ANTI-AMYLOID TREATMENT

Benefits, ARIA Risk, and Safety for Early Alzheimer's Disease

The patient and care-partner guide we use at Los Altos Neurology when discussing lecanemab (Leqembi) and donanemab (Kisunla)

Created by Los Altos Neurology for our patients and care partners. This handout is for informational and educational purposes only and is not a substitute for medical advice. Please contact us or your physician with questions about your diagnosis, treatment options, or individual risk profile.

Read this first

These treatments are intended for carefully selected patients with early, amyloid-confirmed Alzheimer's disease. They do not improve memory or restore abilities that have already been lost. On average, they modestly slow worsening in memory, thinking, and daily function, which may allow some patients to remain independent for longer. They do not stop the disease. The principal risk is amyloid-related imaging abnormalities, or ARIA—changes such as brain swelling or small areas of bleeding seen on MRI. ARIA is often asymptomatic, but it can occasionally cause serious neurologic injury, disability, or death.

Who was studied in clinical trials

- Adults with mild cognitive impairment or mild dementia due to Alzheimer's disease.
- In the pivotal trials, participants were generally 50–90 years old for Leqembi and 60–85 years old for Kisunla.
- Amyloid confirmed by an accepted biomarker test before treatment.
- Patients with moderate or severe dementia were excluded from the pivotal trials.

What treatment may do

- Slow the average rate of worsening.
- Help some patients remain in an earlier stage longer.
- Preserve independence longer for some patients, on average.

What treatment does not do

- Cure Alzheimer's disease.
- Reverse memory loss or restore abilities already lost.
- Guarantee stability or a specific benefit for one person.

How strong is the evidence?

Evidence	What it tells us	How certain is it?
Main trials (about 18 months)	The strongest evidence. Patients were randomly assigned to treatment or placebo.	Shows the average benefit, but cannot predict one person's response.
Longer follow-up (3-4 years)	Suggests that the benefit continues and may grow over time.	There was no ongoing placebo group, so these estimates are less certain.

This handout summarizes what we review with you before and during treatment. It is not a consent form and does not replace your visits with us, the FDA Medication Guide, current prescribing information, MRI review, or our safety protocol.

1 Benefit and treatment logistics

What the clinical trials showed and what treatment requires

Randomized and longer-term benefit

Medicine	What the main trial found	Longer follow-up
Leqembi (Lecanemab)	On a standard measure of memory, thinking, and daily function, patients worsened 0.45 point less over 18 months (27% relative slowing), equal to roughly 5-6 months of time-equivalent slowing.	At 4 years, the average difference is reasonably summarized as about 12 months of time-equivalent slowing.
Kisunla (Donanemab)	On the same type of measure, patients worsened 0.70 point less over 76 weeks (29% relative slowing), equal to roughly 5 months of time-equivalent slowing.	At 3 years, the average difference is reasonably summarized as about 7 months of time-equivalent slowing.

What "time saved" means

It does not mean extra life expectancy. It means that, on average, the treated group reached a similar level of measured worsening later than the comparison group. It is a way to translate slowing into months, not a promise for one person.

How the medicines target amyloid differently

Amyloid builds up in the brain in different forms, ranging from smaller clumps that have not yet formed mature plaques to larger, established plaques. Leqembi targets smaller amyloid clumps called protofibrils and also binds amyloid within plaques. Kisunla mainly targets a modified form of amyloid found in established plaques. Both treatments reduce amyloid plaque seen on PET scans, and neither directly targets tau.

Dosing and required MRI monitoring

	Leqembi	Kisunla
Starting treatment	IV every 2 weeks for 18 months.	IV every 4 weeks: 350 mg, 700 mg, 1,050 mg, then 1,400 mg.
After the initial period	Continue IV every 2 weeks, transition to monthly IV maintenance, or weekly subcutaneous maintenance when appropriate.	Kisunla may be stopped after amyloid PET shows that plaque has fallen to a minimal level. The best schedule for future PET scans or restarting treatment is not yet established.
Scheduled MRI	Baseline; before infusions 3, 5, 7, and 14.	Baseline; before infusions 2, 3, 4, and 7.
Additional MRI	Needed for new symptoms, prior ARIA, or other clinical concerns.	Needed for new symptoms, prior ARIA, or other clinical concerns.

