

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

Intervene at the earliest clinical stages of AD¹

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



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[®] (lecanemab-irmb) 100 mg/mL injection for intravenous use 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

WARNING: AMYLOID-RELATED IMAGING ABNORMALITIES (ARIA)

- **Monoclonal antibodies directed against aggregated forms of amyloid beta, 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 asymptomatic, although serious and life-threatening events, including seizure and status epilepticus, rarely can occur. Serious intracerebral hemorrhages >1 cm, some fatal, have been observed with this class of medications.**
- **Apolipoprotein E ϵ 4 (ApoE ϵ 4) Homozygotes: Patients who are ApoE ϵ 4 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 ϵ 4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. 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 ϵ 4 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	<ul style="list-style-type: none">› 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	<ul style="list-style-type: none">› 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	<ul style="list-style-type: none">› 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	<ul style="list-style-type: none">› No evidence of acute infarction, hemorrhage, or mass› Post-surgical posterior fossa› No microhemorrhages	
Other observations	<ul style="list-style-type: none">› No symptoms to suggest obstructive sleep apnea› Low suspicion for depression or mood disorder	
Current medications	None	
Lifestyle factors	<ul style="list-style-type: none">› No alcohol use› No drug use	

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

CSF	<ul style="list-style-type: none">› 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

A β =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.

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



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 A β 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 ϵ 4 status
- › Evaluated for genetic risk; patient agreed to ApoE ϵ 4 testing to better understand his ARIA risk with treatment
- › Patient indicated LEQEMBI as treatment of choice

✓ Prepared patient for treatment

- › ApoE ϵ 4 test result: ϵ 3/ ϵ 4 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 ϵ 4=apolipoprotein E ϵ 4; ARIA=amyloid-related imaging abnormality.

SELECT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS AMYLOID-RELATED IMAGING ABNORMALITIES

ARIA-E and ARIA-H can occur together. ARIA-E can be observed on MRI as brain edema or sulcal effusions and ARIA-H as microhemorrhage and superficial siderosis. ARIA can occur spontaneously in patients with AD. ARIA-H generally occurs in association 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.

