ECHO IDAHO

Alzheimer's Disease and Related Dementias

Mild Cognitive Impairment (MCI), Biomarkers and Disease Modifying Treatments

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Objectives

1. Discuss use of biomarkers to identify cause(s) of MCI
2. Discuss risks and benefits of disease modifying treatments for MCI-AD

Case study

- Mr. A, a 74-years old pharmacist, is experiencing increasing levels of forgetfulness over the last six months. He had to cut down to working part-time. He reports becoming more forgetful at work. He feels frustrated that it is so hard to find the right words to describe something. His colleague told him that he had missed a couple of meetings. He started to wonder if he has a serious problem.
- His wife has also noticed him to be more anxious and at times depressed.
- Family history of dementia in his older sister and mother.
- Completes a thorough evaluation and MCI is diagnosed.

Biomarkers to clarify cause(s) of MCI

- MRI of the brain without contrast to look for cerebrovascular disease (vascular MCI), hippocampal atrophy (Alzheimer's and LATE [Limbic-predominant Age-related TDP-43 Encephalopathy]) and amygdalar atrophy (LATE)
- Blood-based Alzheimers' biomarker test: Lumipulse G Ptau217 / Abeta42 ratio or Ptau217 or %pTau217
- Amyloid PET for Alzheimer's disease

Biomarkers to clarify cause(s) of MCI

- Cerebrospinal fluid test: alpha synuclein seed amplification assay for Lewy body disease and tests for Alzheimer's disease (Abeta 42/40; Ptau 181 / Abeta 42)
- FDG PET for Fronto-temporal lobar degeneration (FTLD)
- Neurofilament light (NfL) blood levels to identify neurodegeneration (helps differentiate between FTLD and primary psychiatric conditions)

MCI-AD = Mild Cognitive Impairment due to Alzheimer's Disease

"There is almost always diagnostic uncertainty about the contribution of AD in the MCI stage."

- Rabinovici et al. Updated Appropriate Use Criteria for Amyloid and Tau PET: A Report from the Alzheimer's Association and Society for Nuclear Medicine and Molecular Imaging Workgroup. J Nuclear Med 2025

MCI to Dementia Conversion

- MCI subjects, average age 71 were followed up for 3 years
- Out of 351, 85 converted to AD dementia and 19 to non-AD dementia
- 25% of MCI subjects with AD biomarkers did not convert to dementia

  - Lombardo et al. The Interceptor Project. Alzheimer's & Dementia 2026. Italian researchers.

Case

- Mr. A was diagnosed with MCI-AD (pTau217 was elevated)
- Mr. A wanted to know about risks and benefits of disease modifying treatments

Disease modifying treatments for MCI due to Alzheimer's disease

- Lecanemab (intravenous infusion every two weeks for 18 months and weekly subcutaneous autoinjector after that)
- Donanemab (intravenous infusion every four weeks)
- Periodic MRI to detect ARIA (before 3rd, 5th, 7th and 14th infusion and as needed)
- High cost ($30K per year just for the drug [Medicare Part B covers 80%] plus ? 70K cost of ancillary services [infusions, MRI routine and urgent, physician visits])

Potential benefits of DMTs

- Slow disease progression by six months or more
- No objective way to know that the functional decline has slowed
- Benefits accrue over time

  - Van Dyck et al. Long-term safety and efficacy of Lecanemab in early Alzheimer's disease: Results from the clarity AD open-label extension study. Alzheimers Dementia 2025

Potential risks of DMTs

- Death (very rare)
- Strokes (rare)
- Seizures, status epilepticus (rare)
- Small brain bleeds and brain swelling – ARIA (amyloid related imaging abnormalities): symptomatic and asymptomatic
- Infusion-related reactions (typically mild)

Real world experience with Lecanemab: Retrospective analysis

- 234 patients with mean age 74 (male and female equally represented, 98% White) followed for 6.5 months
- 164 (85%) had MCI and 30 (15%) had mild dementia
- 37% had infusion-related reactions (typically mild)
- 22% had asymptomatic ARIA (amyloid related imaging abnormalities – brain bleeds, brain swelling)

- Paczynski et al. Lecanemab treatment in a specialty memory clinic. JAMA Neurology 5-12-25. Washington University

Real world experience with Lecanemab: symptomatic ARIA

- 11 out of 234 (4.7%) patients had symptomatic ARIA (3 in the MCI group, 8 in mild dementia group)
- 3 out of 164 in the MCI group (1.8%)
- 8 out of 30 in the mild dementia group had symptomatic ARIA (27%)
- 1% (two of the 11) had severe clinical symptoms due to ARIA and had to be hospitalized (both had mild dementia, not MCI)

