APP-Led Models in Subspecialty Care:
Expanding Access to Alzheimer's Treatment and Beyond

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Alzheimer's Disease Statistics

- In 2025, 7 million people in the US are living with Alzheimer's Disease. The number will go up to 13 million by 2050.
  - 54,500 Kansans over age 65 are living with AD as of 2020.
  - 122,300 Missourians over age 65 are living with AD as of 2020.
- 1 in 9 people aged 65 and older have Alzheimer's Disease.
  - Racial and Ethic disparities
    - 19% of Black Americans over age 65 and 14% of Hispanic Americans have Alzheimer's dementia compared to 10% of White Americans.

Alzheimer's Disease Statistics

- $384 billion is spent annually in the US for people with dementia. That number is expected to increase to nearly $1 trillion by 2050.
- Nearly 12 million Americans provide unpaid care for people living with Alzheimer's and other dementias. This care is valued to about $413 billion.
    - The total lifetime cost of care for a person living with dementia is estimated at $405,262. Seventy percent of these costs are borne by family caregivers in the forms of unpaid caregiving and out-of-pocket expenses.
- Alzheimer's Disease is the 6th leading cause of death in the US.

Alzheimer's Association. 2025 Alzheimer's Disease Facts and Figures. Alzheimers Dement 2025;21(5)

What can be done to minimize this crushing societal toll?

- The answer likely lies in delaying the onset of symptoms and even stopping the progression of symptoms.
- Delaying onset of AD by 5 years can result in 41% lower prevalence and 40% lower cost of AD in 2050.
- Anti-amyloid drugs are a promising step in the direction to minimizing the burden to society, healthcare providers, patients and families.

Zissimopoulos J, Crimmins E, St Clair P. The Value of Delaying Alzheimer's Disease Onset. Forum Health Econ Policy. 2014 Nov;18(1):25-39. doi: 10.1515/fhep-2014-0013. Epub 2014 Nov 4. PMID: 27134606; PMCID: PMC4851168.

What is Alzheimer’s Disease

- The most common form of dementia accounting for roughly 60-70% of cases.
- It is not a normal part of aging
- It is neurodegenerative disease
- On average, a person with Alzheimer's lives four to eight years after diagnosis but can live as long as 20 years, depending on other factors.
- Pathophysiologic changes mainly beta-amyloid deposition can begin up to 20 years before onset of symptoms.

The Usual Suspects - Abnormal Proteins

Beta Amyloid

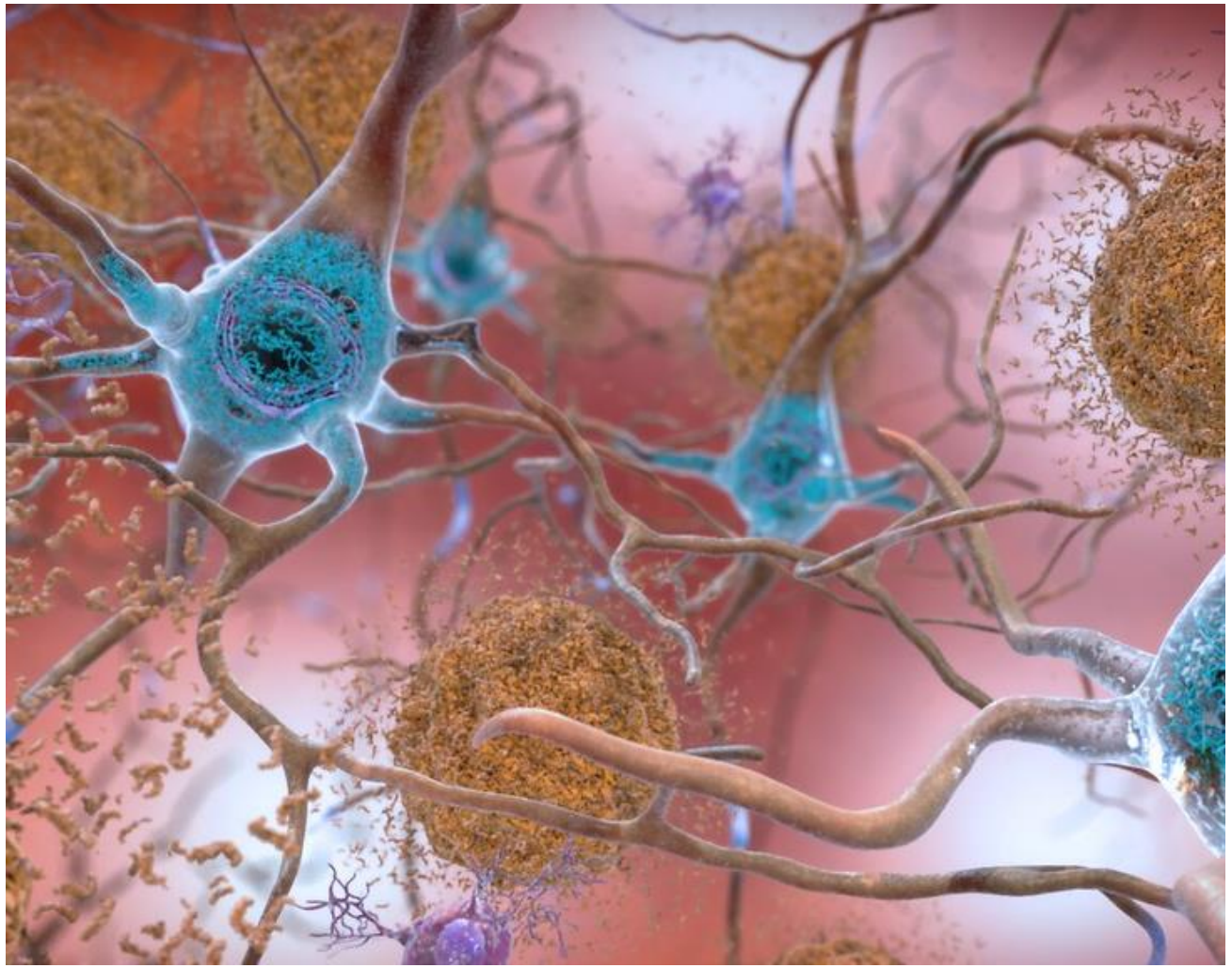
- Protein fragment that accumulates into intercellular plaques