Infusion reactions are separate from ARIA

Leqembi infusion-related reactions occurred in 26% of treated participants; 75% of those reactions occurred with the first infusion. With the current Kisunla titration, infusion-related reactions occurred in 16%, and 88% occurred within the first four infusions. Most were mild or moderate, but serious hypersensitivity can occur. The 16% Kisunla figure comes from a separate study; it should not be compared directly with Leqembi as if the trials were head-to-head.

2 ARIA at a glance

Overall MRI and symptom risks from current U.S. prescribing information

ARIA-E means swelling or fluid seen on MRI. ARIA-H means small areas of bleeding or iron staining in or on the brain. A person can have both types, so the percentages should not be added.

Why ARIA can happen - and why scheduled MRI matters

Amyloid can also collect in the walls of small brain blood vessels. A leading explanation is that, as treatment mobilizes amyloid, these vessels may temporarily become inflamed, leaky, or more fragile. You can feel completely normal while an MRI shows ARIA, so please do not skip a scheduled safety MRI because you feel well.

Outcome	Leqembi 898 treated; 18 months	Kisunla (Modified Titration) 212 treated; 12 months
Any ARIA on MRI	21% (about 1 in 5)	29% (about 3 in 10)
ARIA-E (swelling or fluid)	13% (about 1 in 8)	16% (about 1 in 6)
ARIA-H (small bleeds or iron staining)	17% (about 1 in 6)	25% (1 in 4)
Symptomatic ARIA	3% overall	3% symptomatic ARIA-E; less than 1% symptomatic ARIA-H
Serious ARIA symptoms	0.7%	No single combined rate reported for the current regimen
Brain hemorrhage larger than 1 cm	0.7% (6 of 898)	1% in the 212-person current-regimen study; 0.5% in the larger original-regimen trial

The two studies are not a head-to-head safety comparison

The studies differed in duration, sample size, dosing, MRI schedules, and participant selection. The Kisunla modified-titration regimen study was much smaller. These percentages inform counseling but do not prove that one medicine is safer for a particular patient.

When ARIA tends to occur

- Leqembi: most ARIA-E appeared within the first seven doses; vigilance is especially important during the first 14 weeks.
- Kisunla: most ARIA-E occurred within the first 24 weeks; vigilance is especially important early in treatment.
- ARIA can occur later, can recur, and may be discovered on a scheduled MRI before symptoms appear.

Other factors that can raise risk

- Two APOE ε4 copies (highest established genetic risk).
- Baseline microhemorrhages or superficial siderosis suggesting cerebral amyloid angiopathy.
- A prior brain hemorrhage, extensive small-vessel disease, or other high-risk MRI findings.

3 APOE ε4 and ARIA risk with Leqembi

Detailed genotype breakdown from the CLARITY AD trial plus the current label summary

APOE ε4 is inherited. You may have zero, one, or two copies. The result can also have meaning for relatives, so we discuss the implications of genetic testing with you beforehand.

Current label summary

APOE ε4 result	Participants	Any ARIA	Symptomatic ARIA-E	Serious ARIA
No ε4 copies	278	13%	About 1%	About 1%
One ε4 copy	479	19%	About 2%	About 1%
Two ε4 copies	141	45%	About 9%	3%

Detailed CLARITY AD subgroup rates

APOE ε4 result	ARIA-E	ARIA-H	Symptomatic ARIA-E
No ε4 copies	5.4%	11.9%	1.4%
One ε4 copy	10.9%	14.0%	1.7%
Two ε4 copies	32.6%	39.0%	9.2%

ARIA-E and ARIA-H can occur in the same person, so the percentages should not be added. The tables separate MRI changes from symptoms because most ARIA is typically found before symptoms occur.

Risk with two APOE ε4 copies

In the CLARITY AD trial, about 1 in 3 participants with two ε4 copies developed ARIA-E and about 1 in 11 developed symptomatic ARIA-E. Serious ARIA occurred in 3%. This is a substantially higher risk than with zero or one copy, but it cannot predict whether you will develop ARIA.

