A REAL PATIENT CASE STUDY:
MILD COGNITIVE IMPAIRMENT (MCI) DUE TO AD

LEQEMBI® (lecanemab-irmb) 100 mg/mL
INJECTION FOR INTRAVENOUS USE

Intervene at the earliest clinical stages of AD[1]

Provided by David C. Weisman, MD

Dr. Weisman is the director of the Clinical Trial Center at Abington Neurological Associates, Pennsylvania, which he founded in 2008. He is a leading AD trialist nationwide and has been honored as an ADCS investigator, having conducted numerous clinical trials in MCI and AD.

Dr. Weisman serves as a consultant and speaker for Eisai Inc.

AD=Alzheimer's disease; ADCS=Alzheimer's Disease Cooperative Study.

INDICATION

LEQEMBI® is indicated for the treatment of Alzheimer's disease (AD). Treatment with LEQEMBI should be initiated in patients with mild cognitive impairment (MCI) or mild dementia stage of disease, the population in which treatment was initiated in clinical trials.

SELECT SAFETY INFORMATION: Boxed WARNING

WARNING: AMYLOID-RELATED IMAGING ABNORMALITIES (ARIA)

- **Monoclonal antibodies directed against aggregated forms of beta amyloid, including LEQEMBI, can cause ARIA, characterized as ARIA with edema (ARIA-E) and ARIA with hemosiderin deposition (ARIA-H). Incidence and timing of ARIA vary among treatments. ARIA usually occurs early in treatment and is usually asymptomatic, although serious and life-threatening events, including seizure and status epilepticus, rarely can occur. Serious intracerebral hemorrhages (ICH) >1 cm, some of which have been fatal, have been observed with this class of medications. Because ARIA-E can cause focal neurologic deficits that can mimic an ischemic stroke, consider whether such symptoms could be due to ARIA-E before giving thrombolytic therapy to a patient being treated with LEQEMBI.**
  - **Apolipoprotein E ε4 (ApoE ε4) Homozygotes: Patients who are ApoE ε4 homozygotes (~15% of patients with AD) treated with this class of medications have a higher incidence of ARIA, including symptomatic, serious, and severe radiographic ARIA, compared to heterozygotes and noncarriers. Testing for ApoE ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. Prior to testing, prescribers should discuss with patients the risk of ARIA across genotypes and the implications of genetic testing results. Prescribers should inform patients that if genotype testing is not performed, they can still be treated with LEQEMBI; however, it cannot be determined if they are ApoE ε4 homozygotes and at higher risk for ARIA.**
- **Consider the benefit of LEQEMBI for the treatment of AD and the potential risk of serious ARIA events when deciding to initiate treatment with LEQEMBI.**

Please see additional Select Safety Information throughout and full Prescribing Information, including Boxed WARNING.

Rick, a 72-year-old man presenting with memory changes, was evaluated by Dr. Weisman

1. Dr. Weisman assessed Rick's cognitive function

Symptoms	› Wife noticed subtle memory changes in patient 2 years ago, which have become more noticeable; patient notices the changes with "almost everything" › No reported functional impairment	**Rick showed possible evidence of cognitive impairment, motivating Dr. Weisman to investigate further.**
MMSE	26/30	
Medical history	› Right cerebellar hemangioblastoma (previously removed) › Peripheral neuropathy › Knee replacement	
Family history	Mother and brother diagnosed with AD in their 80s	

2. Dr. Weisman probed whether AD could be the cause of Rick's symptoms

Lab	› Vitamin B12: 440 (normal) › TSH: 1.140 (normal)	**Dr. Weisman's suspicion of MCI due to AD was consistent with Rick's differential diagnosis. He ordered confirmatory tests and began to consider possible treatments.**
MRI	› No evidence of acute infarction, hemorrhage, or mass › Post-surgical posterior fossa › No microhemorrhages	
Other observations	› No symptoms to suggest obstructive sleep apnea › Low suspicion for depression or mood disorder	
Current medications	None	
Lifestyle factors	› No alcohol use › No drug use	

