New Alzheimer's drug: What you need to know about donanemab's promising trial results

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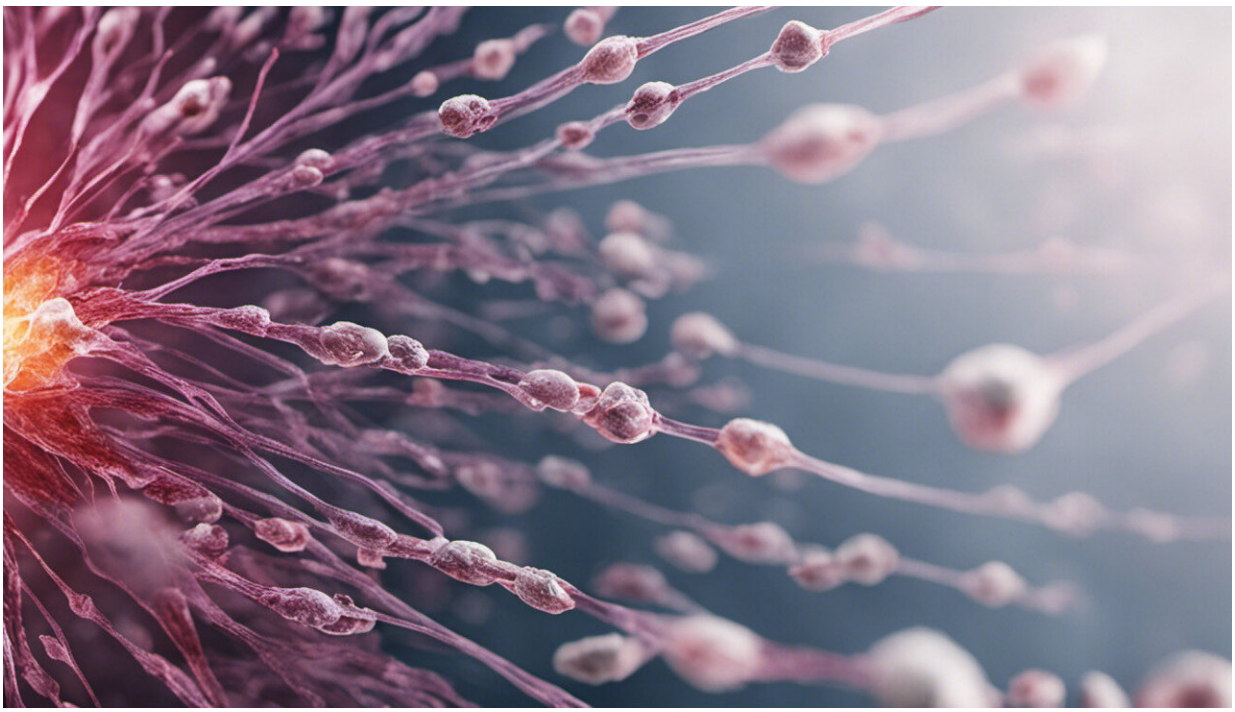

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American pharmaceutical company Eli Lilly announced last week that it had seen encouraging clinical trial results of its new Alzheimer's medication. According to the company, their experimental drug, donanemab, was shown in a late-stage trial to slow cognitive decline by

35%. While these results do sound promising, the full data is not yet released, so there's still a lot we don't know.

Donanemab works by targeting a common hallmark of Alzheimer's disease in the brain: amyloid plaques.

Beta-amyloid is a protein which plays an important role in brain function for everyone. But in patients with Alzheimer's disease, beta-amyloid turns toxic—clumping together and disrupting the connection between brain cells and their function. This leads to cognitive issues such as memory loss.

Donanemab uses the body's immune system system to target these amyloid plaques and remove them from the brain, and while doing so it also manages to reduce the disease-related decline. But what's most significant about this new drug is that it only binds to harmful, established plaques, leaving other forms of beta-amyloid alone.

The trial was conducted in 1,182 people who had early symptoms of Alzheimer's disease and detectable plaques in their brains. Half of the participants received an initial 700mg of donanemab intravenously every four weeks for the first three doses, then 1400mg every four weeks thereafter. The other half of the participants received a placebo treatment.

The duration of each participant's treatment was determined by measuring the plaques in their brains. They stopped treatment only when the plaques in their brain were considered as cleared. Just over half of the participants completed their course of treatment after one year. A further 20% of participants completed treatment after 18 months—meaning that the drug was able to achieve a certain level of plaque clearance for 72% of the participants given donanemab.

Nearly half of the participants who took donanemab showed no signs of an increase in the severity of their disease after one year. In comparison, this was true for only 29% of the placebo group. Importantly, donanemab was also shown to slow down clinical and functional decline by 35% in all cases of those who took the full course of donanemab, when compared to the placebo group.

It was also shown that, compared to the placebo group, participants who took the drug had 40% less decline in their ability to perform daily activities at 18 months, alongside a 39% lower risk of progressing to the next stage of the disease.

The researchers then focused further analysis on an additional 552 patients who had high levels of tau in their brains (a small protein which is typically used as a marker of Alzheimer's disease progression and severity). They found that, when the data was combined with participants who had intermediate tau levels, cognitive decline was slowed by 22%, compared to 35% for the initial study cohort.

However, the trial also showed the drug had concerning side effects. For example, around 24% of participants experienced brain swelling, while 31% experienced microhaemorrhages. These side effects were dangerous in around 1.6% of cases, leading to three deaths.

How it measures up

Overall, these results do sound encouraging. But it's important to note that the full results of the phase 3 trial for donanemab have yet to be published, so it's best to wait until then in order to understand more about this drug.

Donanemab isn't the first amyloid-targeting drug to be developed. Two other drugs that work using a similar mechanism have been approved for

use in the past couple of years. But both of these have had somewhat different results compared to donanemab.

The first drug, called aducanumab, did lead to reduction of plaques in the brain. But there was controversy when it came to its trial results, in that the drug's effectiveness only became significant when certain sub-groups of patients were excluded (or included) from the analysis—such as patients who dropped out. The drug went on to be approved, despite the fact that its clinical benefit might be limited.

The other drug, lecanemab, which was approved for use by the US Food and Drug Administration earlier this year, was shown to reduce both plaques and disease-related decline in early Alzheimer's disease.

Participants in the lecanemab trial had a 27% slower rate of cognitive decline after 18 months of treatment. The drug was also shown to slow decline in a measure of daily living by 37% after treatment compared to the placebo group. But while lecanemab had relatively worse results compared to donanemab, it also had a lower proportion of adverse incidents.

Although donanemab's results may be promising for anyone who's been diagnosed with Alzheimer's, or who may be at risk, there's still a lot researchers don't know—such as why donanemab seems to work differently in different people. There's also no data currently showing which patients may most benefit from this treatment. The only exception to this is data showing patients with less severe disease (as indicated by tau levels and symptoms) benefited more than those with more severe disease. This suggests donanemab may work best when administered to patients who have amyloid plaques early on.

We also have no way of knowing yet which patients are more at risk for developing dangerous side effects, nor whether using donanemab in

patients with no symptoms, but established plaques, acts in a preventative way. Lastly, we also don't know whether or when plaques may reappear, or if these effects are permanent.

Further studies will need to focus on investigating these unknowns, alongside looking at what makes this treatment successful. Nevertheless, the results of this trial make it clear that early intervention and targeting the right brain changes at the right time is key when it comes to Alzheimer's disease. Indeed, perhaps combined with screening for Alzheimer's risk biomarkers, new medications may allow scientists to stop the disease before it starts.

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