4 APOE ε4 and ARIA risk with Kisunla

Results from the current dosing study (TRAILBLAZER-ALZ 6) and the larger earlier trial (TRAILBLAZER-ALZ 2)

TRAILBLAZER-ALZ 6 best estimates ARIA risk with today's Kisunla dosing schedule. The larger TRAILBLAZER-ALZ 2 trial used the earlier schedule but provides more information about symptomatic and serious ARIA risk by APOE status.

Current Kisunla dosing schedule: TRAILBLAZER-ALZ 6

APOE ε4 result	Participants	ARIA-E	ARIA-H	Symptomatic ARIA-E
No ε4 copies	75	13.8%	16.4%	3%
One ε4 copy	115	16.4%	30.8%	4%
Two ε4 copies	21	24.4%	28.6%	Not enough participants to estimate reliably

Larger earlier trial: TRAILBLAZER-ALZ 2

APOE ε4 result	Participants	Any ARIA on MRI	Symptomatic ARIA-E	Serious ARIA
No ε4 copies	255	25%	4%	1%
One ε4 copy	452	36%	7%	2%
Two ε4 copies	143	55%	8%	3%

What two APOE ε4 copies mean for risk

The current-dosing study included too few patients with two APOE ε4 copies to estimate symptomatic ARIA-E reliably. In the larger TRAILBLAZER-ALZ 2 trial, 8% developed symptomatic ARIA-E and 3% developed serious ARIA. Until larger studies of the current dosing schedule are available, we continue to consider patients with two APOE ε4 copies the highest-risk group.

5 Symptoms, emergency care, and medications

When to call us and when to call 911

Call 911 for:

Stroke-like or severe neurologic symptoms

- New weakness or numbness.
- Trouble speaking or understanding.
- New vision loss or inability to walk.
- A seizure, collapse, or major change in alertness.

Other immediately dangerous symptoms

- Sudden severe or rapidly worsening headache.
- Severe breathing difficulty or swelling suggesting an allergic reaction.
- Persistent vomiting with confusion or marked drowsiness.
- Any symptom that feels life-threatening.

Important emergency information:

Do not delay emergency care. Call 911 first. Show the emergency team your medical alert bracelet and tell them when you last received Leqembi or Kisunla. ARIA can cause symptoms that resemble an ischemic stroke, and fatal brain bleeding has occurred when clot-busting treatment was given in the setting of ARIA. The emergency and neurology teams need to weigh the risks and benefits of treatment.

Contact us promptly if you notice new or persistent

- Headache, confusion, unusual sleepiness, dizziness, unsteadiness, vision change, nausea, or difficulty finding words.
- A change that is subtle but clearly different from your usual baseline.
- Symptoms during or after an infusion, including chills, flushing, breathing difficulty, chest discomfort, high or low blood pressure symptoms, or rash.

Aspirin and Other Blood-Thinning Medications

- Do not start or stop aspirin, another antiplatelet medication, or an anticoagulant without first contacting us. We will coordinate with the clinician who prescribed the medication to determine the safest plan.

- Aspirin is an antiplatelet medication. Many patients may continue one antiplatelet medication—most commonly low-dose aspirin and, in selected cases, clopidogrel—after an individualized review. There is less safety information for other antiplatelet medications, and taking two antiplatelet medications at the same time requires additional caution.

- Anticoagulants carry greater concern for serious bleeding in the brain during anti-amyloid treatment. Examples include Eliquis (apixaban), Xarelto (rivaroxaban), Pradaxa (dabigatran), Coumadin (warfarin), Lovenox (enoxaparin), and heparin. In general, Leqembi or Kisunla should not be given while a patient requires therapeutic anticoagulation. If an anticoagulant becomes medically necessary during treatment, contact us promptly because infusions may need to be paused or discontinued.

If your MRI shows ARIA

We may continue, hold, or permanently stop treatment depending on your symptoms, MRI findings, recurrence, and other bleeding risks. We usually repeat MRI to document improvement or stability before treatment resumes. Severe or symptomatic cases may require hospital care and specialist-directed treatment.