Journal of Health Management and Pharmacy Exploration
https://shmpublisher.com/index.php/johmpe
p-ISSN: 2985-4814
e-ISSN: 2985-5543

Effectiveness and safety of the monoclonal antibody drug lecanemab (Leqembi) in reducing beta-amyloid plaques in alzheimer's dementia: a literature review

Adinda Nezma Meidina [1*], Nafilah Ramadhanti [1], Dyah Fatha Istiqomah [1], Yolanda Delia Putri [1], Nabila Az-zahra Hasibuan [1]
[1]Master of Medicine, Universitas Sriwijaya, Indonesia

Article Info

Article history:

Received February 06, 2025
Revised February 25, 2025
Accepted February 27, 2025

Keywords:

Alzheimer's Dementia [MeSH]
Beta-Amyloid Plaques
Lecanemab OR Leqembi
Monoclonal Antibody
Treatment

ABSTRACT

Dementia is a syndrome characterized by cognitive decline, behavioral changes, and impaired self-care, with Alzheimer's disease (AD) being the most common cause. The global prevalence of AD is rising and is expected to reach 152 million cases by mid-century, imposing significant public health and economic burdens, particularly in low- and middle-income countries. AD is marked by synapse loss and neuronal atrophy, beginning in the hippocampus and spreading across the cerebral cortex due to β-amyloid plaque and neurofibrillary tangle accumulation, which disrupt neuronal communication and survival. Current treatments, such as memantine and cholinesterase inhibitors, provide only temporary symptom relief without stopping disease progression. Literature was searched using search engines such as Google Scholar, Science Direct, ResearchGate, and NCBI. Inclusion and exclusion criteria were applied, resulting in 27 relevant references that explored monoclonal antibody-based therapies and multidisciplinary interventions for AD management. Lecanemab has been shown to reduce amyloid accumulation effectively. However, its use is associated with risks such as amyloid-related imaging abnormalities with edema (ARIA-E) and hemorrhage ARIA-H, particularly in ApoE ε4 carriers. Despite these concerns, recent meta-analyses suggest that lecanemab is generally well-tolerated and offers potential as a cost-effective treatment for AD. Monoclonal antibody therapies, such as lecanemab, provide hope for slowing AD progression. Further research is crucial for developing more effective treatments. A multidisciplinary approach that integrates pharmacological therapies with advanced technologies may offer a more effective strategy for managing AD in the future.

* ***Corresponding Author:***
Adinda Nezma Meidina,
Department of Medicine,
Universitas Sriwijaya,
Palembang, Indonesia
Email: adindanezmameidina@gmail.com
DOI: https://doi.org/10.52465/johmpe.v3i1.547

1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that severely affects cognitive function, behavior, and daily activities. As the leading cause of dementia, AD is marked by cortical degeneration, resulting in memory loss, impaired reasoning, and language difficulties. The amnestic form of AD primarily manifests as episodic memory deficits and disorientation, while the non-amnestic variant may involve behavioral changes, language impairments, or visual disturbances [1].

The global prevalence of AD is steadily rising and is expected to reach 152 million cases by the middle of this century. Women are at a higher risk, and AD-related mortality continues to rise, making it the fifth leading cause of death among older adults in the United States. With increasing life expectancy, AD has become a growing public health concern, particularly in low- and middle-income countries, where it imposes significant economic and social burdens [2].

Alzheimer's dementia is marked by synapse loss and neuronal atrophy, starting in the hippocampus and gradually spreading across the cerebral cortex. This deterioration is primarily caused by the buildup of β-amyloid plaques and neurofibrillary tangles (NFTs), which impair neuronal communication and survival. Genetic and environmental factors, such as mitochondrial dysfunction and oxidative stress, further accelerate disease progression by increasing β-amyloid production and synaptic damage. Age is a significant risk factor, with the likelihood of developing AD rising from approximately 3% at age 65 to over 30% by age 85 [3].