3. CSF analysis showed presence of Aβ pathology, confirming Rick's diagnosis

CSF	› CSF analysis consistent with presence of AD › Aβ42/40: 0.042 (low; reference interval 0.058; higher likelihood of AD diagnosis) › Aβ42: 531 (abnormal) › Aβ40: 12679 (abnormal)	**Dr. Weisman and Rick discussed next steps, including available treatments to help slow cognitive and functional decline.**
Diagnosis	**MCI due to AD**	

Patient name is hypothetical in nature to maintain confidentiality.
Clinical details, personal traits, and quotes presented herein are from an actual patient.
Individual results may vary. The efficacy and safety of LEQEMBI have been studied in Clarity AD.[2]

Aβ=amyloid beta; CSF=cerebrospinal fluid; MMSE=Mini-Mental State Examination; MRI=magnetic resonance imaging; TSH=thyroid stimulating hormone.

SELECT SAFETY INFORMATION (cont'd)

CONTRAINDICATION

LEQEMBI® is contraindicated in patients with serious hypersensitivity to lecanemab-irmb or to any of the excipients of LEQEMBI. Reactions have included angioedema and anaphylaxis.

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Treatment rationale for choosing LEQEMBI®

Perspective from Dr. Weisman

✔ Identified and diagnosed patient

- Patient presented with **mild cognitive impairment**, consistent with MMSE score of 26/30
- **Ruled out** possible non-AD causes
- **Diagnosis confirmed** with CSF analysis that showed presence of Aβ pathology

✔ Discussed LEQEMBI as a treatment option

- Patient understood that LEQEMBI may help slow AD, but not reverse it* or its symptoms
- Noted side effects, ARIA risk, and risk based on ApoE ε4 status
- Evaluated for genetic risk; patient agreed to ApoE ε4 testing to better understand his ARIA risk with treatment
- Patient indicated LEQEMBI as treatment of choice

✔ Prepared patient for treatment

- ApoE ε4 test result: ε3/ε4 heterozygote (discussed elevated ARIA risk vs noncarriers)
- Most recent MRI (taken a few months ago) used as baseline

*Based on an 18-month study vs placebo.[2]

Actor portrayal.

Rick expressed to Dr. Weisman why he was motivated to start on LEQEMBI

- Aware of his cognitive changes and family history of AD (mother and brother)
- Determined to stay on top of his health
- Desire to continue role in a family business
- Strong support system from wife, children, and grandchildren

More about Rick: He is a semi-retired owner of a construction company in Philadelphia. Rick is motivated to do anything he can to maintain his active, family-oriented lifestyle.

> “I’m going to fight this. **I will do everything I can to delay progression.**”
>
> – Rick

ApoE ε4=apolipoprotein E ε4; ARIA=amyloid-related imaging abnormality.

SELECT SAFETY INFORMATION (cont’d)

WARNINGS AND PRECAUTIONS

AMYLOID-RELATED IMAGING ABNORMALITIES

Medications in this class, including LEQEMBI, can cause ARIA-E, which can be observed on MRI as brain edema or sulcal effusions, and ARIA-H, which includes microhemorrhage and superficial siderosis. ARIA can occur spontaneously in patients with AD, particularly in patients with MRI findings suggestive of cerebral amyloid angiopathy (CAA), such as pretreatment microhemorrhage or superficial siderosis. ARIA-H generally occurs with ARIA-E. Reported ARIA symptoms may include headache, confusion, visual changes, dizziness, nausea, and gait difficulty. Focal neurologic deficits may also occur. Symptoms usually resolve over time.

Incidence of ARIA

Symptomatic ARIA occurred in 3% and serious ARIA symptoms in 0.7% with LEQEMBI. Clinical ARIA symptoms resolved in 79% of patients during the period of observation. ARIA, including asymptomatic radiographic events, was observed: LEQEMBI, 21%; placebo, 9%. ARIA-E was observed: LEQEMBI, 13%; placebo, 2%. ARIA-H was observed: LEQEMBI, 17%; placebo, 9%. No increase in isolated ARIA-H was observed for LEQEMBI vs placebo.

