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IVD Kits - articles

ApoE Genetic testing – a tool to prevent side effects during Lecanemab/Leqembi® treatment

What the Lecanemab actually is?

Lecanemab belongs to the antibody-based treatment approach as might be easily derived from its name Lecanemab where specifically the mab end cap refers to a monoclonal antibody. Lecanemab is registered commercially as **Leqembi®** and it has been approved by the FDA (Food and Drug Administration) in an accelerated approval pathway in January 2023 however this status changed in the summer of this year when the FDA converted the **Leqembi®** to traditional approval [1], [2].

What is the Leqembi® used for?

Leqembi® has proved its clinical benefit in reducing the amyloid plaques that occur in the brain of affected patients with **Alzheimer's disease** [3]. A clinical study called **Study 301** was Leqembi® administered to patients with mild cognitive impairment or mild dementia stages of the disease after confirmation of amyloid beta pathology presence [1].

How are the amyloid plaques formed?

Amyloid plaques belong to the most important diagnostic proof of Alzheimer's disease development. These plaques are formed due to the accumulation of soluble β-amyloid peptides [4] which then aggregate to an insoluble form of amyloid fibrils or even plaques [5].

Are there any side effects associated with Leqembi®?

As Leqembi® is by its structure a monoclonal body it naturally binds to amyloid plaques in the brain thus the side effects are associated with headaches. A very specific side effect known as **ARIA** (amyloid-related imaging abnormalities) has been observed as in other antibody-based treatments targeting β-amyloid with no significantly higher incidence [3], [6]. **ARIA** is not necessarily accompanied by the presence of side effects such as headache, dizziness or nausea but during the imaging studies swelling spots have been observed. Rarely, the life-threatening brain oedema or intra-cerebral haemorrhages might occur. However, these finding occurs most frequently at the beginning of the Leqembi® administration and resolve months later [1], [3]. Besides, patients under anticoagulant treatment should be carefully monitored due to the higher probability of intra-cerebral haemorrhage development in such patients.

Why the genetic testing might be useful?

Before the administration of Leqembi, the prescribing information states that testing for the APOE ε4 allele is beneficial for the determination of potential **ARIA-associated risks** [1]. Homozygots bearing the APOE ε4 allele have in higher incidence of development of ARIA in comparison to heterozygots and noncarriers [1], [7]–[9].

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What is the APOE ε4?

Gene APOE is responsible for encoding the production of a protein called **Apoliproprotein E**. This gene naturally occurs in humans in three alleles: ε2, ε3, and ε4 [4], [5]. All three alleles produce **Apolipoprotein E**, which plays a crucial role in lipid metabolism as well as in β-amyloid binding. Besides, the APOE gene has been observed as an important risk factor for Alzheimer's disease, especially the allele ε4 associated with sporadic and early onset Alzheimer's disease [4], [5], [10]–[12]. On the other hand, the allele ε2 is considered more protective against the disease onset. Third, the ε3 allele is the most common and has a neutral effect on disease onset [4], [5], [10].

How the allele APOE ε4 can be detected?

Genetic testing is the field employing various methods. One of the most suitable, fast, precise and reproducible methods is PCR (Polymerase Chain Reaction). GENERI BIOTECH offers a CE-marked in vitro diagnostic kit **gb GENETIC APOE** suitable for implementation in any certified diagnostic laboratory or healthcare provider facility. This kit is designed as a ready-to-use assay suitable for the determination of ε2, ε3, and ε4 alleles in patient samples by using any PCR cycler with FAM and HEX channels (see more about validated cyclers). The final output of the analysis is a determination of wild-type, mutant or heterozygote genotype based on the alleles present in the sample.

GENERI BIOTECH has successfully passed the IVDR certification process and is ready to place on the market IVDR compliant kits from spring 2024.

Literature:

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More info on website:
www.generi-biotech.com/products/gb-genetic-apoe
www.generi-biotech.com/wp-content/uploads/2023/10/075F011_Validated_cyclers_www.pdf

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