LECANEMAB IN THE EARLY TREATMENT OF ALZHEIMER'S DISEASE: EVIDENCE AND PERSPECTIVES

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Abstract

This chapter aims to analyze recent scientific evidence regarding the use of lecanemab in the early treatment of Alzheimer's disease, focusing on its efficacy, safety, and clinical implications. The methodology consisted of a narrative literature review based on randomized clinical trials, observational

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studies, and reports from regulatory agencies published between 2018 and 2025. The results indicate that lecanemab, a monoclonal antibody targeting beta-amyloid protein, has shown the ability to reduce amyloid plaque burden in the brain and slow cognitive decline in patients at early stages of the disease. Phase III studies demonstrated modest but statistically significant clinical benefits, particularly when administered early. However, adverse events such as amyloid-related imaging abnormalities were reported, requiring careful monitoring. It is concluded that lecanemab represents a significant advancement in disease-modifying therapy for Alzheimer's disease, although challenges related to safety, cost, and accessibility still limit its widespread clinical use.

Keywords: Alzheimer, Beta-amyloid, Early therapy, Lecanemab, Monoclonal antibodies.

INTRODUCTION

Alzheimer's disease is a progressive and irreversible neurodegenerative disorder characterized by cognitive decline, behavioral changes, and functional impairment, being the leading cause of dementia in the elderly worldwide (Alzheimer's Association, 2023). It is estimated that millions of people are affected globally, with a growing trend due to population aging, which reinforces the need for effective therapeutic strategies, especially in the early stages of the disease (WHO, 2021).

From a pathophysiological perspective, the disease is associated with the abnormal accumulation of beta-amyloid and tau proteins in the brain, leading to the formation of senile plaques and neurofibrillary tangles, which contribute to synaptic dysfunction and neuronal death (Hardy; Selkoe, 2002). In this context, the so-called "amyloid hypothesis" has guided the development of disease-modifying therapies, focusing on the removal or reduction of these pathological proteins (Selkoe; Hardy, 2016).

Recently, lecanemab, a humanized monoclonal antibody, has gained prominence as a promising approach in the early treatment of Alzheimer's disease. This drug acts selectively on soluble beta-amyloid protofibrils, promoting their clearance and potentially delaying the clinical progression of the disease

(Van Dyck et al., 2023). Phase III clinical trials, such as the CLARITY AD study, have shown that lecanemab was able to significantly reduce cognitive decline in patients with mild cognitive impairment or mild dementia associated with Alzheimer's disease (Van Dyck et al., 2023).

Despite promising results, the use of lecanemab still raises debates regarding its safety, particularly due to the occurrence of amyloid-related imaging abnormalities (ARIA), in addition to issues involving cost, accessibility, and patient eligibility criteria (Cummings et al., 2023). Moreover, regulatory agencies such as the Food and Drug Administration (FDA) have approved the drug under specific conditions, reinforcing the need for strict monitoring and careful patient selection (FDA, 2023).

Given this scenario, it becomes essential to understand the available scientific evidence regarding lecanemab, as well as its future prospects in the management of Alzheimer's disease. Thus, this chapter aims to discuss the advances, limitations, and clinical implications of the use of this drug in the early treatment of the disease, contributing to the updating of knowledge in the field and to evidence-based practice.

METHODOLOGY

TYPE OF STUDY

This is a qualitative, descriptive study developed through a narrative literature review. This design was chosen because it allows the integration and critical interpretation of different scientific evidence available on the use of lecanemab in the early treatment of Alzheimer's disease, providing a broad and contextualized view of the topic. In addition, the narrative review enables the discussion of clinical, therapeutic, and future perspectives in a more flexible manner, without the methodological restrictions of systematic reviews.

SEARCH STRATEGY

The bibliographic search was carried out in widely recognized electronic health databases, including PubMed/MEDLINE, Scopus, Web of Science, and the Virtual Health Library (VHL). The search period included publications from 2018 to 2025, aiming to encompass recent and updated evidence. Controlled descriptors and keywords in Portuguese and English were used, combined with Boolean operators (AND and OR), such as: "Alzheimer's disease," "lecanemab," "beta-amyloid," "monoclonal antibodies," and "early treatment." The search strategy was adapted according to the specificities of each database, ensuring greater coverage and sensitivity in identifying studies.

INCLUSION AND EXCLUSION CRITERIA

Previously defined criteria were adopted for study selection. Inclusion criteria included:

a) original articles and relevant reviews;

b) randomized clinical trials and observational studies;

c) publications directly addressing the use of lecanemab in early stages of Alzheimer's disease;

d) documents from regulatory agencies and scientific consensus statements;

e) studies published between 2018 and 2025, available in full text.

Exclusion criteria were:

a) duplicate studies across databases;

b) publications without access to the full text;

c) works that did not address the proposed objective;

d) studies focusing on other therapies unrelated to lecanemab;

e) articles outside the established time frame.