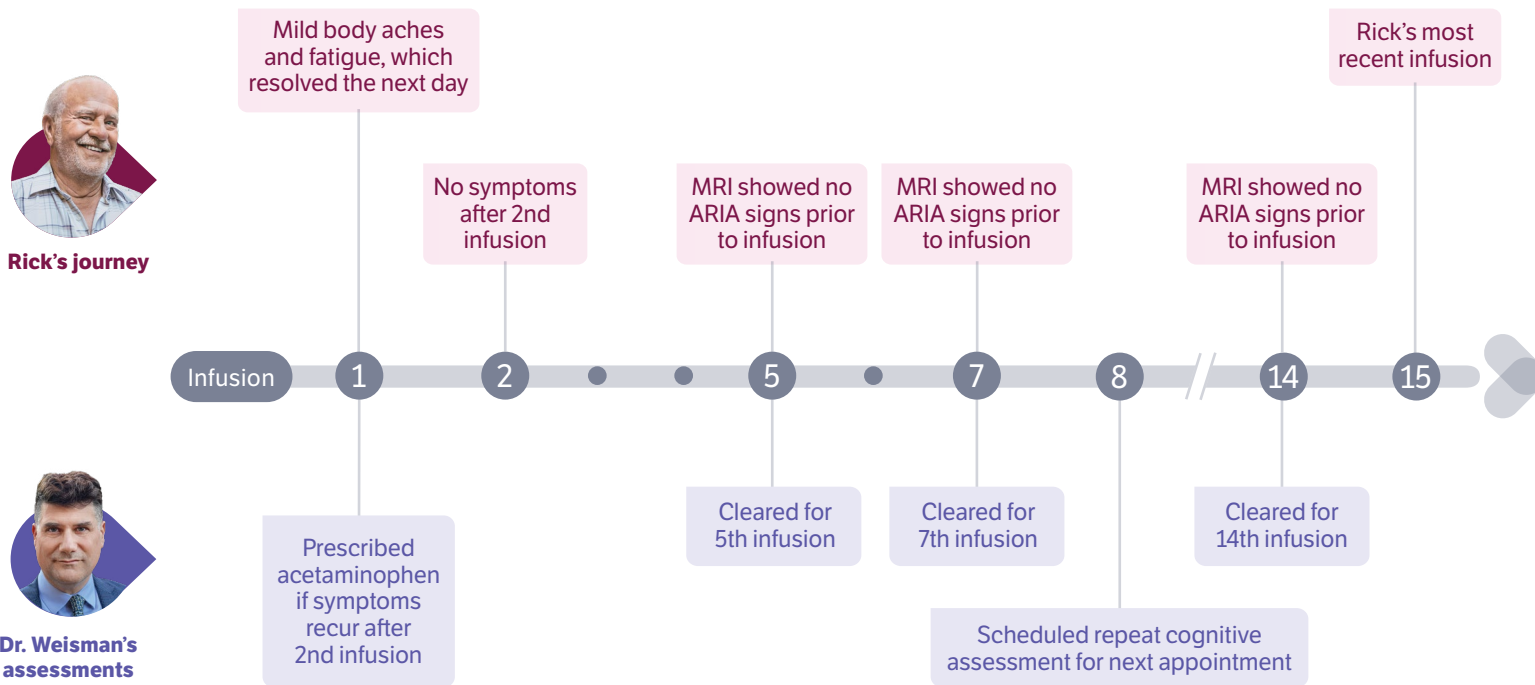
Incidence of ARIA

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



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.

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

SELECT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS AMYLOID-RELATED IMAGING ABNORMALITIES (cont'd)

ApoE ϵ 4 Carrier Status and Risk of ARIA

Of the patients taking LEQEMBI[®], 16% were ApoE ϵ 4 homozygotes, 53% were heterozygotes, and 31% were noncarriers. With LEQEMBI, ARIA was higher in ApoE ϵ 4 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 ϵ 4 homozygotes vs 2% of heterozygotes and 1% of noncarriers. Serious ARIA events occurred in 3% of ApoE ϵ 4 homozygotes and in ~1% of heterozygotes and noncarriers. The recommendations on management of ARIA do not differ between ApoE ϵ 4 carriers and noncarriers.

Radiographic Findings

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 of ARIA-E on MRI occurred in 52% of 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 ϵ 4 homozygotes (5%) vs heterozygotes (0.4%) or noncarriers (0%). With LEQEMBI, the rate of severe radiographic ARIA-H was highest in ApoE ϵ 4 homozygotes (13.5%) vs heterozygotes (2.1%) or noncarriers (1.1%).

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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 AMYLOID-RELATED IMAGING ABNORMALITIES (cont'd)

Intracerebral Hemorrhage

Intracerebral hemorrhage >1 cm in diameter was reported in 0.7% LEQEMBI vs 0.1% placebo. Fatal events of intracerebral hemorrhage in patients taking LEQEMBI have been reported.

Concomitant Antithrombotic Medication and Other Risk Factors for Intracerebral Hemorrhage:

- 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 intracerebral hemorrhage: 0.9% LEQEMBI with a concomitant antithrombotic medication vs 0.6% no antithrombotic; 2.5% LEQEMBI with an anticoagulant alone or with antiplatelet medication/aspirin vs none receiving placebo.
- Patients were excluded from Clarity AD if neuroimaging indicated increased risk for intracerebral hemorrhage including cerebral amyloid angiopathy (prior cerebral hemorrhage >1 cm in greatest diameter, >4 microhemorrhages, superficial siderosis, vasogenic edema) or other lesions (aneurysm, vascular malformation). The presence of an ApoE ε4 allele is also associated with cerebral amyloid angiopathy.
- Caution should be exercised when considering the administration of anticoagulants or a thrombolytic agent (e.g., tissue plasminogen activator) to a patient already being treated with LEQEMBI and in patients with factors that indicate an increased risk for intracerebral hemorrhage.

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



1. Check for cognitive impairment³⁻⁶

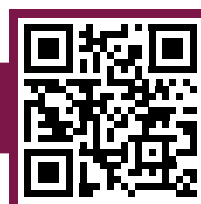


2. Differential diagnosis for AD^{3,7,8}



3. Confirm AD diagnosis^{9,10}

Explore resources to help your patients start treatment



SELECT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS AMYLOID-RELATED IMAGING ABNORMALITIES (cont'd)

ARIA Monitoring and Dose Management Guidelines

Obtain a recent baseline brain MRI prior to initiating treatment with LEQEMBI[®] and prior to the 5th, 7th, and 14th infusions. 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 $\geq 5\%$ with LEQEMBI and $\geq 2\%$ 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'Caomh 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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