

Patients, doctors await FDA decision on experimental Alzheimer's drug

January 6 2023, by Ernie Mundell



Lecanemab: It's an experimental medication that's been shown in trials to

slow cognitive decline in people with Alzheimer's disease.

It's also up for accelerated approval by the U.S. Food and Drug Administration, with a decision expected by Jan. 6.

However, the [drug](#) has also been linked to two deaths from brain bleeds among people who've used it in [trials](#), so safety concerns could threaten any approval.

If approved, the drug—made by Japanese pharmaceutical company Eisai—would follow the controversial drug Aduhelm to become only the second medication ever approved to slow Alzheimer's disease.

Not every patient would stand to benefit from lecanemab, stressed the Cleveland Clinic's [Dr. Babak Tousi](#). He led the portion of the clinical trial that was conducted at the Cleveland Clinic, in Ohio.

"The trial was designed for patients in the earlier stage of Alzheimer's disease, people with mild cognitive impairment or early stage of dementia," Tousi noted. "If this medication gets approval, it will probably be for people who have early stage of disease, with no to minimal assistance needed for activities of daily living."

The results of the 18-month trial, which involved about 1,800 patients, gained wide attention when they were published Dec. 1 in the [New England Journal of Medicine](#), Tousi noted.

In the trial, early-stage Alzheimer's patients who took lecanemab showed a 27% reduction in their mental decline compared to patients in the placebo arm of the trial. The drug's users also showed less evidence of amyloid protein plaques in their brain compared to non-users.

Amyloid buildup in the brain has long been a hallmark of Alzheimer's

disease.

"Lecanemab clearly did what it was designed to do—it removed [amyloid plaque](#)," said Tousi, who heads the Clinical Trials Program at the Cleveland Clinic Center for Brain Health.

"Lecanemab identifies this amyloid and helps the body get rid of it," he explained. "The results demonstrated all the downstream effects we hoped would happen in terms of reduction of biomarkers and less clinical decline on several functional and cognitive measures. So, this difference will likely translate to a longer period of independent living for patients."

Two patient deaths raise questions

Still, the deaths of two patients enrolled in the trial cast a cloud on these hopeful findings. Both died from brain hemorrhages that seem linked to the use of lecanemab.

In one case, a 65-year-old woman with early-stage Alzheimer's died from a massive brain bleed that some researchers link to lecanemab, according to a report published Nov. 27 in [Science Insider](#).

The woman suffered a stroke, as well as a type of brain swelling and bleeding that's been previously seen with such antibodies, the report noted.

ER doctors at Northwestern University Medical Center in Chicago treated the woman with a common but powerful clot-busting drug, tissue-plasminogen activator (t-PA). She immediately had substantial bleeding throughout her brain's outer layer.

"As soon as they put it in her, it was like her body was on fire," her

husband told *Science Insider*. "She was screaming, and it took like eight people to hold her down. It was horrific."

The woman died a few days later, the case report said.

The death follows that of an 80-year-old man who was taking part in lecanemab's phase 3 clinical trial. His death was linked to a possible interaction between the experimental drug and a blood thinner called apixaban (Eliquis).

[Rudolph Castellani](#), a Northwestern neuropathologist who autopsied the woman, determined that she had amyloid deposits surrounding many of her brain's [blood vessels](#).

The woman had been receiving biweekly infusions of lecanemab, which appears to have inflamed and weakened her blood vessels, Castellani said. These vessels then burst when exposed to the clot-buster, something that can happen even in conventional stroke cases.

"It was a one-two punch," Castellani told *Science Insider*. "There's zero doubt in my mind that this is a treatment-caused illness and death. If the patient hadn't been on lecanemab, she would be alive today."

While Eisai declined to comment on the woman's case, the company did issue a [statement](#) saying that "All the available safety information indicates that lecanemab therapy is not associated with an increased risk of death overall or from any specific cause."

The woman might have received either lecanemab or a placebo during the 18-month trial, but she was definitely given the drug during the month preceding her death. She'd opted to receive it as part of an open-label extension of the clinical trial.

Weakened blood vessels

The woman and the man both had widespread cerebral amyloid angiopathy (CAA), a condition in which amyloid deposits gradually replace the smooth muscle of blood vessel walls.

Nearly half of Alzheimer's patients have CAA, and many also suffer from heart ailments that are normally treated with blood thinners, the report noted.

Experts explained to *Science Insider* that in these types of patients, stripping the amyloid away—as drugs like lecanemab are meant to do—could weaken the blood vessels and make them vulnerable to bleeds if exposed to [blood thinners](#) or clot busters.

More details on the woman's case—including autopsy results—were released Wednesday in the [New England Journal of Medicine](#) by doctors at Northwestern Medicine in Chicago. The autopsy confirmed extensive brain bleeding and amyloid deposits within many blood vessels.

The Northwestern team believes that exposure to t-PA triggered burst blood vessels throughout the patient's brain, causing death.

"The extensive number and variation in sizes of the cerebral hemorrhages in this patient would be unusual as a complication of t-PA solely related to cerebrovascular amyloid," they wrote, but prior use of lecanemab may have tipped the balance, triggering the hemorrhages.

In a [journal response](#) to the article Drs. Marwan Sabbagh and Christopher H. van Dyck said they "agree that this case raises important management issues for patients with Alzheimer's disease."

But factors other than the patients' use of lecanemab could have been at

play, they pointed out. In the woman's case, an extended period of very high blood pressure could have been a contributing factor. In the man's case, a drug he was taking to counter atrial fibrillation might have played a role in the hemorrhaging.

Sabbagh and van Dyck also noted that [amyloid deposits](#) within blood vessels have been seen before in people who died after getting t-PA.

Besides the two fatal cases, the clinical trial also showed that 2.8% of participants who took the drug had a symptomatic side effect called ARIA-E, which involves swelling in the brain. ARIA-E was not seen among any participants who got the placebo.

Risks versus benefits

However, for the millions of Americans affected by Alzheimer's, any beneficial drug could be welcome.

The anticipation building around lecanemab follows the controversial June [approval](#) of a similar Alzheimer's drug, Aduhelm, even though studies didn't prove the treatment worked and showed serious safety risks.

After Medicare [limited](#) its coverage of Aduhelm, citing risks and unclear benefit, the expensive drug was essentially sidelined.

Like Aduhelm, lecanemab—given via infusion every two weeks—is a monoclonal antibody that targets a protein, amyloid, that tends to clump in the brains of people with Alzheimer's. Years of research have uncovered precious little evidence that clearing these plaques actually helps with memory and thinking problems. Earlier this month, another anti-amyloid monoclonal antibody, [gantenerumab](#), failed to show any benefit.

For his part, Tousi stressed that lecanemab will not produce a dramatic turnaround in the cognitive health of people with Alzheimer's disease.

"It is not that you take this medication and your memory gets better," he said. "It is a newer concept for many patients. It is not treating the symptoms but it slows down the decline. ... It is a small benefit but is still a benefit. The findings are promising when we don't have any other treatments available."

More information: Visit the U.S. National Institute on Aging for more on [Alzheimer's](#).

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Citation: Patients, doctors await FDA decision on experimental Alzheimer's drug (2023, January 6) retrieved 5 May 2024 from <https://medicalxpress.com/news/2023-01-patients-doctors-await-fda-decision.html>

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