Tau

- An abnormal form of tau proteins that cause neurofibrillary tangles inside of neurons

Both abnormal beta amyloid and tau accumulation impairs neuronal function and leads to neuronal death. These are the hallmark findings that are used as biomarkers for diagnosis.

Other brain changes include impaired glucose metabolism and inflammation



Alzheimer's Disease Staging Continuum

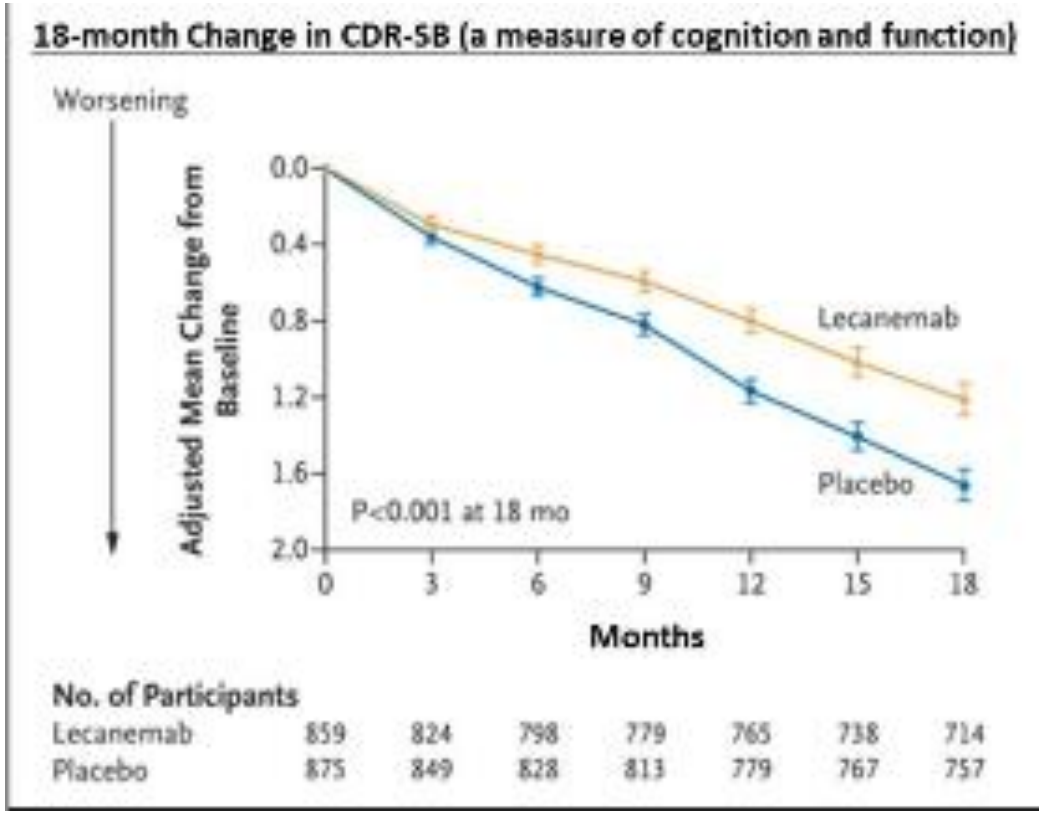
Newer model including both biological and clinical staging

Jack CR, Andrews JS, Beach TG, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. Alzheimer's Dement. 2024; 20: 5143–5169. https://doi.org/10.1002/alz.13859

How does Anti-Amyloid Therapy Work?

Anti-amyloid therapies, such as lecanemab and donanemab, have demonstrated efficacy in slowing cognitive decline in patients with early-stage Alzheimer's disease [1–3]. These therapies target aggregated forms of amyloid-beta (Aβ) and require strict diagnostic confirmation due to the potential for adverse events, including ARIA and cerebral hemorrhages. Appropriate patient selection is essential to optimize therapeutic outcomes and mitigate risks.

