Eisai to seek FDA approval for lecanemab, one of dozens of drugs in the Alzheimer pipeline

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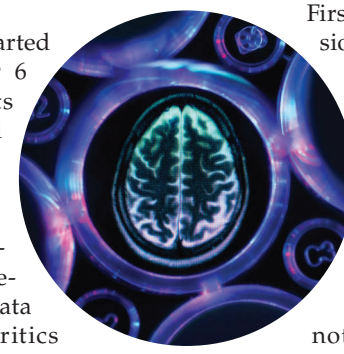
This fall, biotech Biogen and pharmaceutical company Eisai released topline data on their new antiamyloid monoclonal antibody lecanemab. In the confirmatory phase 3 Clarity AD study, a double-blind, placebo-controlled clinical trial that included 1,795 participants with mild cognitive impairment and early Alzheimer disease (AD), the drug slowed cognitive decline by 27% over 18 months compared to placebo.

This drug may represent a second chance for Biogen after the failure of its aducanumab (Aduhelm–Biogen) hit the market last year. Both drugs are antiamyloid monoclonal antibodies, which seem to be where the field's focus currently lies in its efforts to change the course of the disease at an earlier stage.

"I think we are going to see a lot happening in the monoclonal antibodies space," said Kristin Zimmerman, PharmD, associate professor in the department of pharmacotherapy and outcomes science at Virginia Commonwealth University School of Pharmacy. "When it comes to early, prodromal disease, it's mostly biologics—that is, monoclonal antibodies—in the pipeline. So, pharmacists will need to be oriented toward those."



endpoint. The drug started to show effects after 6 months and patients continued to respond to it at 18 months.

While some groups responded, such as Alzheimer's Association in an official statement, to the initial data with enthusiasm, critics argue that the effect on cognitive decline was too small to be meaningful.

"There's some controversy over using the CDR-SB as the primary endpoint. Cognitive assessments like the Alzheimer's Disease Assessment Scale for Cognition are considered the gold standard," Zimmerman said.

"Pharmacy has a role to play in potentially assisting in the screening and med review process."

Lecanemab and other monoclonal antibodies for Alzheimer disease

Like aducanumab, lecanemab is a monoclonal antibody that targets amyloid beta. Patients receive it by I.V. infusion.

In the clinical trial, the drug slowed cognitive decline, based on the Clinical Dementia Rating-Sum of Boxes (CDR-SB) scale, which was the study's primary endpoint. The drug also reduced amyloid levels in the brain as measured by PET scan, the study's secondary

"So some people weren't swayed by the use of this scale and the degree of change in the scale. There's not a lot of agreement on what would be clinically significant change."

Along with the release of its topline data, Eisai announced that it will publish its findings in a peer-reviewed journal and file for traditional FDA approval by the end of March 2023. This regulatory distinction may help ensure the drug earns the Medicare coverage that its predecessor aducanumab did not.

Also in clinical trials is Eli Lilly's donanemab, another amyloid-targeted monoclonal antibody. Researchers published results of a positive phase 2 trial in the *New England Journal of Medicine* last year. Biologics that target tau are currently in the works as well.

I.V. drugs come with access challenges

Pharmacists should be aware of the barriers that come with monoclonal antibody therapies for AD and the role pharmacists might play in helping mitigate them.

First, a shortage of I.V. infusion centers may make it difficult for patients to access these drugs.

"Some drugmakers are looking at subcutaneous formulations, which would help enhance accessibility," Zimmerman said.

Next, Zimmerman notes, the health care workforce is not well-trained to screen patients for mild cognitive impairment and mild dementia, the stages for which these new drugs would be approved. Patients will also need biomarker testing to be eligible for the drugs and ongoing MRI monitoring.

"I can't emphasize these barriers enough," she said. "Pharmacy has a role to play in potentially assisting in the screening and med review process."

Small molecules hold lion's share of drug pipeline

While I.V.-infused monoclonal antibodies seem to garner more attention, small molecule oral medications occupy a much larger proportion of the Alzheimer's drug development pipeline from phase 1 to phase 3 clinical trials, according to a recent review in *Alzheimer's & Dementia: Translational Research & Clinical Interventions.*

Many of these drugs, however, are repurposed drugs, such as metformin and levetiracetam, which pharmacists already know well. Unlike biologics for AD, the focus of many small molecules in development is later stage dementia. ■