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A New Alzheimer's Drug Offers Hope for Patients and Evidence for New Theories on What Causes the Disease

Alzheimer's disease is a brain disorder that causes deterioration of memory, thinking, and learning abilities; eventually, it can result in the inability to complete basic tasks. Alzheimer's is the leading cause of dementia in older adults, typically occurring around age 60 (Alzheimer's Association, n.d.). While the cause of the disease is not yet fully understood, many evidence-based theories exist, of which the leading one is known as the Amyloid hypothesis.

The Amyloid hypothesis suggests that Alzheimer's is caused by the buildup of amyloid plaques in the brain. These plaques are created when the amyloid-beta protein, which usually plays a role in neural growth and repair (Goodsell, 2006), hardens from a soluble protein into clumps between nerve cells (Alzheimer's Association, n.d.). The hypothesis also postulates that buildup of Tau protein tangles factor into Alzheimer's (Alzheimer's Association, n.d.). While most people do develop some amyloid plaques and tangles as they age, those suffering from Alzheimer's develop many more of them and in a predictable manner (Alzheimer's Association, n.d.).

However, new research from the University of Cincinnati suggests that the increase of amyloid plaques could just be a side effect of the actual cause of Alzheimer's: a decrease of soluble amyloid proteins (University of Cincinnati, 2022). The amyloid-beta protein is usually soluble, and people with the disease have a large decrease of these soluble proteins in their brain (University of Cincinnati, 2022). Researchers studied a subgroup of patients who have a genetic mutation thought to make them more susceptible to amyloid plaque buildup in the brain. They compared this data to a control group of members from the general population and found that, at

a baseline of above 270 picograms/L of soluble amyloid protein, the experimental group showed no difference from the control regardless of the amount of plaque buildup in their brains.

Many pharmaceutical companies have tried to create a drug that helps slow the progression of Alzheimer's and improve quality of life for those living with it, though none have been truly successful. Despite this lack of success, a Tokyo-based pharmaceutical company named Eisai has developed a drug, lecanemab, that has shown favorable results in clinical trials. During lecanemab's phase III trials, it ran for 18 months and slowed mental decline in patients to a statistically significant degree (Prillaman, 2022). The trial was conducted on approximately 1,800 patients living with early-stage Alzheimer's disease in over 12 countries. The drug targets the amyloid plaques in the brain, and patients saw a significant decrease of those plaques. As a result, they also scored, on average, 0.45 points higher on an 18-point Clinical Dementia Rating–Sum of Boxes test compared to the placebo group. Caleb Alexander, an internal-medicine specialist and epidemiologist, called the results "quite promising" while adding that the degree of benefit is quite small (Prillaman, 2022). However, even small benefits could be consequential for those who are fighting Alzheimer's.

The results are also starkly preferable to those of aducanumab, a drug introduced last year, which did not present a clear sign of cognitive aid (Prillaman, 2022). While 20% of patients receiving lecanemab in the trial showed brain scans of abnormal bleeding and swelling, 40% of patients that had been receiving aducanumab showed these abnormalities, which is a striking difference. Lecanemab's lower risk rate and higher success rate could make it a breakthrough drug, while it is still important to continue developing drugs with lower rates of abnormal bleeding and swelling, as well as even higher success rates.

Interestingly, one distinction between lecanemab and other Alzheimer's drugs is it does something the others do not: increase the levels of soluble amyloid-beta proteins in the brain. This shows that the positive results of this trial not only support the Amyloid hypothesis, but also provide evidence that it is not the only source of Alzheimer's disease.

The Food and Drug Administration is currently reviewing lecanemab for "accelerated approval" based on its phase II clinical trials, and should release its decision on January 6th (Prillaman, 2022).

Works Consulted

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