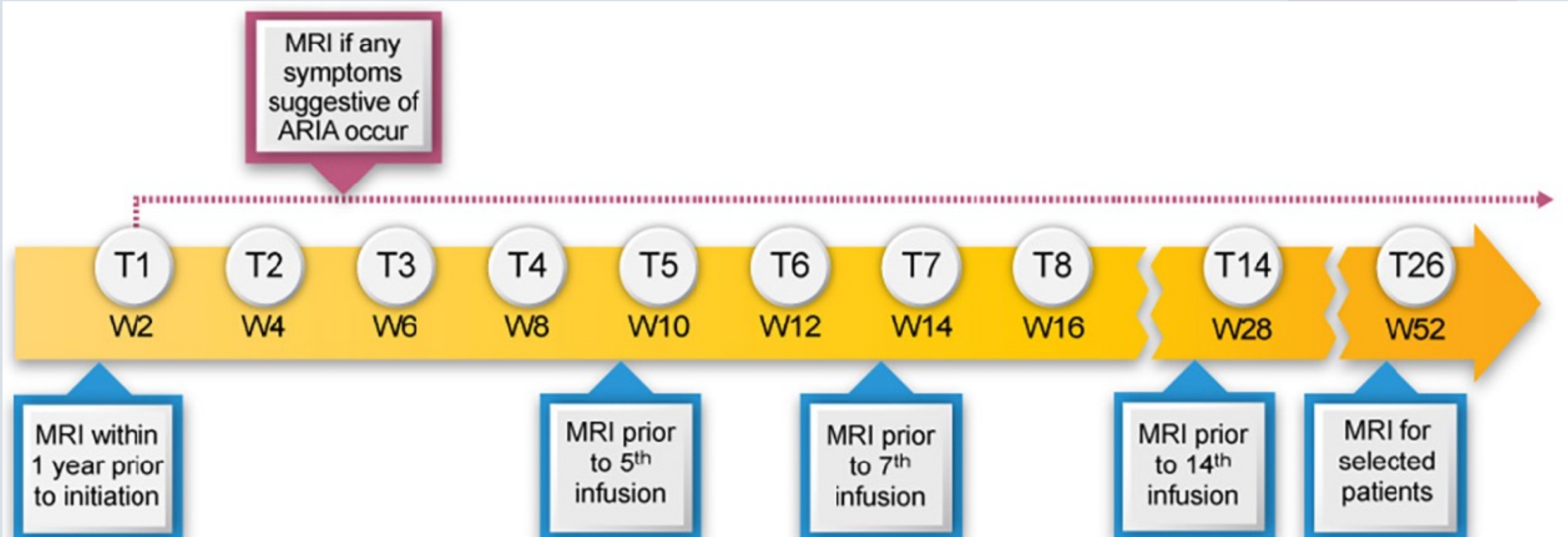
# My Approach to Treatment

- I treat patients with Lecanemab who:
  - Meet the published appropriate use guidelines' inclusion and exclusion criteria.
  - Demonstrate understanding of the logistics, uncertainty around potential benefits, and the risk of side effects.
  - Have care partner(s) who commit to helping them navigate the process, accompany them to infusions, and monitor for side effects.





# Lecanemab Administration & Monitoring



*An injectable version of lecanemab that can be given at home is in development and may be available in early 2025*

# Unanswered Questions

- There are outstanding questions about diagnosis, particularly in early disease.
- How do we identify patients most likely to benefit from treatment?
- How do we identify patients at high risk of serious side effects?
- What is the optimum duration of therapy? Do benefits accrue over time?
- What is the optimum management of side effects?
- Can Lecanemab treatment prevent the development of cognitive impairment?



# What to do if you're worried about your memory and thinking?

- If you or your loved ones have concerns about your memory, make an appointment at the Duke Memory Disorders clinic or the Duke Geriatrics and Evaluation (GET) Clinic.
- The GET Clinic is better for patients  $\geq 65$  with moderate or severe dementia.
- It's never too early to get checked out!
- We do specialized testing to diagnose Alzheimer's disease, Lewy Body Disease, and other causes of changes in memory and thinking.
- We also have several ongoing research studies.



# Questions?

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**Thank you for joining us today!**

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