Five on Friday | Musings on Mental Health

Prescription Problems

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Last month, the U.S. Food and Drug Administration approved Biogen's new medication, aducanumab, for the treatment of Alzheimer's Disease.

Photo Credit

Marketed with the brand name, Aduhelm, this is the first medication that targets the fundamental pathophysiology of Alzheimer's disease and the first new treatment approved for Alzheimer's since 2003. With 44 million people worldwide who have Alzheimer's Disease, shouldn't that be good news?

1. Why is aducanumab's approval so controversial? When testing a new drug, the FDA enlists scientific experts to advise on its approval. In the case of aducanumab, ten of the eleven expert panel members voted against approval of aducanumab; the eleventh member abstained. Since the FDA's decision, three members of the advisory panel have resigned. The committee's scientific assessment was that the data did not demonstrate sufficient evidence for the effectiveness of aducanumab. The crux of the controversy is that the FDA overruled the scientific advisory recommendation and proceeded with approval of aducanumab via its accelerated approval process (same as for the COVID-19 vaccines), allowing it to bypass typical requirements.

2. How does aducanumab work? Aducanumab is a monoclonal antibody that targets an amyloid (protein) that clumps into plaques in the brains of people with Alzheimer's disease. Aducanumab aims to attack amyloids

early in the lifecycle of the disease to slow its progression. Many other amyloid-reducing drugs have been tested, and some have also succeeded in reducing amyloid deposits, but none have provided clinical benefit. According to the expert panel and many other scientists, aducanumab is no different.

3. Who is aducanumab designed to serve? Aducanumab is a potential medication for individuals with minimal cognitive impairment, a precursor to dementia, and those who have mild Alzheimer's-related cognitive decline. In the U.S. alone, roughly two million Americans show early signs of Alzheimer's. About 44 million individuals have Alzheimer's Disease globally, so the promise of a medication that could slow down or eliminate the symptoms of this devastating and progressive disease should be cause for joy, but not so fast.

4. What do the data say? Biogen, the pharmaceutical corporation responsible for developing aducanumab, conducted two large Phase III clinical trials: "EMERGE" and "ENGAGE." Phase III clinical trials compare the safety and effectiveness of a new treatment against the current standard treatment. In the EMERGE and ENGAGE studies, participants had mild cognitive impairment and early dementia. The ENGAGE trial showed no benefit. The EMERGE trial, which used higher dosages, was initially reviewed by the FDA with negative results. At the same time, the FDA Office of Neurological Drugs reported positive results, whereas the statisticians' conclusions were negative. Thus, in 2020, the FDA did not approve the drug. However, with longer follow-up and re-analysis, Biogen arrived at a different verdict: a significant benefit was achieved for a subgroup in one arm of the study. The scientific panel was not convinced.

5. What is the rationale for approving aducanumab? Proponents of moving forward claim that approval will herald the arrival of a new, modern treatment era for Alzheimer's, akin to what statins signified for cholesterol management and what AZT meant for HIV treatments. They claim that its implementation will generate further data that will help determine who benefits from this treatment, which will pave the way for other therapeutic interventions. Maybe. It also may be a case of power and commercial interests trumping science. Biogen reports that the yearly maintenance plan per person for the drug (and this is just what Biogen plans to charge) will be $56,000. When we add the costs for monthly infusions of the drug and testing for eligibility and side effects, the total cost will be substantially higher. Some health economists estimate that this single drug could double the overall budget for Medicare.

As we approach the Fourth of July in the US, a day centered on the value of freedom, I find myself troubled by what appears to be a corruption of science driven by commercial opportunity. At the same time, I am reminded of a comment from a family member in Italy who said that one of the things she marvels at is the way in which the U.S. "airs its laundry in the piazza." The intense public debate – with strong supporters and detractors, including a powerful opinion piece entitled, What A Bad Day Science Had by Director of the Einstein-Cardozo Master of Science in Bioethics Dr. Tia Powell – reflects this core cultural value of freedom of speech and public debate in American society. My fervent hope is that this dialogue moves us forward so that science and society win the day.