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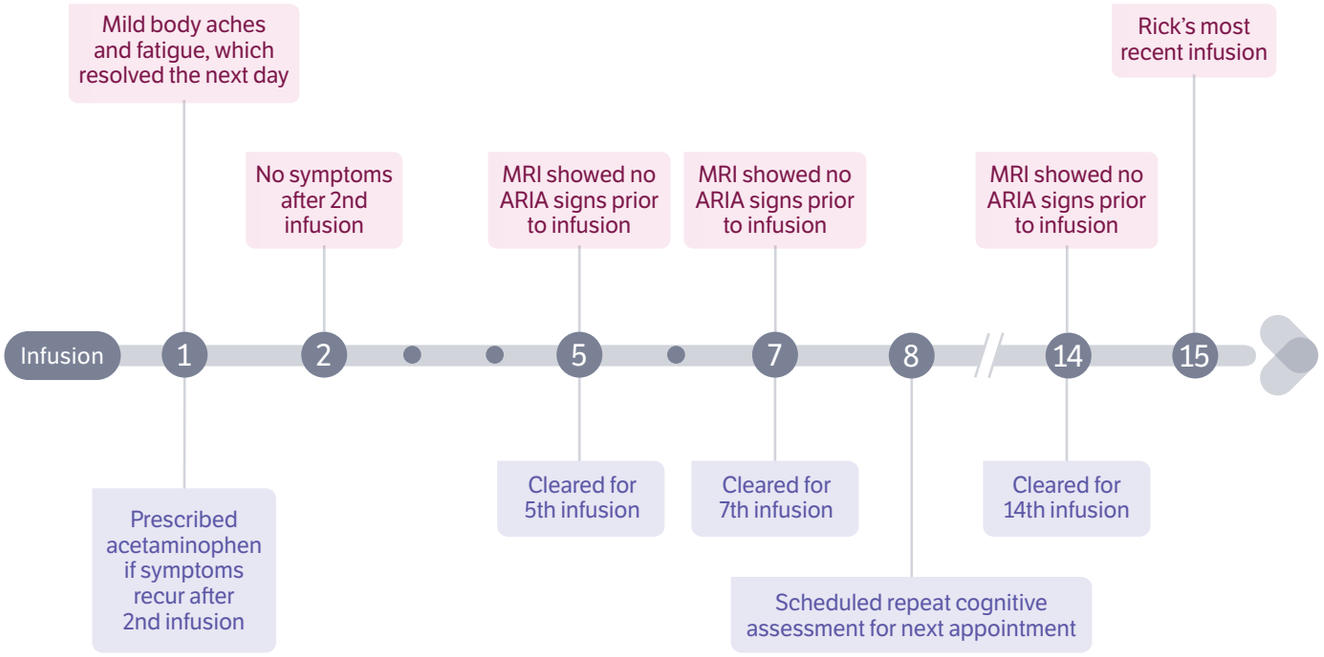
Dr. Weisman continues to monitor Rick's individual treatment plan

Rick's journey

Dr. Weisman's assessments



As of June 2024, Rick has not experienced any new neurologic symptoms. His care team continues to monitor for any changes or adverse reactions.

With the support of Dr. Weisman and his care team, Rick is staying on track with treatment.

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SELECT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

AMYLOID-RELATED IMAGING ABNORMALITIES (cont'd)

Incidence of ICH

ICH >1 cm in diameter was reported in 0.7% with LEQEMBI® vs 0.1% with placebo. Fatal events of ICH in patients taking LEQEMBI have been observed.

Risk Factors of ARIA and ICH

ApoE ε4 Carrier Status

Of the patients taking LEQEMBI, 16% were ApoE ε4 homozygotes, 53% were heterozygotes, and 31% were noncarriers. With LEQEMBI, ARIA was higher in ApoE ε4 homozygotes (LEQEMBI: 45%; placebo: 22%) than in heterozygotes (LEQEMBI: 19%; placebo: 9%) and noncarriers (LEQEMBI: 13%; placebo: 4%). Symptomatic ARIA-E occurred in 9% of ApoE ε4 homozygotes vs 2% of heterozygotes and 1% of noncarriers. Serious ARIA events occurred in 3% of ApoE ε4 homozygotes and in ~1% of heterozygotes and noncarriers. The recommendations on management of ARIA do not differ between ApoE ε4 carriers and noncarriers.