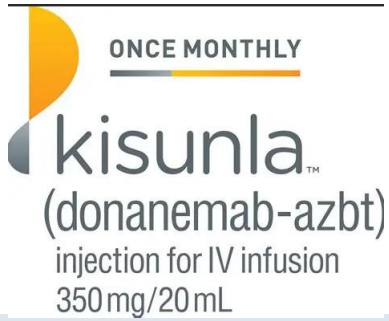
The CLARITY AD trial for lecanamab demonstrated 27% slowing of progression vs placebo with increasing separation over time.



Current Anti-Amyloid Therapies

- **Lecanemab (Leqembi)**
  - Recombinant humanized immunoglobulin gamma 1 (IgG1) anti-amyloid monoclonal antibody
  - Received full FDA approval in Jan 2023.
  - Intravenous infusion 10 mg twice a month for 18 months.
- **Donanemab (Kisunla)**
  - Humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody.
  - Received full FDA approval July 2023
  - Intravenous infusion once every month for 12 months.
  - Modified dosing schedule: 350 mg for first infusion, 700 mg for second, 1050 mg for third, and 1400 mg for remaining infusions.

Cummings J, Apostolova L, Rabinovici GD, et al. Lecanemab: appropriate use recommendations. J Prev Alzheimers Dis. 2023;10(3):362-377. doi:10.14283/jpad.2023.30
Rabinovici GD, Selkoe DJ, Schindler SE, Aisen P, Apostolova LG, Atri A, Greenberg SM, Hendrix SB, Petersen RC, Weiner M, Salloway S, Cummings J. Donanemab: Appropriate use recommendations. J Prev Alzheimers Dis. 2025 May;12(5):100150. doi: 10.1016/j.tjpad.2025.100150. Epub 2025 Mar 27. PMID: 40155270; PMCID: PMC12180672.



Diagnostics Workup for Anti-Amyloid Therapy

- **Cognitive and Clinical Assessment**
  - Patients must meet clinical criteria for **amnestic MCI or mild dementia** due to Alzheimer's disease, as per **NIA-AA** or **DSM-5** guidelines. A structured neuropsychological evaluation is used to assess memory and other cognitive domains and rule out alternative causes. If someone has amyloid pathology but no objective evidence of mild cognitive impairment, recommend monitoring symptoms over time and can consider repeat neuropsychological evaluation once symptoms are more apparent.

Albert, M. S., et al. (2011). The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging and the Alzheimer's Association workgroup. Alzheimer's & Dementia, 7(3), 270–279. https://doi.org/10.1016/j.jalz.2011.03.008

Diagnostics Workup for Anti-Amyloid Therapy

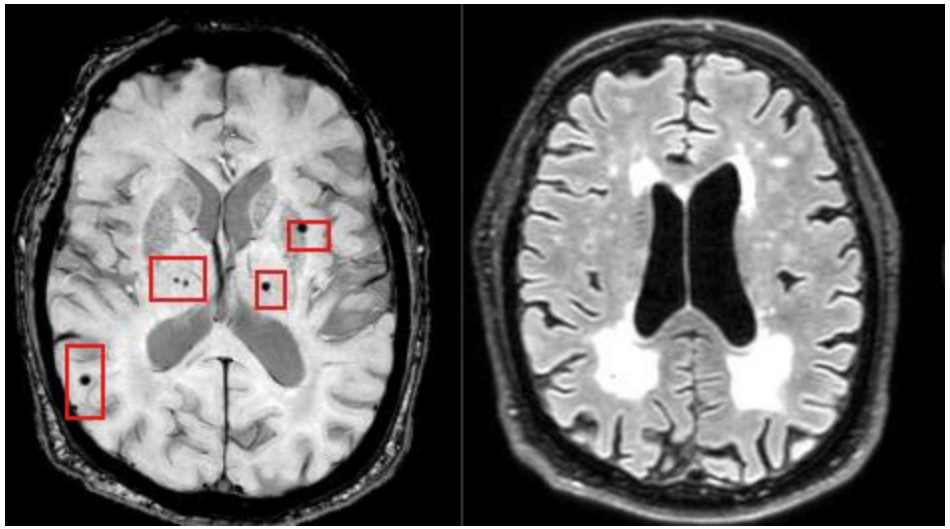
- **Confirmation of Amyloid Pathology**
  - Biomarker confirmation of amyloid pathology is required before initiating treatment. This can be confirmed with either amyloid PET scans of cerebrospinal fluid (CSF) analysis via lumbar puncture. Amyloid PET scans are able to visualize cortical amyloid deposition in the brain, while CSF analysis would be consistent with decreased Aβ42 and elevated p-tau/ratio confirm AD pathology. These biomarkers align with the AT(N) framework for AD diagnosis.

