

Aducanumab (Aduhelm™) Information

What is aducanumab (Aduhelm™)?

Aducanumab (brand name Aduhelm™) is a drug that was recently approved by the Food and Drug Administration (FDA) for the treatment of Alzheimer's disease.

How does aducanumab work?

Aducanumab is an antibody directed at the amyloid protein that builds up abnormally as plaques in the brain when someone has Alzheimer's disease. By binding to amyloid, aducanumab allows the immune system to remove the amyloid buildup.

How is it given?

Aducanumab is given as an infusion (through a vein) every 4 weeks. The dose is based on the patient's weight (10 milligrams/kilogram).

How can you tell if it is removing amyloid from the brain?

In research studies, specialized brain scans called amyloid Positron Emission Tomography (PET) scans were done before and after treatment with aducanumab. These scans showed that treatment with aducanumab led to removal of brain amyloid.

Does removing brain amyloid help the symptoms of Alzheimer's disease?

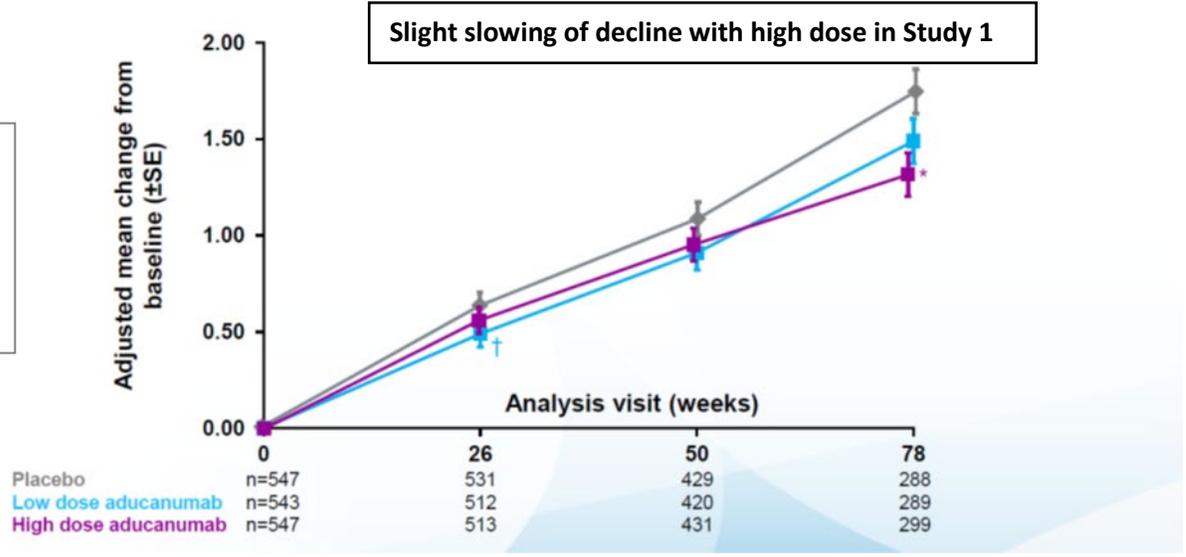
Possibly. Two large studies looked at the potential benefit of treatment with aducanumab in persons with mild symptoms of Alzheimer's disease. These studies were stopped earlier than planned due to lack of anticipated benefit. The available data were reviewed by looking at the change in Alzheimer's symptoms in persons treated with aducanumab compared to persons receiving an inactive substance (placebo). Study 1 showed less decline in persons receiving a high dose of aducanumab (10 mg/kg) compared to persons receiving the placebo. Study 2 did not show a difference between aducanumab and placebo.

What does "less decline" in Study 1 mean?

This is hard to describe because the Alzheimer's disease symptoms were measured by questionnaires and interviews that are used primarily in research rather than at a clinic visit. For the main measure of symptoms, persons receiving the high dose (10 mg/kg) of aducanumab had symptoms at 18 months that were similar to the expected symptoms of the placebo group at 14 months. In other words, decline was slowed by about 4 months with aducanumab, but both groups still got worse. Study 2 did not show a difference in the decline between aducanumab and placebo.

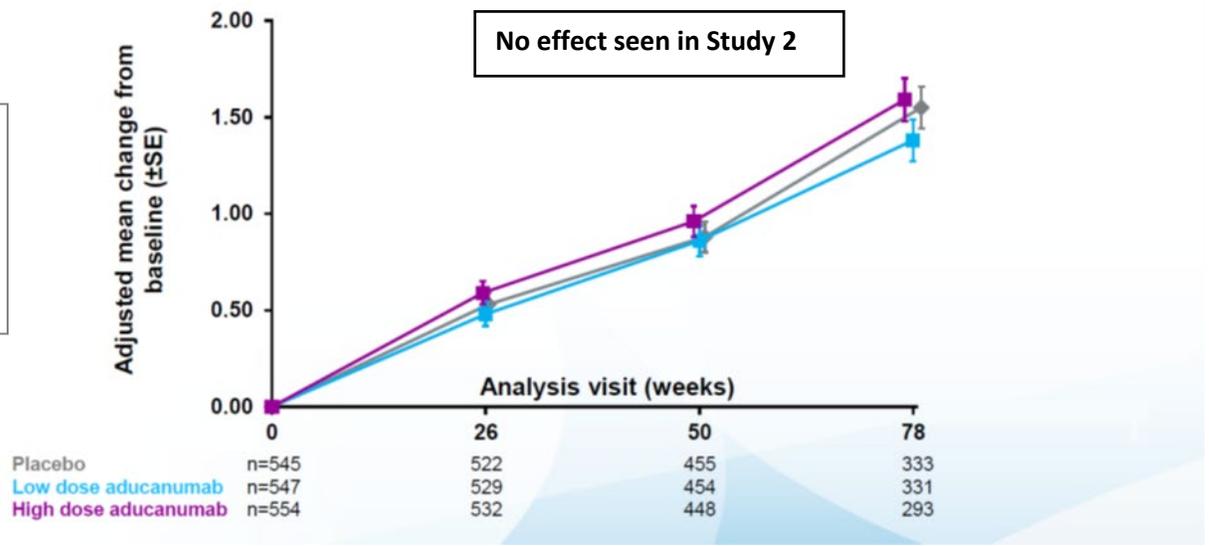
EMERGE: Longitudinal change from baseline in CDR-SB