Radiographic Findings of CAA

- Neuroimaging findings that may indicate CAA include evidence of prior ICH, cerebral microhemorrhage, and cortical superficial siderosis. CAA has an increased risk for ICH. The presence of an ApoE ε4 allele is also associated with CAA.
- The baseline presence of at least 2 microhemorrhages or the presence of at least 1 area of superficial siderosis on MRI, which may be suggestive of CAA, have been identified as risk factors for ARIA. Patients were excluded from Clarity AD for the presence of >4 microhemorrhages and additional findings suggestive of CAA (prior cerebral hemorrhage >1 cm in greatest diameter, superficial siderosis, vasogenic edema) or other lesions (aneurysm, vascular malformation) that could potentially increase the risk of ICH.

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“I feel so grateful that we caught this early so that I can take steps to **slow how fast my disease progresses.**”

– Rick

Actor portrayals.

Since Rick was diagnosed with MCI due to AD, he is able to be treated with LEQEMBI®.[1,2]

SELECT SAFETY INFORMATION (cont’d)
WARNINGS AND PRECAUTIONS (cont’d)
AMYLOID-RELATED IMAGING ABNORMALITIES (cont’d)
Risk Factors of ARIA and ICH (cont’d)

Concomitant Antithrombotic or Thrombolytic Medication

- In Clarity AD, baseline use of antithrombotic medication (aspirin, other antiplatelets, or anticoagulants) was allowed if the patient was on a stable dose. Most exposures were to aspirin. Antithrombotic medications did not increase the risk of ARIA with LEQEMBI. The incidence of ICH: 0.9% in patients taking LEQEMBI with a concomitant antithrombotic medication vs 0.6% with no antithrombotic and 2.5% in patients taking LEQEMBI with an anticoagulant alone or with antiplatelet medication such as aspirin vs none in patients receiving placebo.
- Fatal cerebral hemorrhage has occurred in 1 patient taking an anti-amyloid monoclonal antibody in the setting of focal neurologic symptoms of ARIA and the use of a thrombolytic agent.
- Additional caution should be exercised when considering the administration of antithrombotics or a thrombolytic agent (e.g., tissue plasminogen activator) to a patient already being treated with LEQEMBI. Because ARIA-E can cause focal neurologic deficits that can mimic an ischemic stroke, treating clinicians should consider whether such symptoms could be due to ARIA-E before giving thrombolytic therapy in a patient being treated with LEQEMBI.
- Caution should be exercised when considering the use of LEQEMBI in patients with factors that indicate an increased risk for ICH and, in particular, patients who need to be on anticoagulant therapy or patients with findings on MRI that are suggestive of CAA.

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Do you suspect early AD in patients you see in your practice?

1. Check for cognitive impairment[3-6]

2. Differential diagnosis for AD[3,7,8]

3. Confirm AD diagnosis[9,10]

Explore resources to help your patients start treatment

SELECT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

AMYLOID-RELATED IMAGING ABNORMALITIES (cont'd)

Radiographic Severity With LEQEMBI®

Most ARIA-E radiographic events occurred within the first 7 doses, although ARIA can occur at any time, and patients can have >1 episode. Maximum radiographic severity of ARIA-E with LEQEMBI was mild in 4%, moderate in 7%, and severe in 1% of patients. Resolution on MRI occurred in 52% of ARIA-E patients by 12 weeks, 81% by 17 weeks, and 100% overall after detection. Maximum radiographic severity of ARIA-H microhemorrhage with LEQEMBI was mild in 9%, moderate in 2%, and severe in 3% of patients; superficial siderosis was mild in 4%, moderate in 1%, and severe in 0.4% of patients. With LEQEMBI, the rate of severe radiographic ARIA-E was highest in ApoE ε4 homozygotes (5%) vs heterozygotes (0.4%) or noncarriers (0%). With LEQEMBI, the rate of severe radiographic ARIA-H was highest in ApoE ε4 homozygotes (13.5%) vs heterozygotes (2.1%) or noncarriers (1.1%).

