

Role of Lecanemab in Early Alzheimers Disease

Dr. Shaktibala Dutta¹, Dr. Jyotsna Sharma², Dr. Vaishali Lote³,
Dr. Isha Ramesh⁴

¹Professor and HOD, Department of Pharmacology, Santosh Medical College, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

²Professor, Department of Pharmacology, Santosh Medical College, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

³Assistant Professor, Department of Pharmacology, Santosh Medical College, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

⁴M.D Student, Department of Pharmacology, Santosh Medical College, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

ABSTRACT:

Alzheimer's disease is a slow and progressive neurodegenerative disorder resulting from the accumulation of amyloid beta protein around neurons resulting in progressive loss of memory and disordered cognitive functions. We reviewed multiple previous studies on Lecanemab and observed that phase 3 clinical trials showed the potential of the drug Lecanemab in the treatment of Alzheimer's disease. Lecanemab targets amyloid beta and reduces its accumulation around neurons resulting in slowing down the progression of the disease. But this drug is also related to its adverse events so longer studies needed to determine its safety and efficacy.

INTRODUCTION:

Alzheimer's disease (AD) was on the name of German psychiatrist Alois Alzheimer [1]. Alzheimer's disease (AD) is the most prevalent form of dementia which does not have any previous cause such as stroke, brain trauma, or alcohol toxicity. It is a neurodegenerative disorder and it causes brain cell degeneration. It is slow and progressive in nature. It is characterized by the accumulation of the abnormal amount of amyloid beta extracellular as amyloid plaques and intra cellularly as a neuro fibrillary tangle in the affected area of the brain and affects neuronal functioning which results in progressive loss of brain function [2]. The cardinal features of AD are progressive loss of memory and disordered cognitive functions with short-term memory loss that usually precedes long-term memory loss. Both genetics and environmental factor plays role in AD. Few cases are due to dominant genetic mutations [3], but widely, AD is sporadic and has not only a single genetic cause. It is believed that environmental and metabolic risk factors like diabetes, CVA, poor diet, head trauma, and stress are related to an increased risk of dementia.

Current Treatment of Alzheimer's disease

Alzheimer's disease can't be cured but available treatment methods can slow down the dementia symptoms and decrease incidence of behavioral problems.

Food and Drug Administration (FDA) has approved four drugs from two drug classes to treat patient's symptoms suffering from Alzheimer's disease. These two drugs classes are

1. Cholinesterase inhibitors
2. NMDA antagonist

Cholinesterase inhibitors. This drug is approved to treat mild to moderate symptoms of Alzheimer's disease (AD). It includes:

- Donepezil (FDA-approved to treat moderate to severe symptoms)
- Rivastigmine
- Galantamine

Mechanism of action of CHOLINESTERASE INHIBITORS - Acetylcholine is a chemical that helps nerve cell to communicate. Reduced levels of acetylcholine is believed to cause symptoms of AD and acetylcholine esterase enzyme destroy acetylcholine in the brain. Cholinesterase inhibitors blocks this enzyme and hence concentration of acetylcholine increases in brain as a result of which there is improve in symptoms of AD. Common Side effects of this class of drugs are GI upset (nausea, diarrhoea and vomiting). Few people may experience loss of appetite, insomnia, bad dreams, etc.

NMDA antagonist : Used to treat moderate to severe symptoms of Alzheimer's disease. It include:

1. Memantine

MOA- NMDA receptors on nerve cells are activated by glutamate neurotransmitter. Memantine blocks this glutamate keeping the cells healthier. It can be taken alone or it can also be taken in combination taken with cholinesterase inhibitor.

Drugs for Managing behavioral changes :

1. Antidepressant drugs:- It is used to treat various symptoms like anxiety, restlessness, aggression and depression.
2. Anti-anxiety drugs:- it may used to treat agitation.
3. Anticonvulsants:- Are also used to treat aggression.
4. Antipsychotics:- It can be used to treat symptoms like paranoia, hallucinations, and agitation.