Jack, C. R., et al. (2018). NIA-AA Research Framework: Toward a biological definition of Alzheimer’s disease. Alzheimer's & Dementia, 14(4), 535–562. https://doi.org/10.1016/j.jalz.2018.02.018

Diagnostics Workup for Anti-Amyloid Therapy

MRI

- **MRI for Risk Stratification**
  - MRI is used to exclude contraindications, including:
    - More than **4 microhemorrhages**
    - Presence of **superficial siderosis**
    - **Significant vascular disease**
    - **>2 lacunar infarcts**
    - Pre-existing **macrohemorrhage**
- MRI also serves as a baseline for ARIA surveillance.
- SWI, SWAN or GRE sequencing needed to assess for microhemorrhages/macrohemorrhages.



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Diagnostics Workup for Anti-Amyloid Therapy

- **APOE Genotyping**
  - **APOE ε4** allele presence increases the risk and severity of ARIA-E. Homozygous carriers require more frequent monitoring or adjusted treatment strategies [7]. Initially did not recommend donanemab for homozygous E4 carriers, but with new modified dosing with similar risk of ARIA compared to lecanemab, we feel more comfortable prescribing this to patients.

Budd Haeberlein, S., et al. (2022). Clinical development of anti-amyloid therapies for Alzheimer's disease. Journal of Prevention of Alzheimer's Disease, 9(2), 197–209. https://doi.org/10.14283/jpad.2022.15

Diagnostics Workup for Anti-Amyloid Therapy

- **Further Inclusion/Exclusion Criteria**
  - Individuals ages 50-90 were included during the Clarity AD Trial of Lecanemab. While ages 60-85 were included during Donanemab TRAILBLAZER-ALZ2 Phase 3 Trial. Clinician discretion is used when determining eligibility for those outside of these age ranges. Patients cannot be taking two monoclonal anti-bodied simultaneously. Patients need to have a care partner or family member who can ensure the patient has support needed when on treatment.

Cummings J, Apostolova L, Rabinovici GD, et al. Lecanemab: appropriate use recommendations. J Prev Alzheimers Dis. 2023;10(3):362-377. doi:10.14283/jpad.2023.30

Exclusion Criteria

Exclusion Criteria
Any neurological condition that may be contributing to cognitive impairment above and beyond that caused by the participant's AD
More than 4 microhemorrhages (defined as 10 millimeter [mm] or less at the greatest diameter); a single macrohemorrhage >10 mm at greatest diameter; an area of superficial siderosis; evidence of vasogenic edema; multiple lacunar infarcts or stroke involving a major vascular territory; severe small vessel; or other major intracranial pathology
Evidence of other clinically significant lesions on brain MRI at Screening that could indicate a dementia diagnosis other than AD
History of transient ischemic attacks (TIA), stroke, or seizures within 12 months of Screening
Any psychiatric diagnosis or symptoms (example, hallucinations, major depression, or delusions) that could interfere with study procedures in the participant
Geriatric Depression Scale (GDS) score > 8 at Screening
Any immunological disease which is not adequately controlled, or which requires treatment with immunoglobulins, systemic monoclonal antibodies (or derivatives of monoclonal antibodies), systemic immunosuppressants, or plasmapheresis during the study
Participants with a bleeding disorder that is not under adequate control (including a platelet count <50,000 or international normalized ratio [INR] >1.5 for participants who are not on anticoagulant treatment, example, warfarin)
Participants who are on anticoagulant therapy should have their anticoagulant status optimized and be on a stable dose for 4 weeks before Screening
Any other medical conditions (example, cardiac, respiratory, gastrointestinal, renal disease) which are not stably and adequately controlled, or which could affect the participant's safety or interfere with the study assessments

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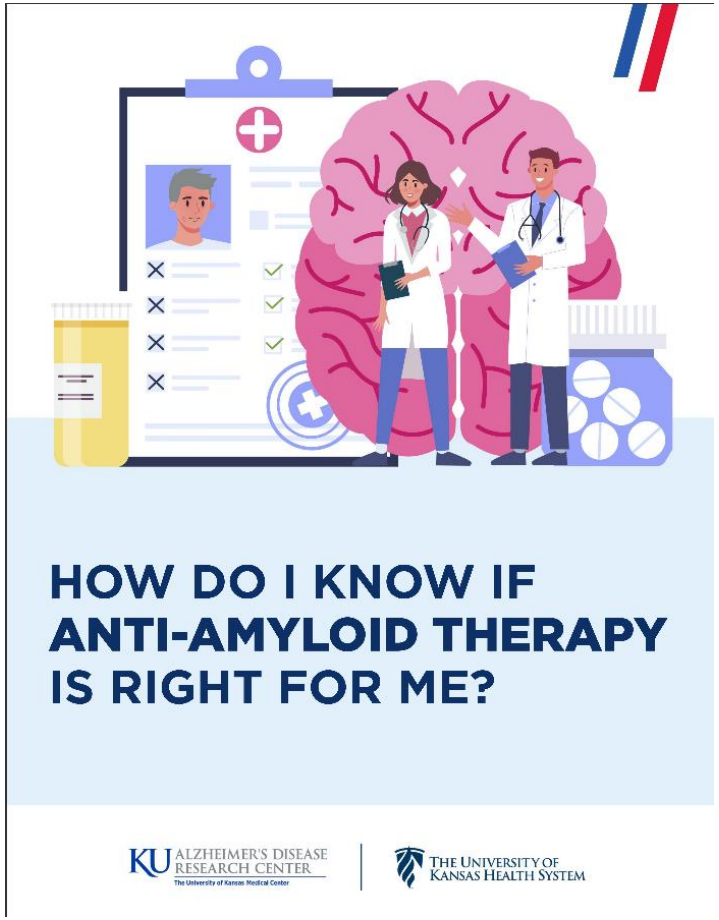
Shared Decision-Making Model