Monitoring and Dose Management Guidelines

Baseline brain MRI and periodic monitoring with MRI are recommended. Enhanced clinical vigilance for ARIA is recommended during the first 14 weeks of treatment. Depending on ARIA-E and ARIA-H clinical symptoms and radiographic severity, use clinical judgment when considering whether to continue dosing or to temporarily or permanently discontinue LEQEMBI. If a patient experiences ARIA symptoms, clinical evaluation should be performed, including MRI if indicated. If ARIA is observed on MRI, careful clinical evaluation should be performed prior to continuing treatment.

HYPERSENSITIVITY REACTIONS

Hypersensitivity reactions, including angioedema, bronchospasm, and anaphylaxis, have occurred with LEQEMBI. Promptly discontinue the infusion upon the first observation of any signs or symptoms consistent with a hypersensitivity reaction and initiate appropriate therapy.

INFUSION-RELATED REACTIONS (IRRs)

- IRRs were observed—LEQEMBI: 26%; placebo: 7%—and most cases with LEQEMBI (75%) occurred with the first infusion. IRRs were mostly mild (69%) or moderate (28%). Symptoms included fever and flu-like symptoms (chills, generalized aches, feeling shaky, and joint pain), nausea, vomiting, hypotension, hypertension, and oxygen desaturation.
- In the event of an IRR, the infusion rate may be reduced or discontinued, and appropriate therapy initiated as clinically indicated. Consider prophylactic treatment prior to future infusions with antihistamines, acetaminophen, nonsteroidal anti-inflammatory drugs, or corticosteroids.

ADVERSE REACTIONS

The most common adverse reactions reported in ≥5% with LEQEMBI and ≥2% higher than placebo were IRRs (LEQEMBI: 26%; placebo: 7%), ARIA-H (LEQEMBI: 14%; placebo: 8%), ARIA-E (LEQEMBI: 13%; placebo: 2%), headache (LEQEMBI: 11%; placebo: 8%), superficial siderosis of central nervous system (LEQEMBI: 6%; placebo: 3%), rash (LEQEMBI: 6%; placebo: 4%), and nausea/vomiting (LEQEMBI: 6%; placebo: 4%).

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References: 1. Alzheimer's Association. 2024 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2024;20(5):1-149. **2.** LEQEMBI (lecanemab-irmb) injection, for intravenous use [package insert]. Nutley, NJ: Eisai Inc. **3.** Alzheimer's Association. Medical tests for diagnosing Alzheimer's. Accessed May 28, 2024. https://www.alz.org/alzheimers-dementia/diagnosis/medical_tests **4.** O'Caoimh R, Timmons S, Molloy DW. Screening for mild cognitive impairment: comparison of "MCI specific" screening instruments. *J Alzheimers Dis*. 2016;51(2):619-629. **5.** Tariq SH, Tumosa N, Chibnall JT, Perry MH 3rd, Morley JE. Comparison of the Saint Louis University Mental Status Examination and the Mini-Mental State Examination for detecting dementia and mild neurocognitive disorder—a pilot study. *Am J Geriatr Psychiatry*. 2006;14(11):900-910. **6.** Usarel C, Dokuzlar O, Aydin AE, Soysal P, Isik AT. The AD8 (Dementia Screening Interview) is a valid and reliable screening scale not only for dementia but also for mild cognitive impairment in the Turkish geriatric outpatients. *Int Psychogeriatr*. 2019;31(2):223-229. **7.** Budson AE, Solomon PR. Evaluating the patient with memory loss or dementia. In: Budson AE, Solomon PR, eds. *Memory Loss, Alzheimer's Disease, and Dementia: A Practical Guide for Clinicians*. 3rd ed. Elsevier; 2022:4-37. **8.** National Institute on Aging. How biomarkers help diagnose dementia. Accessed August 24, 2023. https://www.nia.nih.gov/health/alzheimers-symptoms-and-diagnosis/how-biomarkers-help-diagnose-dementia **9.** Schindler SE, Bollinger JG, Ovod V, et al. High-precision plasma β-amyloid 42/40 predicts current and future brain amyloidosis. *Neurology*. 2019;93(17):e1647-e1659. **10.** Nakamura A, Kaneko N, Villemagne VL, et al. High performance plasma amyloid-β biomarkers for Alzheimer's disease. *Nature*. 2018;554(7691):249-254.

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