New Alzheimer's drug: US expert panel greenlights FDA approval for Donanemab

When it comes to Alzheimer's, even a modest benefit is worthwhile, say experts

After much debate on the cost-benefit analysis and whether the new Alzheimer's drug, Donanemab, was worth administering given its modest benefits and side effects, a committee of independent advisers to the US Food and Drug Administration (FDA) voted unanimously that the benefits outweigh the risks.

The drug, made by Eli Lilly, had generated much excitement as it slowed cognitive decline in patients in the early stages of the disease. But given that the effects were modest and there were risks such as swelling and bleeding in the brain, the FDA withheld approval in March. It had then said that it would have to undergo the scrutiny of an independent advisory committee. That panel has now concluded that when it comes to Alzheimer's, even a modest benefit is worthwhile. The FDA usually goes by the committee's recommendations.

What is Donanemab?

Just like its predecessor Lecanemab, Eli Lilly's Donanemab is a monoclonal antibody that targets amyloid beta protein plaques in the brain, one of the defining features of Alzheimer's disease that can be seen on imaging. Similar amyloid-fighting drugs, Leqembi and Biogen, were approved by FDA last year.

What did phase III clinical trials show?

The phase III study shows that Donanemab slows down cognitive decline in early Alzheimer's patients by 35.1 per cent in 76 weeks. The result was based on a study with 1,736 patients, of whom 860 received the infusion every four weeks till the amyloid beta plaque cleared. "This 35 per cent less decline was measured by testing memory and motor skills. This translates into small daily activities like talking to another person. Though the therapy slows down the progression of the disease, it does not ultimately treat the disease," said Dr Pravat Mandal, senior researcher from the National Brain Research Centre.

What about side effects?

According to studies, Donanemab may result in slightly higher adverse events than its predecessor Lecanemab. Other than infusion-related reactions, the main adverse effect with drugs that clear out amyloid beta proteins is amyloid-related imaging abnormalities (ARIA) such as swelling or bleeding in the brain. Most of this is asymptomatic. The study showed that 24 per cent participants given Donanemab had ARIA involving brain swelling and 19.7 per cent had ARIA involving brain bleeds. Three treatment-related deaths were reported in the study. Many experts had then still preferred Donanemab as the infusion needs to be given every four weeks instead of every two weeks with Lecanemab.

Why is there a need to focus on other modalities?

"Alzheimer's disease has multiple modalities and we would need various therapies. While the amyloid beta protein therapy has been in focus, there is a need to investigate other targets as well," said Dr Mandal, whose team is investigating the impact of iron build-up and oxidative stress in the brain as a result of declining levels of an antioxidant called glutathione.

What are cost challenges?

An editorial in the journal JAMA had argued that there was a simultaneous need for validated tools and expertise at the primary care level to grade the disease as the most significant impact of Donanemab was felt in the early stages. This is costly.

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