Adverse Effects of Anti-Amyloid Therapy

Amyloid-Related Imaging Abnormalities (ARIA)

ARIA is a treatment-emergent effect unique to anti-amyloid monoclonal antibodies. These abnormalities are generally monitored via MRI and include:

- **ARIA-E (Edema/Effusion):** Vasogenic edema or sulcal effusion, which may present with symptoms such as headache, confusion, dizziness, changes in vision/gait but is often asymptomatic. Risk is notably higher in APOE ε4 carriers.
- **ARIA-H (Hemosiderin deposition):** Includes microhemorrhages and superficial siderosis, which can accumulate over time with continued therapy and may predispose to macrohemorrhage.

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Adverse Effects of Anti-Amyloid Therapy

Macrohemorrhage

- Although rare, macrohemorrhage can occur, particularly in APOE ε4 carriers or patients with extensive cerebral small-vessel disease. The FDA has issued warnings regarding the increased risk of intracerebral hemorrhage in these populations [8]. The use of anticoagulants increases risk of macrohemorrhage from 0.7% to 2.5%.

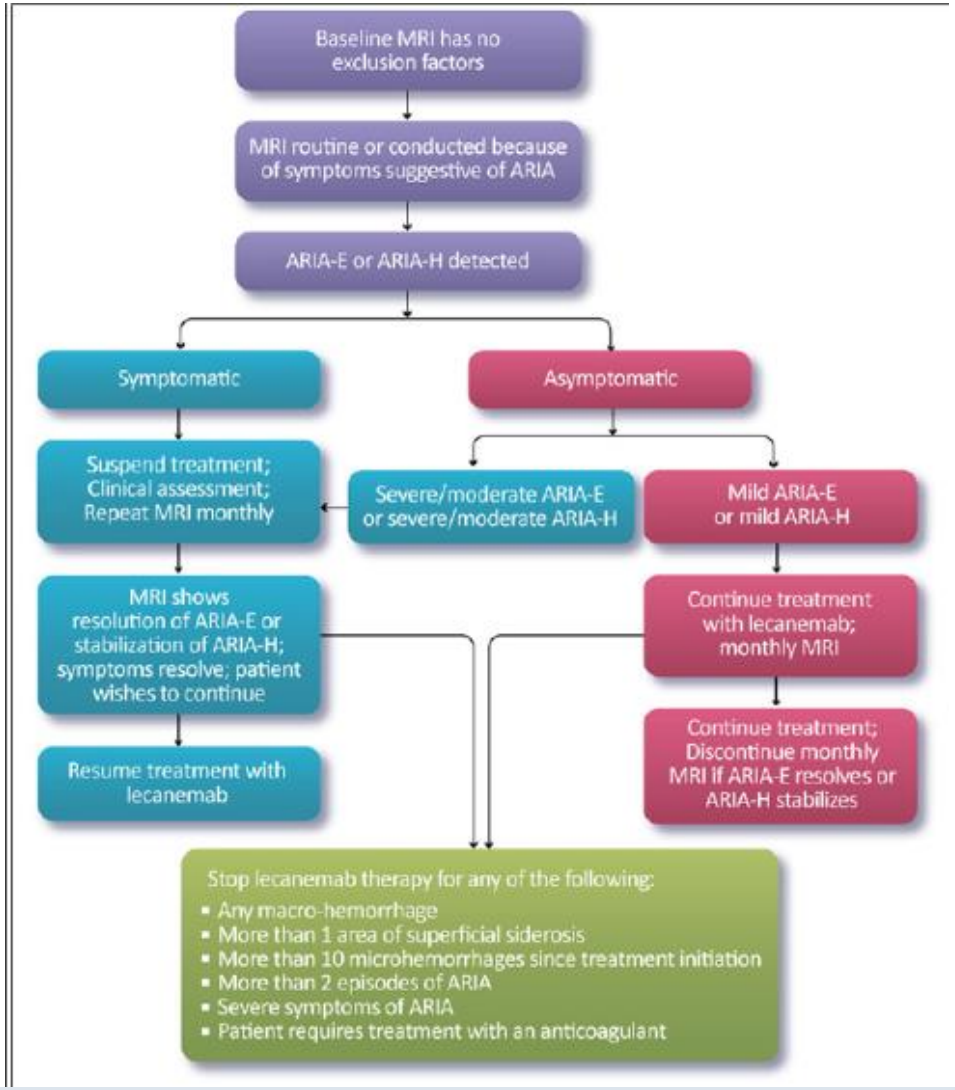
Cummings J, Apostolova L, Rabinovici GD, et al. Lecanemab: appropriate use recommendations. J Prev Alzheimers Dis. 2023;10(3):362-377. doi:10.14283/jpad.2023.30

