

What we know about aducanumab, the new drug to treat Alzheimer's disease

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Earlier this week, the federal Food and Drug Administration (FDA) [approved the use of the drug aducanumab](#) to treat Alzheimer's disease—making it the first new drug in nearly 20-years to treat the

disease. Aducanumab is the first of a new generation of drugs that target the underlying damage in the brain. Anton Porsteinsson, M.D., is director of the Alzheimer's Disease Care Research and Education Program (AD-CARE) at the University of Rochester Medical Center. He has spent the past 10-plus years as the principal investigator of Biogen's clinical trial for aducanumab at the Medical Center. And in the past year, he was hired as a consultant for Biogen to help with the Biologics License Application for aducanumab and testified before the FDA on the clinical findings of the drug—findings he is hopeful will change how Alzheimer's disease is evaluated and treated. Dr. Porsteinsson is also the William B. and Sheila Konar Professor of Psychiatry, Neurology, Neuroscience, and Medicine at the University of Rochester. We caught up with Dr. Porsteinsson to share his insight about aducanumab and what it means for the disease that afflicts nearly 6 million Americans.

Describe your Alzheimer's research and role in the clinical trials for aducanumab.

For more than a decade, AD-CARE has been involved in studies of humanized monoclonal antibodies that target beta amyloid—a protein thought to play a central contributing role in Alzheimer's disease by accumulating in the brain, disrupting communication between brain cells, and eventually killing those cells. We were involved in one of the two phase three of Biogen's [clinical trials](#) for aducanumab and provided pivotal data in the studies that eventually lead to the FDA's approval.

This approval was not without controversy. Can you explain what happened?

The studies, referred to as ENGAGE and EMERGE were stopped prematurely due to a late-stage interim analysis that suggested the studies

failed based on a futility analysis. After all the data was collected the findings from the studies went in two different directions. One study (ENGAGE) was convincingly negative, and the other (EMERGE) was convincingly positive. Furthermore, limitations were found in the data—this treatment needs to be given with care, over a long period of time to people who meet very particular benchmarks, and has potential side effects that need to be monitored closely, such as swelling of the brain. Yet the clinical end sees hope in this [drug](#) delaying the disease progression in patients who meet those specific requirements necessary to receive the drug when compared to placebo. Currently, the FDA's approval is provisional and is based on aducanumab's ability to lower amyloid propensity. Clinical efficacy needs to be validated with at least another confirmatory controlled study and Biogen has committed to completing that study. Our lab is one of the locations that expects to collect data for this study.

What makes aducanumab different from other drugs currently approved to treat Alzheimer's? How does it work?

This is the first drug approved by the FDA for Alzheimer's disease in 18 years. It is also the first drug that treats the underpinning of the Alzheimer's disease. Other drugs on the market only treat symptoms. Aducanumab instead binds to and removes the beta amyloid plaques—and slows down this process that would eventually lead to widespread destruction of brain cells. In clinical trials, this drug delayed the progression of the disease by about 20 to 40 percent depending on the outcome measure, in the patients who had success with the treatment. Aducanumab is administered intravenously through a monthly infusion, starting with a low dose that increases over the first six months of treatment. It is extremely important that a patient continues these infusions through the highest dose to see the potential benefits, which

are generally not seen for first year of treatment. As it stands, this is a long term treatment with no recommended end.

Who will potentially benefit and what needs to happen before a patient starts receiving this drug?

Before a patient is recommended for this treatment they will undergo a series of tests to determine if they meet the disease criteria that has the best chance of seeing a positive outcome. I would say that the appropriate people are people with [mild cognitive impairment](#) due to Alzheimer's disease, and people with very mild stage Alzheimer's disease that are confirmed to have an elevated amyloid burden, so there's biomarker verification that they have Alzheimer's disease and not another form of dementia or cognitive impairment. That can happen through a PET scan, cerebral spinal fluid or, in the near future, through blood biomarkers. It is also important that patients are otherwise healthy and don't have medical conditions or are on medications that increase their risk of developing and being harmed by amyloid related imaging abnormalities (ARIA). Patient selection needs to be extremely thoughtful and careful.

What will the follow-up care look like for patients who receive the drug?

Patients will need clinical and MRI monitoring for side effects particularly for amyloid related imaging abnormalities edema (ARIA-E) – swelling, or amyloid related imaging abnormalities hemorrhage (ARIA-H) –pinhead size bleeding. These symptoms are directly related to the mechanism of action of the drug. Removing beta amyloid (the plaque) out of the vessel walls in the depth of brain can often leave them temporarily leaky. This is what can cause the increased fluid content in the surrounding tissue that can result in swelling. Sometimes a small

amount of blood can leak out as well. While some patients will have mild to moderate symptoms like headaches, confusion, walking and balance issues, as well as visual disturbances—65 to 75 percent of patients will have what we call clinically silent findings that can only be detected by an MRI. It is why all patients need to be closely monitored and if meaningful ARIA-E and or ARIA-H develops, then the dosing should be withheld to let the ARIA resolve before moving forward with dosing.

How soon could someone who meets the criteria to receive aducanumab start treatment?

That date is still an unknown. We don't know when the drug will be on the market, although Biogen says soon. We also need the right space to properly administer the infusions for these patients. Furthermore, it is unclear how health insurance companies will cover the treatment. It's estimated the medication will cost \$56,000 per year for each patient with significant additional cost associated with the infusion delivery, clinical monitoring and imaging. We need to understand the cost so that we can be transparent with people because there is no benefit for you to go on this treatment for six months and quit. That will only thing expose you to the potential risks. This drug is a long term commitment; the therapeutic benefits arise well down the road.

What does this aducanumab mean for the future of treating Alzheimer's disease?

We are on the forefront of a change in how we evaluate and treat Alzheimer's and it is incredibly exciting. This medication does not cure Alzheimer's disease, it does not stop Alzheimer's [disease](#), but it delays progression in those treated. We need to do this work carefully. The researchers and clinicians at the forefront of this need to be thoughtful and cautious. We need to continue with research and clinical trials to,

first of all, validate that this treatment really is clinically beneficial, and hopefully, then move other drugs that at least comparable in terms of efficacy and comparable in terms of tolerability and side effects. But we hope to leapfrog this treatment and find even better treatments. I hope the approval of this drug reinvigorates research, and changes how we view and use blood biomarkers in a clinical setting—they are less intrusive and more cost effective than a PET scan or cerebral spinal fluid test. Biomarkers also offer a more accurate diagnosis, which is important for patients so they can understand their health and their treatment options.

Provided by University of Rochester Medical Center

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