Eli Lilly hopeful of Alzheimer's drug approval after promising results

July 22 2023

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A second Alzheimer's drug proven to slow cognitive decline was a step closer to US approval on Monday after clinical trial results published in a top journal confirmed its efficacy.

Many experts have hailed the developments as major breakthroughs

after years of little progress in the field, although others have urged caution, casting the benefits as modest while noting the high costs and risks of life-threatening side effects.

In an analysis of nearly 1,200 people with the early stages of Alzheimer's disease, the drug called donanemab slowed the progression of symptoms by 35 percent over a period of 18 months compared to placebo, according to a paper in the *Journal of the American Medical Association* (*JAMA*).

This was measured by the people's results on cognitive tests and ability to carry out daily tasks.

The drug—taken as an intravenous injection every four weeks—is made by drugmaker Eli Lilly, which said it expects regulatory action in the United States by the end of the year.

The new paper comes days after the US Food and Drug Administration took a step that made Leqembi, produced by Biogen and Eisai, available on the government-run insurance program for the elderly called Medicare.

Both work by targeting amyloid beta, a protein that impairs cognition when it accumulates in the brain.

"These first-generation drugs are by no means perfect, but represent an important breakthrough," Giles Hardingham, interim director of the UK Dementia Research Institute, said in a statement.

At the same time, however, he said it was important to realize that Alzheimer's is a complex disease, and amyloid beta was just one element in its genesis.

But in an editorial in JAMA that accompanied the new results, Eric Widera of the University of California, San Francisco and colleagues said it was too early to declare the new medicines would be beneficial over the long run.

Donanemab and Leqembi, also known as lecanemab, do not cure Alzheimer's—rather they lead to "slightly less worsening" in patients, they said.

"The modest benefits would likely not be questioned by patients, clinicians, or payers if amyloid antibodies were low risk, inexpensive, and simple to administer. However, they are none of these," the authors wrote.

Even once 80 percent of the costs are offset by Medicare, patients will still need to pay costs totalling thousands of dollars out of pocket.

There were also three deaths in the studies of donanemab and Leqembi that were probably caused by the treatments that lead to brain bleeds.

As the treatments move into real world use, it will be essential to gather more data to find out if they continue to slow cognitive decline beyond 18 months—or if they backfire, given that anti-amyloid treatments also accelerate brain atrophy, according to research.

Moreover, 96 percent of the patients in the donanemab trial were white, while Black and Latino people have far higher rates of Alzheimer's, meaning that key demographics were left understudied.

More information: John R. Sims et al, Donanemab in Early Symptomatic Alzheimer Disease, *JAMA* (2023). DOI: 10.1001/jama.2023.13239 , jamanetwork.com/journals/jama/ … 1001/jama.2023.13239