Adverse Effects of Anti-Amyloid Therapy

Monitoring and Management of ARIA

Table 8. Management of ARIA depending on the severity of symptoms and the severity of the radiographic ARIA-E or ARIA-H on MRI

	Symptom Description			
	No Symptoms	**Mild Symptoms**	**Moderate Symptoms**	**Severe Symptoms**
Severity of Changes Observed on MRI	None	Discomfort noted; no disruption of daily activity	Discomfort sufficient to reduce or affect normal daily activity	Incapacitating, with inability to work or to perform normal daily activity
ARIA-E on MRI				
Mild	Continue dosing	Suspend dosing	Suspend dosing	Discontinue dosing
Moderate	Suspend dosing	Suspend dosing	Suspend dosing	Discontinue dosing
Severe	Discontinue dosing	Discontinue dosing	Discontinue dosing	Discontinue dosing
ARIA-H on MRI				
Mild	Continue dosing	Suspend dosing	Suspend dosing	Discontinue dosing
Moderate	Suspend dosing	Suspend dosing	Suspend dosing	Discontinue dosing
Severe	Discontinue dosing	Discontinue dosing	Discontinue dosing	Discontinue dosing



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Adverse Effects of Anti-Amyloid Therapy

Kisunla (Donanemab) and Modified Dosing Strategy

Recent clinical data from the TRAILBLAZER-ALZ 2 trial demonstrated that Kisunla (donanemab) uses a biomarker-guided, time-limited dosing strategy, where treatment is discontinued after amyloid plaque clearance is confirmed via PET imaging. This approach showed:

- Sustained clinical benefit after treatment cessation
- Lower cumulative risk of ARIA, particularly ARIA-E, due to shorter treatment duration
- Reduced treatment burden and improved safety profile

Adverse Effects of Anti-Amyloid Therapy

Kisunla (Donanemab) and Modified Dosing Strategy

Table 1: Recommended Dosage* and Dosing Schedule Intravenous Infusion (every 4 weeks) KISUNLA Dosage (administered over approximately 30 minutes)

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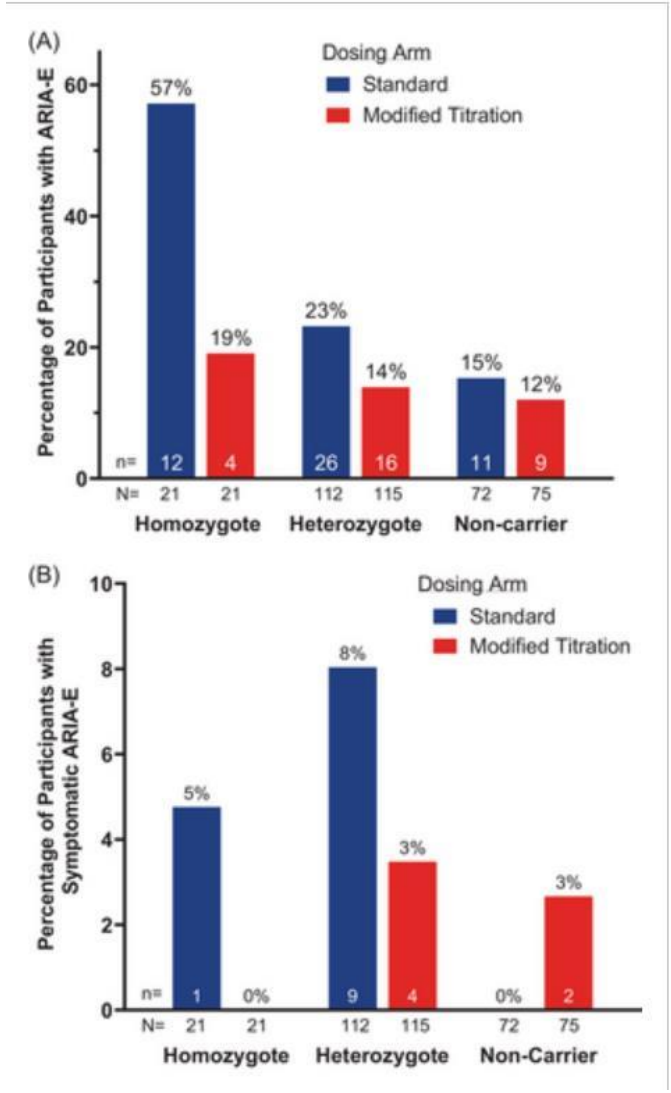
Infusion 1 350 mg

Infusion 2 700 mg

Infusion 3 1,050 mg

Infusion 4 and beyond 1,400 mg

This dosing model contrasts with continuous administration protocols used for other agents (e.g., lecanemab), potentially redefining anti-amyloid treatment paradigms [9].