Higher number indicates more decline



ENGAGE: Longitudinal change from baseline in CDR-SB

Higher number indicates more decline



How do we know if aducanumab is helpful since Study 1 and Study 2 had different results?

We don't. The FDA approved aducanumab as a drug to reduce brain amyloid and is requiring an additional study to determine if there is a clinical benefit. The FDA approval allows aducanumab to be used while awaiting this additional study, which will likely not be complete for many years.

Does aducanumab have side effects?

Yes. Aducanumab can have side effects, including Amyloid Related Imaging Abnormalities (ARIA). ARIA is most commonly seen as temporary swelling in areas of the brain. Some people may also have small spots of bleeding in or on the surface of the brain with the swelling. In Studies 1 and 2, ARIA was observed in 41% of patients in the aducanumab 10 mg/kg group compared to 10% of patients in the placebo group. Although most people with ARIA do not have symptoms, some people (24 % of those with ARIA in the aducanumab group and 5% of those with ARIA in the placebo group) do have symptoms, such as:

- o headache
- o confusion
- o dizziness
- o vision changes
- o nausea

Brain Magnetic Resonance Imaging (MRI) scans are done before and during treatment to look for ARIA and to determine if treatment with aducanumab needs to be stopped temporarily or permanently. ARIA brain swelling and any associated symptoms usually resolve over time (months).

Serious allergic reactions (swelling of the face, lips, mouth, or tongue and hives) can occur during aducanumab infusion, but were rare in Studies 1 and 2.

Are certain persons at higher risk of side effects?

Yes. Individuals who have a type of the apolipoprotein E gene known as E4 have approximately twice the risk of ARIA brain swelling compared to persons who do not have this gene type. Genetic testing can be done to determine if someone has the E4 type. This testing may not be covered by insurance.

Could aducanumab slow decline in anyone with Alzheimer's disease?

Aducanumab has only been studied in persons with early symptoms of Alzheimer's disease, such as individuals with memory loss who are still able to function independently or with minimal assistance. The effects of aducanumab in persons with later symptoms of Alzheimer's disease are not known, but there are reasons to believe that there could be greater risks and less potential benefit.

Is a clinical diagnosis of Alzheimer's disease accurate enough to know that someone has amyloid buildup in the brain?

No. A clinical diagnosis of Alzheimer's disease is not 100% accurate. Other conditions can cause similar symptoms but do not have the amyloid buildup that occurs with Alzheimer's disease. Aducanumab is not an appropriate treatment if there is no buildup of amyloid.

Can someone with suspected Alzheimer’s disease get a PET scan to determine if they have amyloid buildup?

A PET scan can be performed to detect brain amyloid buildup. However, an amyloid PET scan is not currently covered by insurance, though this could change now that a drug targeting amyloid is available.

Is aducanumab useful in persons with other types of dementia, such as Lewy Body Dementia or vascular dementia?

Lewy Body Dementia may or may not have brain amyloid buildup. However, aducanumab has not been studied in persons with Lewy Body Dementia to know if it is helpful or safe. Therefore, aducanumab is not recommended for Lewy Body Dementia, even if someone with Lewy Body Dementia has evidence of brain amyloid buildup. Aducanumab is not recommended for vascular dementia or other non-Alzheimer’s dementias.

Based on the available information, who should receive aducanumab?

The most appropriate person for aducanumab treatment is someone who is medically similar to the patients in the aducanumab studies and who understands the potential risks and uncertainty about clinical benefit.

Who was able to enroll in the main aducanumab studies?

Patients in aducanumab studies 1 and 2 were age 50-85 and had:

Mild symptoms of Alzheimer’s disease (based on several tests of thinking and daily function, including an MMSE of 24-30):

An amyloid Positron Emission Tomography (PET) scan showing evidence of amyloid buildup

And could not have:

Any medical or neurological condition other than Alzheimer's Disease that might be a contributing reason for thinking difficulties

A stroke or Transient Ischemic Attack (TIA) or unexplained loss of consciousness in the past year

A significant, unstable psychiatric illness in the past 6 months

Significant heart disease in the past year

Impaired kidney or liver function

Human immunodeficiency virus (HIV) infection

A significant illness or infection in the past 30 days

Significant brain vascular disease or bleeding disorder

Any contraindications to brain MRI or PET scans

Alcohol or substance abuse in past 1 year

Treatment with blood thinners (except for aspirin)

For patients who choose to receive aducanumab, how long should it be continued?

The duration of treatment is unknown. The main aducanumab studies used a treatment period of 18 months.

Is aducanumab covered by insurance?

Insurers are in the process of determining if they will cover aducanumab and if so, for which individuals.

What is the cost of aducanumab without insurance?

The anticipated cost for aducanumab (the drug only, not including the costs of infusion, brain scans, examinations, and other monitoring) is \$56,000 per year.

Prepared by the University of Michigan Cognitive Disorders Clinic