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Pharm in Action: New Hopes for Alzheimer's Treatment

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A new drug, Lecanemab, is creating excitement that a treatment for Alzheimer's disease is on the horizon

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Currently, Alzheimer's disease has no cure. This neurodegenerative disease affects 6.5 million Americans age 65 and older, the most common cause of dementia in the US. The onset of Alzheimer's is insidious, starting with vague effects like trouble thinking, slowly worsening social skills, and a growing trouble remembering words. Eventually, however, persons with Alzheimer's disease become unable to carry out the normal tasks of living. The disease progression is often devastating for patients and families alike.

Many companies have tried and failed at developing a drug to treat or stop Alzheimer's disease. Recently, Biogen and Eisai, the makers of Lecanemab, completed their latest clinical trial with a finding of a 27 percent slowing of deterioration in patients receiving the drug twice per month. The results are far from definitive, but more promising than other drugs' results to date.

One of the reasons that this new drug is so interesting is because Alzheimer's disease has defied easy treatment. One of the disease characteristics is the buildup of amyloid plaques – a type of abnormal protein – in the brain. Most earlier drugs have targeted these plaques, but proved no better (and sometimes worse) than a placebo.

The new drug, Lecanemab, takes a direct approach to amyloid plaques. Its name is a clue for how the drug works: the *-mab* identifies it as a monoclonal antibody. Monoclonal antibodies

are molecules produced by specially grown white blood cells, designed to bind to and neutralize a target. Our immune systems produce a broad array of antibodies naturally; a monoclonal antibody drug provides a strong dose of antibodies directed against a target. Monoclonal antibodies are grown in vats of cultivated cells, then extracted and purified to be given as a drug.

Lecanemab works by targeting a very specific type of amyloid protein called amyloid beta. In Alzheimer's disease, amyloid beta proteins build up in the brain and spinal fluid. Over time, the concentration increases, and the proteins stick to nerves and the walls of brain arteries, forming amyloid plaques.

We know that Alzheimer's disease is associated with these plaques, but how to stop them has been a moving target. Some drugs have tried chemically interrupting the process by which floating proteins condense and combine into plaques. Others have tried interrupting the chemical synthesis of the proteins in the first place. The results have been generally poor, making Lecanemab's early results especially interesting.

Lecanemab works by intercepting amyloid beta proteins while they're still floating in circulation. First, the drug is administered via IV. From the bloodstream, it crosses the blood-brain barrier and enters the cerebral spinal fluid (CSF) as well, where high levels of amyloid beta proteins circulate in Alzheimer's disease patients. The Lecanemab molecules bind to the proteins, stopping them from combining and condensing into plaques, while making it easier for the body to recognize and eliminate these monoclonal antibody-amyloid beta complexes.

Given the scope of the problem and the challenge of finding any effective treatment, the "27% improvement" number is a milestone. This is the first, albeit incremental, treatment to have shown efficacy. Hopefully, this milestone represents the first of more incremental

improvements in curing this debilitating and deadly disease. Ultimately, more effective treatments may require a multi-drug solution as seen with HIV/AIDS. The combination of Lecanemab with other novel treatments may have greater success in future trials.

The author has no conflicts to report.