New Experimental Drug Signficantly Slows Alzheimer's Disease

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Donanemab is the third in a class of monoclonal antibody drugs that slow the cognitive and functional decline associated with Alzheimer's disease. Does this new, improved version of the medication mean that we are close to curing Alzheimer's disease? We can safely say that donanemab leaves us optimistic that we now have promising treatments for early-stage Alzheimer's disease.

Key takeaways:

- Donanemab and other drugs in its class do not cure Alzheimer's disease, but it does significantly slow the decline of memory loss, thinking, and the ability to engage in daily living.
- Donanemab is a monoclonal antibody that creates an immune system response, targeting amyloid plaque between nerve cells in the brain.
- None of the medications in the class of monoclonal antibodies can be used to prevent Alzheimer's disease.
- There are significant potential side effects, such as brain swelling and mini-brain hemorrhages.

Donanemab and Alzheimer's disease

On May 3, 2023, it was announced that donanemab, a new monoclonal antibody, decreased mental decline by 35% in a clinical trial of 1,736 people with early Alzheimer's disease. This rate was similar to a 2022 FDA-approved monoclonal antibody, lecanemab, which slowed a decline in memory and thinking by 27%.

Alzheimer's & monoclonal antibody therapy

The first case of Alzheimer's Disease was diagnosed in 1906. Since then, it has become the seventh leading cause of death. It affects more than six million Americans today. The cost of care for those living with Alzheimer's was $321 billion in 2022 due to the significant toll the disease takes on an individual's ability to think and handle self-care activities like grooming, taking medication, toileting, and dressing.

Alzheimer's disease often begins to develop 10 or more years before symptoms show. Therefore, the National Institute on Aging and the Alzheimer's Association created guidelines to diagnose Alzheimer's disease. For instance, three biomarkers must be present for a definitive diagnosis to be made:

- **Tau tangles.** Abnormal proteins that twist inside brain cells and interfere with

communication and the transportation of nutrients.

- **Amyloid plaques (plaques).** Proteins that clump between nerve cells, causing them to die.
- **Neurodegeneration.** Death of nerve cells in the brain.

These proteins, plaques and tangles, build up over years and trigger an inflammatory response that destroys brain cells. Donanemab and two earlier drugs, lecanemab and aducanumab, are special antibodies engineered in the laboratory that trigger an immune system attack on the plaques that clump between nerve cells in the brain and destroy them. Destruction of the plaques slows the progression of Alzheimer's disease, giving people more time to function independently.

Medication benefits

The donanemab study is promising, with the strongest results to date. In addition to removing a substantial amount of the plaque clumped between nerve cells in the brain, donanemab also slows the deposits of tau in brain nerve cells. With the removal of these destructive proteins:

- 47% of study participants showed no additional mental decline after one year of treatment.
- 40% of study participants had less decline after 18 months in their ability to handle

things like finances, daily care activities, and driving.

Further studies are needed to learn how long people stay in "remission" once the monoclonal antibody medication substantially removes the amyloid plaques and decreases the amount of tau. investigation.

Side effects

Donanemab is administered intravenously once every four weeks. Most side effects are minor, including:

- Nausea
- Urinary tract infection
- Vomiting
- Anxiety
- Diarrhea

As with the other two medications in this group of monoclonal antibodies, the most serious side effects of donanemab were:

- Brain swelling
- Mini-brain bleeds

However, most cases of brain swelling or brain bleeds were mild to moderate and resolved on their own or were responsive to treatment. Researchers believe that all three medications, which are manufactured antibodies, weaken the blood vessels in the brain as they attack the plaques. Three deaths were connected to these side effects in the brain in a donanemab study.

Furthermore, mini hemorrhages could also be more pronounced in those who take anticoagulants. It is likely that this group of medications would be contraindicated for those taking blood thinners.

Medicare denies coverage

With monoclonal antibody medications potentially changing the trajectory of Alzheimer's disease, why has the Centers for Medicare and Medicaid (CMS) issued a National Coverage Determination (NCD) denying coverage for this group of medications, more specifically, lecanemab and aducanumab, which already have FDA accelerated approval? This NCD will apply to donanemab once it receives FDA approval.

The annual cost of these medications is approximately $26,000 per year or more, which puts them out of reach for the average person.

The reasons cited for CMS' denial of coverage include the potentially serious side effects of the medications, such as brain swelling and mini-brain hemorrhages. The Alzheimer's Association has been advocating for CMS to review new evidence, especially that produced by the donanemab study, which shows significant life-changing benefits for those with early Alzheimer's disease. Slowing the progression of a fatal illness and preserving mental and functional independence for a longer period should outweigh CMS' concerns

regarding potential side effects, most of which resolve or can be treated.

Donanemab, and to a lesser extent, the other two monoclonal antibody medications, promises to extend the ability of those with early Alzheimer's disease to participate fully in and enjoy their daily lives. Slowing the progression of the disease will extend lives and reduce the costs of care caused by mental and functional decline. Full results of the donanemab study will be presented at the Alzheimer's Association International Conference in July 2023. It will be an opportunity for CMS to re-evaluate its coverage decision for monoclonal antibody therapy.

Resources:

1. Association of Amyloid Reduction After Donanemab Treatment with Tau Pathology and Clinical Outcomes The TRAILBLAZER-ALZ Randomized Clinical Trial.
2. Alzheimer's drug donanemab: what promising trial means for treatments.
3. Alzheimer's Association Statement on Donanemab Phase 3 Topline Data Release.
4. Medicare Coverage Policy for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease.