Wang H, Serap Monkul Nery E, Ardayfio P, et al. Modified titration of donanemab reduces ARIA risk and maintains amyloid reduction. Alzheimer's Dement. 2025; 21:e70062. https://doi.org/10.1002/alz.70062

KU Anti-Amyloid Treatment Clinic Model

KU ALZHEIMER'S DISEASE RESEARCH CENTER

The University of Kansas Medical Center

A Call For New Models of Care

- Anti-amyloid therapies represent a paradigm shift in Alzheimer's treatment.
- Traditional memory clinics are not equipped for the scale and complexity of delivery.
- A dedicated "Treatment Clinic" offers a model for safe, efficient, and scalable care.
- Launched mid-2023 within the KU Memory Care Clinic.
  - **Goal**: Fast-track evaluation, eligibility, and initiation of anti-amyloid therapies.
  - Multidisciplinary team-led approach.

KU Anti-Amyloid Treatment Clinic

Journal of the American Geriatrics Society

Journal of the
American Geriatrics Society

Scaling Alzheimer's Care: The Case for Specialized Treatment Clinics

Eric D. Vidoni[1] | Adam C. Parks[1,2] | Amanda Brunette[1,2] | Katelynn Kreszyn[2] | Ryan A. Townley[1,2] | Anne K. Arthur[1,2] | Lindsey Gillen[2] | Jaime Perales Puchalt[1] | Tina Lewandowski[1] | Dinesh P. Mudaranthakam[1] | Jill K. Morris[1] | T. Ryan Smith[1,2] | Jennifer Woodward[1,2] | Jeffrey M. Burns[1,2]

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Support selection of appropriate patients → Initiate and support mAb Treatment → Optimize safety through monitoring and addressing AEs → Enroll patients in required CMS Registry

Collaboration and communication with referring PCPs

APP Role in the Anti-Amyloid Treatment Clinic

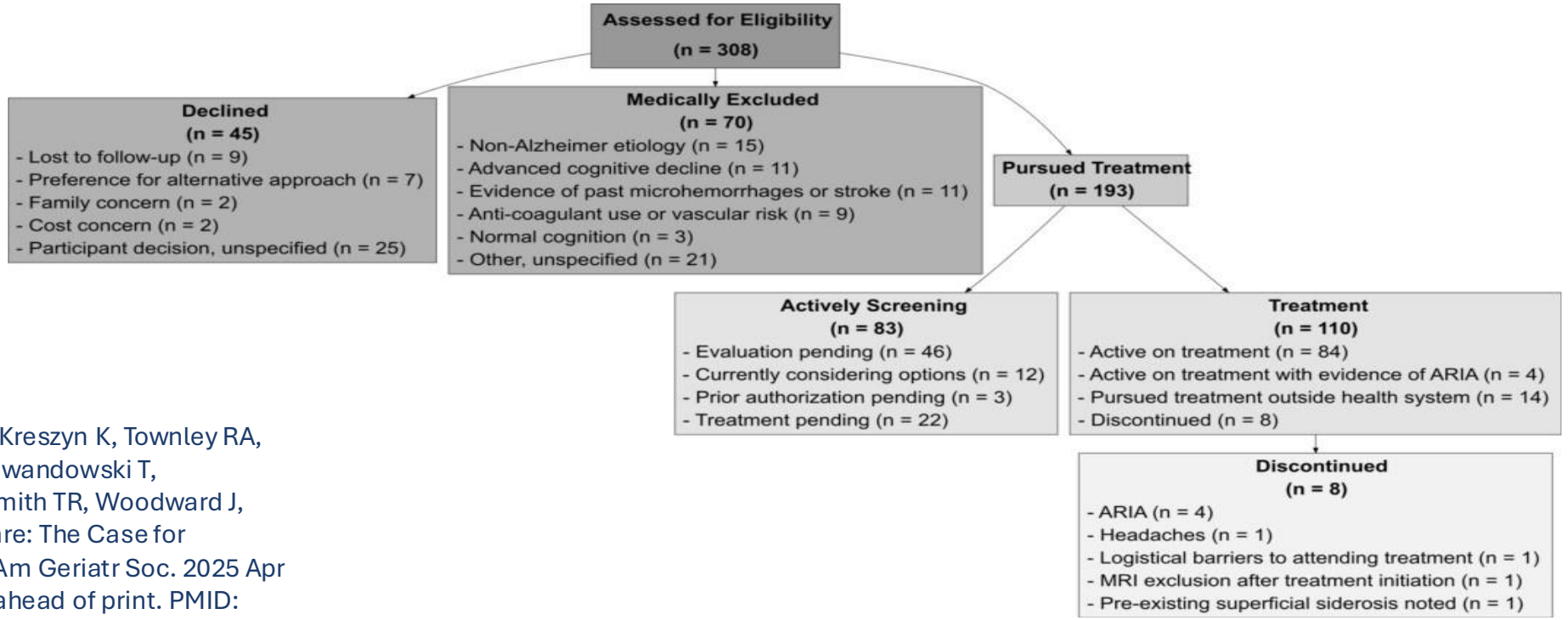
“The APP is trained in dementia evaluation and appropriate use guidelines for monoclonal antibody therapy, serves as the clinical backbone of the clinic, performing initial evaluations, assessing eligibility, guiding shared decision-making, and monitoring patient safety.”

