Alzheimer’s Disease Treatment Clinic: Genetic Testing

The Alzheimer’s Disease Treatment Clinic is designed to support patients eligible for new medications such as lecanemab, approved by the U.S. Food and Drug Administration in 2023. New therapies like lecanemab are given through IV infusions to treat the presence of a protein in your brain called amyloid.

As part of your evaluation in the Alzheimer’s Disease Treatment Clinic, it is recommended that you have genetic testing. The genetic test will look for the apolipoprotein E gene, also called the APOE gene. Results from the genetic test may affect how likely you are to experience benefits and side effects from treatment.

FORMS OF APOE
Everyone has two copies of the APOE gene. Each of your biological parents gives you one copy. Each copy of APOE can have 3 different forms, known as ε2, ε3, or ε4.

• ε2: This is the least common form of the gene. The ε2 form may modestly protect against risk of developing Alzheimer’s disease.

• ε3: This is the most common form of the gene. There is no increased risk between the ε3 form and risk of Alzheimer’s disease.

• ε4: This form is found in approximately 25% of people. People with one copy of the ε4 form have a higher risk of developing Alzheimer’s disease. People with two copies of the ε4 form of the APOE gene have an even higher risk of developing Alzheimer’s disease.

The APOE gene is one of many factors that affect the risk of developing Alzheimer’s disease. Lifestyle and the environment are other factors that affect risk. We are still learning about these and other risk factors.

An APOE result cannot predict for sure whether a person will – or won’t – develop dementia. Many people with the ε4 form of APOE never develop Alzheimer’s disease. Others develop Alzheimer’s disease or other causes of dementia without having the ε4 form of APOE.

CONSIDERING THE BENEFITS AND RISKS OF TREATMENT IN RELATION TO THE APOE GENE
Treatment that removes amyloid from your brain has risks. One risk is brain swelling, also called edema. Another risk is brain bleeding. These risks are known as ARIA, or amyloid-related imaging abnormalities. In the clinical trial for lecanemab, the risk of ARIA was higher in patients who had one copy of the ε4 form of APOE. The risk was much higher in patients who had two copies of the ε4 form of APOE.

Some data but not all also suggested that patients who had the ε4 form of APOE (especially those with two copies of the ε4 form) may be less likely to benefit from treatment.

TESTING FOR APOE IN THE ALZHEIMER’S DISEASE TREATMENT CLINIC
It is strongly recommended that all patients considering treatment with lecanemab or other similar drugs be tested for the APOE gene in order to determine the risks and benefits of treatment.

This genetic test is completed through a blood draw and results will be shared with you to help decide whether treatment is the best fit for you. The cost of this test may or may not be covered by your insurance.

If it is determined very early in the course of your evaluation that you are not a candidate for lecanemab or similar drugs, APOE gene testing may be cancelled.

RISKS OF APOE TESTING
Genetic testing may affect you and your loved ones beyond your treatment plan. If you are found to have at least one copy of the ε4 form of the APOE gene, your children, siblings, parents, and possibly later generations of your family would be considered at risk of having the ε4 form of the APOE gene themselves. Knowing your APOE result might lead to anxiety about risk for your family members, or might affect relationships between you and your loved ones.

Also, it is possible that results of APOE testing could affect your eligibility and/or premiums for life, disability, or long-term care insurance.

Currently, APOE testing is not recommended in clinical care outside of the context of treatment decisions (related to lecanemab and similar drugs) for patients with early symptomatic Alzheimer’s disease.

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