  - Paczynski et al. Lecanemab treatment in a specialty memory clinic. JAMA Neurology 5-12-25. Washington University

Real world experience with Lecanemab: Symptoms of ARIA

- Headache (most common symptom – 46%)
- Subacute decline in cognition (increased confusion) (15%)
- Dizziness (11%)
- Aphasia
- Visual disturbance, changes in visual acuity, color perception

  - Paczynski et al. Lecanemab treatment in a specialty memory clinic. JAMA Neurology 5-12-25. Washington University and Pivotal Trials

Real world experience with Lecanemab: Symptoms of ARIA

- Shuffling gait and other gait disturbances
- Arm tremor
- Agitation
- Lethargy and delirium

- Paczynski et al. Lecanemab treatment in a specialty memory clinic. JAMA Neurology 5-12-25. Washington University and Pivotal trials

Real world experience with Lecanemab: Symptoms of ARIA

- 92 urgent MRIs
- Only two of these MRIs demonstrated ARIA

  - Paczynski et al. Lecanemab treatment in a specialty memory clinic. JAMA Neurology 5-12-25. Washington University

Donanemab

- Higher rates of ARIA and symptomatic ARIA than Lecanemab
- Faster clearance of amyloid plaques

Case

- Mr. A declines DMT
- Mr. A takes an early retirement and initiates a host of brain healthy lifestyle-based interventions to slow the progression of functional and cognitive decline

Dr. Atul Gawande: Confronting reality

We’re caught in a transitional phase. However miserable the old system has been, we are all experts at it. We know the dance moves. With this new way, in which we together try to figure out how to face mortality and preserve the fiber of a meaningful life with its loyalties and individuality, we are plodding novices. We are going through a societal learning curve, one person at a time.

Book: Being Mortal – Medicine and What Matters in the end.

References

- Palmqvist S, Whitson HE, Allen LA, et al. Alzheimer's association clinical practice guideline on the use of blood-based biomarkers in the diagnostic workup of suspected Alzheimer's disease within specialized care settings. Alzheimers Dement. 2025;21(7): e70535. doi:10.1002/alz.70535
- Chin and Erickson. Alzheimer's disease, biomarkers, and mAbs – What does primary care need? NEJM June 2024
- American Psychiatric Association 2022. Diagnostic and Statistical Manual of Mental Disorders, 5th Edition Text Revision (DSM 5-TR).

References

- Atri et al. Alzheimer's Association clinical practice guideline for the Diagnostic Evaluation, Testing, Counseling, and Disclosure of Suspected Alzheimer's Disease and Related Disorders (DETeCD-ADRD): Executive summary of recommendations for primary care. Alzheimer's & Dementia 2024
- Rabinovici et al. Updated Appropriate Use Criteria for Amyloid and Tau PET: A Report from the Alzheimer's Association and Society for Nuclear Medicine and Molecular Imaging Workgroup. J Nuclear Med 2025

Resources

- Biomarkers for Mild Cognitive Impairment (MCI) and Dementia: Practical Guide for Clinicians (Abhilash Desai, MD)
- Helping Your Patients Understand the New Amyloid-Targeting Therapies for Alzheimer's Disease (Alzheimer's Association)
- Donanemab-azbt Criteria for Use (VA Pharmacy Benefits Management Services, VA National Formulary Committee)
- Lecanemab Eligibility Checklist
- Lecanemab Appropriate Use Recommendations (Alzheimer's Association)
- Lecanemab Patient Eligibility Criteria (Alzheimer's Association)
- MCI, Promoting Hope and Fostering Dementia Positive Communities (Abhilash Desai, MD)
- MCI- Why Early Diagnosis Matters (Abhilash Desai, MD)
- MCI Dementia Prevention (Abhilash Desai, MD)
- MCI Fact Sheet (Boston University Alzheimer's Disease Center)
- MCI or Dementia Care Process Model (Intermountain Health Neurosciences Clinical Program)
- Alzheimer's Forum website (for Nerds)
- Dementia Matters Podcast by Dr. Nathaniel Chin (University of Wisconsin ADRC Director)
- Webinar: Healthy Living with MCI. Free quarterly education and support series by the University of Wisconsin ADRC. March topic: Ultra processed foods. June 12 topic: Navigating Alzheimer Biomarker Testing and Results
- Book: Dr. Chin. When Memory Fades. 2026.

Thank you

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