STUDY SELECTION PROCESS

The selection of studies occurred in sequential stages. Initially, titles and abstracts were read to identify potentially relevant works. Subsequently, full-text reading of the selected articles was carried out to verify their suitability according to the established criteria. This process allowed refinement of the final sample, ensuring the inclusion of studies with greater scientific relevance and alignment with the research objective.

DATA ANALYSIS AND SYNTHESIS

The data extracted from the selected studies were systematically organized and qualitatively analyzed. The synthesis of information included aspects related to the mechanism of action of lecanemab, its clinical efficacy, safety profile, adverse events, and implications for clinical practice. The analysis was conducted descriptively, seeking to identify convergences, divergences, and gaps in the literature.

ETHICAL ASPECTS

As this study is based on secondary data available in public databases and does not directly involve human subjects, submission to a Research Ethics Committee was not required, in accordance with the guidelines for studies of this nature. However, ethical principles related to scientific integrity and proper citation of sources were observed.

RESULTS AND DISCUSSION

The analysis of the included studies showed a predominance of phase II and III randomized clinical trials, as well as systematic reviews and recent reports from regulatory agencies. Most studies focused on patients with mild cognitive impairment or mild dementia associated with Alzheimer's disease, considered ideal stages for disease-modifying interventions. There was also a significant increase in publications from 2021 onwards, reflecting advances in therapies targeting beta-amyloid protein.

Table 1

General characteristics of the included studies

Author/Year	Type of study	Sample	Main findings
Van Dyck et al. (2023)	Phase III clinical trial	1795 patients	Reduction in cognitive decline
Swanson et al. (2021)	Phase II clinical trial	856 patients	Reduction of amyloid plaques
Cummings et al. (2023)	Systematic review	—	Evidence of moderate efficacy
FDA (2023)	Regulatory report	—	Approval with restrictions

The results demonstrate that lecanemab presents modest but statistically significant clinical efficacy in slowing cognitive decline in patients at early stages of the disease. The CLARITY AD study showed an approximately 27% reduction in clinical progression, measured by scales such as CDR-SB. In addition, there was a consistent reduction in beta-amyloid plaque burden in the brain, confirmed by imaging exams, reinforcing the hypothesis that early intervention can alter the course of the disease.

Table 2

Main efficacy outcomes

Assessed outcome	Observed result
Cognitive decline	Significant reduction (≈27%)
Beta-amyloid burden	Marked reduction
Clinical progression	Moderate delay
Daily function	Partial preservation

Despite the benefits, concerns related to treatment safety were identified. The main adverse event associated with lecanemab use was the occurrence of amyloid-related imaging abnormalities (ARIA), including brain edema (ARIA-E) and microhemorrhages (ARIA-H). These events were more frequent in individuals carrying the APOE ε4 allele, although in most cases they were mild or asymptomatic.

Table 3

Adverse events associated with lecanemab

Adverse event	Frequency	Severity
ARIA-E (edema)	Moderate	Mild to moderate
ARIA-H (microhemorrhages)	Low to moderate	Variable
Headache	Frequent	Mild
Infusion reactions	Occasional	Mild

The interpretation of the findings indicates that lecanemab represents a relevant advancement in the treatment of Alzheimer's disease, as it acts directly on the disease's pathophysiology, unlike traditional therapies focused only on symptom control. The results are consistent with recent literature, which points to greater efficacy when intervention occurs in early stages, before more advanced neuronal impairment. However, the clinical benefits are still considered modest, raising questions about its cost-benefit ratio, especially in resource-limited settings.

Furthermore, the need for monitoring through imaging exams and the occurrence of adverse events reinforce the importance of careful patient selection. Issues related to accessibility and the high cost of treatment also represent significant challenges for its large-scale implementation. Thus, although promising, the use of lecanemab still requires further investigation, particularly regarding long-term effects and its association with other therapeutic approaches.

CONCLUSION

This chapter aimed to analyze the scientific evidence regarding the use of lecanemab in the early treatment of Alzheimer's disease, focusing on its efficacy, safety, and clinical implications. Based on the literature review, it was possible to identify that the drug represents a relevant advancement in the field of disease-modifying therapies, particularly because it acts directly in reducing beta-amyloid plaques, one of the main pathophysiological markers of the disease.

The main findings showed that lecanemab is capable of promoting a statistically significant slowing of cognitive decline in patients at early stages of the disease, in addition to reducing cerebral amyloid burden. However, the observed clinical benefits are still considered moderate and are accompanied by potential risks, such as amyloid-related imaging abnormalities (ARIA), which require rigorous monitoring and careful patient selection.

As a contribution, this study reinforces the importance of early intervention in the course of Alzheimer's disease and highlights lecanemab as a promising therapeutic alternative in the context of evidence-based medicine. In addition, it expands the understanding of recent advances in disease treatment, assisting healthcare professionals in clinical decision-making.

Finally, future research is suggested to investigate the long-term effects of lecanemab, its efficacy in different population profiles, and its possible association with other therapeutic approaches, such as treatments targeting tau protein. It is also necessary to analyze aspects related to cost-effectiveness and accessibility, especially in public health systems, in order to enable its broader and more equitable implementation.

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