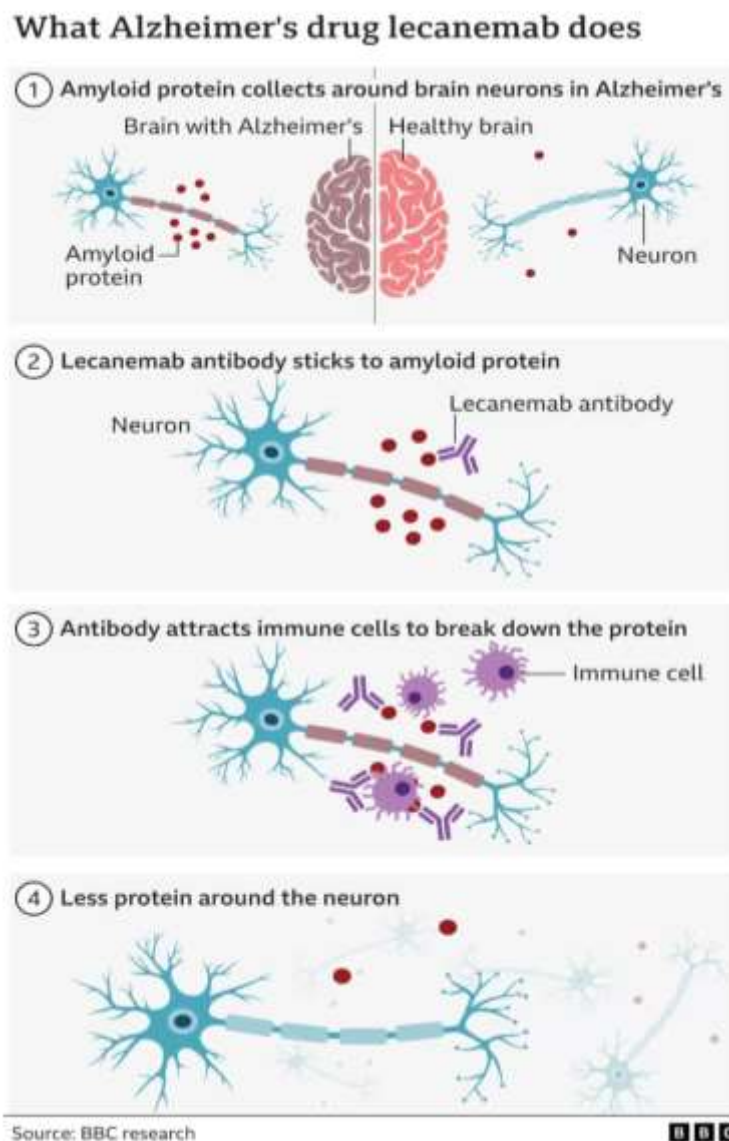
Side effects of these drugs are confusion, dizziness this lead to increase risk of falls. Therefore these drugs are used for short periods, when behavioral problems are severe, and after other therapies have been tried before.

Newer Drug for Alzheimer's disease

Lecanemab is a humanized monoclonal antibody that targets amyloid beta and currently, it shows potential to treat AD in phase III clinical trials [4].

Mechanism of action of lecanemab

Lecanemab is a humanized IgG1 monoclonal antibody. It binds amyloid beta ($A\beta$) soluble protofibrils and reduces the accumulation of amyloid beta around the neurons resulting in slowing down the destruction of the brain.



METHODS:

In this study, we reviewed previously conducted studies for lecanemab, its safety, and its efficacy. A study was conducted for a period of 18 months. The study was a double-blind, multicentre phase 3 trial. The participants were of 50yrs to 90yrs of age group diagnosed with early AD and the diagnosis was confirmed by PET or cerebrospinal fluid testing for amyloid. The participants were divided into n = 1:1 ratio randomly and one group received intravenous lecanemab 10mg/kg body weight every two weeks and the other group received placebo [6].

RESULT:

The results of the Clinical Trials of lecanemab are not a miracle in curing Alzheimer's disease Alzheimer's disease Alzheimer's disease but the progression of the disease over the period of 18 months. Infusion of Lecanemab resulted in reactions in 26.4% of the patient's participated in phase 3 clinical trial study and also amyloid-related imaging abnormalities associated with edema or effusions in 12.6% of patients who participated in the study.[6]

CONCLUSIONS:

Lecanemab does reduce the accumulation of amyloid beta and hence progression of the disease slows down but it is also associated with adverse events. So more and longer studies required to determine the safety and efficacy of lecanemab.

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