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Louisville doctor: New FDA approved drug is not the solution for people with Alzheimer's

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There has not been a new treatment for Alzheimer's disease approved in the United States since 2003. This disappointing record is despite intense scientific activity to develop effective therapies.

On June 7, the FDA approved Aducanumab, a monoclonal antibody, for the treatment of the disease. What does this mean for the many patients and families?

In Alzheimer's, there are abnormal protein deposits called amyloid beta (AB) plaques. It has been proposed that removal of the plaques will limit progression of the disease. This idea, called the amyloid cascade hypothesis, is based on the uncommon genetic forms of the illness and does not explain the origins of the more common nongenetic form, which accounts for 99% of cases.

Aducanumab was developed by Biogen to bind to the plaques and remove them from the brain. Two Phase 3 clinical trials demonstrated the effective removal of the plaques, but only modest clinical improvement was seen in one of the trials and not the other.

In November 2020, an FDA panel recommended 10 to 0 that the data on Aducanumab were not sufficient for approval. To the great surprise of the medical community, the FDA approved the antibody on June 7 because of the reduction in AB deposits, not because of an improvement in memory.

The treatment will require infusions and several MRI scans to monitor potentially hazardous side effects seen in 41% of patients. Biogen’s cost will be $56,000 a year.

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This decision by the FDA to approve Aducanumab is highly disturbing for several reasons. First, AB plaques are biomarkers – an indicator of disease, not the disease itself. It already has been shown that removal of the plaques does not provide significant benefit. Second, the high cost of treatment will produce enormous monetary challenges and is not reasonable for a treatment without demonstrated efficacy.

Third, the approval could diminish the search for novel treatments involving other mechanisms of disease. Subjects might hesitate to participate in clinical trials because of the availability of an approved agent. Because of these concerns, three scientists on the FDA advisory panel have resigned in protest.

Alzheimer's causes profound suffering worldwide. It is dangerous to allow our longing for an effective therapy distort our understanding of clinical trials. It is a fundamental principle of medicine that biomarkers cannot be the sole indicator of clinical outcome.

As a physician, I am concerned primarily with my patient’s welfare, not the values of a blood test or neuroimaging outcome. The billions of dollars spent on Aducanumab therapy could be better spent on developing truly effect agents focused on new targets.

I agree with the FDA advisory panel that did not support the approval. The data from the trials are incomplete, contradictory and, critically, do not show improvement in the lives of the subjects.

To use a biomarker such as AB plaque density as a sole outcome measure for a new drug is a serious error. Additionally, the high cost of the therapy is inappropriate and the risks of the therapy are significant.

In my clinical practice, I will counsel patients and families about this newly approved Alzheimer treatment, discussing the risks of this therapy as well as costs and possible benefit. Out of concern for my patient’s welfare, I will be reluctant to prescribe this new therapy.

We need to know what the cause of Alzheimer’s is in the many cases not caused by genes and we need to identify better targets for therapy. I have been caring for patients with Alzheimer’s for the past 44 years and have a profound desire for effective disease modifying therapies. Aducanumab is not the solution.

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