Other essential team members:

- Board-certified neurologist
- Neuropsychologist and psychometrist
- 2 RNs and clinic manager
- Cognitive Care Network (Note: The CCN was developed in 2018 by the KU ADRC) to enhance dementia by integrating Social Work Navigators who connect patients and caregivers with essential resources and provide ongoing support.

APP Role in the Anti-Amyloid Treatment Clinic

Scaling Alzheimer's Care: The Case for Specialized Treatment Clinics



Vidoni ED, Parks AC, Brunette A, Kreszyn K, Townley RA, Arthur AK, Gillen L, Puchalt JP, Lewandowski T, Mudaranthakam DP, Morris JK, Smith TR, Woodward J, Burns JM. Scaling Alzheimer's Care: The Case for Specialized Treatment Clinics. J Am Geriatr Soc. 2025 Apr 7. doi: 10.1111/jgs.19461. Epub ahead of print. PMID: 40192212.

Scalable Blueprint for the Future

- Dedicated anti-amyloid clinics = scalable, high-quality model.
- Centralize expertise → empower community referrals.
- Adaptable across rural, urban, academic, and community settings.

Thanks!

References

- Albert, M. S., et al. (2011). The diagnosis of mild cognitive impairment due to Alzheimer’s disease: Recommendations from the National Institute on Aging and the Alzheimer’s Association workgroup. Alzheimer's & Dementia, 7(3), 270–279. https://doi.org/10.1016/j.jalz.2011.03.008
- Alzheimer’s Association. 2025 Alzheimer’s Disease Facts and Figures. Alzheimers Dement 2025;21(5)
- Budd Haeberlein, S., et al. (2022). Clinical development of anti-amyloid therapies for Alzheimer’s disease. Journal of Prevention of Alzheimer's Disease, 9(2), 197–209. https://doi.org/10.14283/jpad.2022.15
- Cummings J, Apostolova L, Rabinovici GD, et al. Lecanemab: appropriate use recommendations. J Prev Alzheimers Dis.
- 2023;10(3):362-377. doi:10.14283/jpad.2023.30
- Jack, C. R., et al. (2018). NIA-AA Research Framework: Toward a biological definition of Alzheimer’s disease. Alzheimer's & Dementia, 14(4), 535–562. https://doi.org/10.1016/j.jalz.2018.02.018
- Jack CR, Andrews JS, Beach TG, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. Alzheimer's Dement. 2024; 20: 5143–5169. https://doi.org/10.1002/alz.13859
- Mintun, M. A., et al. (2021). Donanemab in early Alzheimer’s disease. New England Journal of Medicine, 384(18), 1691–1704. https://doi.org/10.1056/NEJMoa2100708
- Rabinovici GD, Selkoe DJ, Schindler SE, Aisen P, Apostolova LG, Atri A, Greenberg SM, Hendrix SB, Petersen RC, Weiner M, Salloway S, Cummings J. Donanemab: Appropriate use recommendations. J Prev Alzheimers Dis. 2025 May;12(5):100150. doi: 10.1016/j.tjpad.2025.100150. Epub 2025 Mar 27. PMID: 40155270; PMCID: PMC12180672.
- Salloway, S., et al. (2022). Amyloid-related imaging abnormalities in aducanumab phase 3 trials: Risk factors and clinical outcomes. JAMA Neurology, 79(1), 13–21. https://doi.org/10.1001/jamaneurol.2021.4161
- Sims, J. R., et al. (2023). Donanemab in early symptomatic Alzheimer’s disease. JAMA, 330(1), 33–43. https://doi.org/10.1001/jama.2023.12033

References

- Sperling, R. A., et al. (2021). The A4 Study: Lessons learned and next steps. Alzheimer's & Dementia, 17(5), 734–755. https://doi.org/10.1002/alz.12249
- U.S. Food and Drug Administration (FDA). (2023). Drug Safety Communication: Serious risks of ARIA with anti-amyloid treatments. https://www.fda.gov
- van Dyck, C. H., et al. (2023). Lecanemab in early Alzheimer’s disease. New England Journal of Medicine, 388(1), 9–21. https://doi.org/10.1056/NEJMoa2212948
- Vidoni ED, Parks AC, Brunette A, Kreszyn K, Townley RA, Arthur AK, Gillen L, Puchalt JP, Lewandowski T, Mudaranthakam DP, Morris JK, Smith TR, Woodward J, Burns JM. Scaling Alzheimer's Care: The Case for Specialized Treatment Clinics. J Am Geriatr Soc. 2025 Apr 7. doi: 10.1111/jgs.19461. Epub ahead of print. PMID: 40192212.
- Wang H, Serap Monkul Nery E, Ardayfio P, et al. Modified titration of donanemab reduces ARIA risk and maintains amyloid reduction. Alzheimer's Dement. 2025; 21:e70062. https://doi.org/10.1002/alz.70062
- Zissimopoulos J, Crimmins E, St Clair P. The Value of Delaying Alzheimer's Disease Onset. Forum Health Econ Policy. 2014 Nov;18(1):25-39. doi: 10.1515/fhep-2014-0013. Epub 2014 Nov 4. PMID: 27134606; PMCID: PMC4851168.