

Lilly ConnectAD™

Welcome to ConnectADTM, a clinical case series created by the Eli Lilly and Company Neuroscience medical education team. This series is intended to connect healthcare professionals to resources that help them detect, diagnose, and manage Alzheimer's disease.

Disclaimer

The content for this case was created by Eli Lilly and Company and is inspired by scenarios clinicians may encounter while caring for patients with Alzheimer's disease.

Inclusion of a specific approach to treatment and monitoring in this clinical case does not imply endorsement or recommendation by Lilly.

Learning Objective

Through completing this course, you will have a deeper understanding of:

Potential options to approach treatment initiation and monitoring in Alzheimer's disease





Diagnosis: MCI Due to AD



Patient overview:

Maria is a 72-year-old Hispanic female who reports being in good health with controlled chronic conditions:

- Type 2 diabetes
- Hypertension

Initial clinical assessment

- Alert and insightful
- Placed good effort into the testing
- Independent in activities of daily living
- Cognitive impairment (MoCA below threshold)

Additional testing

Maria's cognitive assessment results led to further testing. The additional tests selected included:

- Blood work
- Brain MRI
- CSF Testing

CSF testing

Low $A\beta_{42}/A\beta_{40}$, high P-tau and high T-tau

 Findings consistent with changes in the accumulation of amyloid and tau neuropathology, supporting diagnosis of Alzheimer's disease¹

Treatment Options

Non-pharmacologic or behavioral interventions:

- Non-pharmacologic interventions that may improve or maintain cognition/function, help to support independence in usual activities of daily living, or address behavioral symptoms¹
- Eg, cognitive therapy, physical exercise, nutrition

Symptomatic therapy:

 Pharmacotherapy that may improve cognitive and behavioral symptoms, but does not alter the course of the disease²



Disease-modifying therapy:

- Pharmacotherapy that modifies the clinical course of disease but does not stop or reverse the disease³
- Eg, amyloid-targeting therapy (ATT)



Note: The treatment plan is under the discretion of the HCP and patient via shared decision making and a combination of treatments may be chosen

Why Could Maria Be Considered an Appropriate

Candidate for an ATT?

- Diagnosis of MCI due to AD with confirmed Aβ pathology
- No other known cause for cognitive decline
- 3 No contraindications to treatment
- Brain MRI has no evidence of edema or cerebral amyloid angiopathy

Note: APOE £4 genotyping would provide additional information to inform the treatment risk-benefit discussion



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ATT Class Boxed Warning: APOE ε4 & ARIA

Among patients treated with the ATT class of medications, those who are APOE \$\varepsilon 4\$ homozygotes have a higher incidence of amyloid-related imaging abnormalities (ARIA) – including symptomatic and serious ARIA – than those who are heterozygotes or noncarriers.^{1,2}

Testing for $APOE \ \epsilon 4$ status should be performed prior to initiation of treatment to inform the risk of developing ARIA.^{1,2}

ATT Class Boxed Warning: Risk of ARIA

ATTs are monoclonal antibodies directed against aggregated forms of Aβ and can cause amyloid-related imaging abnormalities (ARIA), as ARIA with edema or effusion (ARIA-E) and ARIA with hemosiderin deposition (ARIA-H). ARIA is usually asymptomatic, although serious and life-threatening events can rarely occur. Serious intracerebral hemorrhages >1 cm have occurred in patients treated with this class of medications. ARIA-E can cause focal neurologic deficits that can mimic ischemic stroke.^{1,2}

Consider the benefit for the treatment of Alzheimer's disease and risk of ARIA when deciding to treat with an ATT.^{1,2}

After Discussion of Treatment Options with Maria and Her Loved One, Maria Expressed an Interest in ATT

Maria is an appropriate candidate for ATT as she:

- Has a diagnosis of MCI due to AD with confirmed Aβ pathology
- Has no contraindications
- Understands the risks and benefits of treatment, including the rationale, process, and resulting impact of APOE ε 4 genotype testing
- Understands the requirements for treatment and monitoring, including infusion and MRI schedule, and communicating new symptoms to the clinician
- Has additional support from loved ones

Initiation and Monitoring of an ATT

Maria begins ATT infusions

She tolerates the infusions well without any infusion-related reactions like dyspnea, change in blood pressure, chills, or chest pain

She receives scheduled MRI scans with no evidence of ARIA

In addition to her treatment, she has started to participate in non-pharmacological interventions including regular exercise and social activities



Note: ATTs carry warnings and precautions about the risk of developing serious hypersensitivity and infusion-related reactions during and after completion of the infusion. In addition, ATTs are contraindicated in patients with a known serious hypersensitivity to the active ingredient or to any of the excipients^{1,2}

ARIA=Amyloid-related Imaging Abnormalities; ATT=Amyloid-targeting Therapy; MRI=Magnetic Resonance Imaging. 1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC.

^{2.} Legembi (lecanemab-irmb) injection, for intravenous use [package insert]. Nutley, NJ: Eisai Inc.

Monitoring of an ATT

- ATTs require periodic monitoring for ARIA with MRI at baseline and throughout treatment. If a patient experiences symptoms suggestive of ARIA, clinical evaluation should be performed, including an MRI if indicated.
- Dose adjustments for ARIA depend on type, radiographic severity, and clinical symptoms.^{1,2}



Key Learnings in Maria's Case

Initiating and monitoring treatment with ATTs requires patient and loved one education and multidisciplinary collaboration.

Patients and their loved ones must be educated about:

- The potential risks and benefits of treatment to engage in shared treatment decision-making^{1,2}
- The symptoms associated with ARIA and the importance of communicating new symptoms immediately if they occur^{1,3}
- The importance of adhering to the MRI monitoring schedule^{2,3}

Multi-disciplinary collaboration and communication are necessary to ensure appropriate treatment monitoring.^{1,2}

Comprehensive patient management includes ATTs⁴, symptomatic treatment⁵, and non-pharmacological interventions.⁵



Treat · Monitor

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