Given the significant challenges posed by AD, innovative treatments are needed to not only provide symptomatic relief but also address its underlying pathology. Current pharmacological therapies, including acetylcholinesterase inhibitors (e.g., donepezil, rivastigmine) and N-methyl-D-aspartate receptor antagonists (e.g., memantine), offer temporary benefits without stopping disease progression [4,5,6]. Lecanemab (Leqembi), a monoclonal antibody targeting beta-amyloid (Aβ) plaques, has shown promise in treating AD. The Phase III CLARITY AD trial demonstrated that lecanemab effectively reduced Aβ plaque accumulation and slowed cognitive decline in patients with mild AD or mild cognitive impairment [7]. Additionally, it has improved cognitive and functional outcomes, as measured by the AD Assessment Scale-Cognitive Subscale (ADAS-Cog) and the Mini-Mental State Examination (MMSE) [8]. While lecanemab effectively lowers amyloid levels, its safety profile includes risks such as amyloid-related imaging abnormalities with edema (ARIA-E) and hemorrhage (ARIA-H), particularly in ApoE ε4 carriers [9]. Despite these concerns, a meta-analysis confirmed its overall tolerability and potential as a cost-effective treatment for AD [10].

This manuscript takes an innovative approach by evaluating the potential of monoclonal antibody-based therapies and multidisciplinary interventions for managing AD. Unlike previous studies, it not only focuses on pharmacological treatments but also explores the integration of advanced technologies for early diagnosis and disease progression

monitoring. As the global prevalence of AD continues to rise, investigating therapies that can alter the disease trajectory is crucial to offering new hope for patients while alleviating the social and economic burden worldwide.

2. Method

The method used in writing this literature review is a literature review using the keywords "Alzheimer′s Dementia [MeSH]", "Beta-Amyloid Plaques", "Lecanemab OR Leqembi", "Monoclonal Antibody", and "Treatment". The literature search was carried out using search engines such as Google Scholar, Science Direct, ResearchGate, and NCBI. The inclusion criteria for this literature search were in narrative review, literature review, clinical trials and meta-analysis with publication requirements within the last 5 years. The exclusion criteria used were studies that had not been completed at the time of the literature search, studies that could not be accessed in full paper, and studies that used languages other than English and Indonesian. From the results of the literature search, the evaluation of inclusion and exclusion criteria was carried out by assessing the title and abstract as a first step, and then the full text was reviewed to see if there was a correlation between keywords in the journal so that it could support writing descriptions or analysis in this literature review. From the results of a literature search using inclusion and exclusion criteria, 27 references from articles and journals were used in this work.

3. Results and Discussion

3.1. About Alzheimer

Dementia is a syndrome caused by a disease that causes cognitive impairment, behavioral changes, and impaired self-care. Alzheimer's dementia is the most common type of dementia and has a gradual progression of symptoms associated with loss of cortical function. In the amnestic form, this disease begins with reduced memory for recent events or conversations (episodic memory) and time orientation problems as well as decreased understanding, judgment, thinking, and language difficulties that develop over time. In the non-amnestic form, the disease begins with behavioral changes, depression, language difficulties, orientation difficulties, or vision problems [1].

According to the epidemiology journal of Zhang et al. (2021), the number of Alzheimer's patients is projected to reach 152 million by mid-century worldwide, with the largest increase expected to occur in low- and middle-income countries. The age-specific global prevalence in women is 1.17 times greater than in men and the age-standardized mortality rate of women is also higher than that of men. The death rate due to Alzheimer's is increasing and is the fifth largest cause of death in older Americans. As life expectancy increases and demographic aging, the global prevalence of AD is expected to continue to increase, especially in developing countries, leading to a costly disease burden.

The etiology of Alzheimer's involves a combination of genetic, biological, environmental, and lifestyle factors. Factors such as genetic factors (APOE gene and genetic mutations), age, environmental and metabolic factors, including inflammation and vascular disorders, contribute to the development of this disease. Meanwhile neuronal atrophy and loss of synapses occurs throughout the cerebral cortex. The hallmark of AD is structural changes in the brain that include amyloid-β plaques and neurofibrillary tangles [3].

The biggest risk factor that plays a role in the manifestation of Alzheimer's dementia is age. At age 65, the chance of suffering from Alzheimer's is about 3%, increasing to more than 30% at age 85. AD can be classified into early-onset AD (EOAD), which occurs before the age of 65 years, and late-onset AD (LOAD), which accounts for more than 95% of cases and manifests after the age of 65 years [3].

Alzheimer's dementia patients will have confusing problems and symptoms in many domains. Many risk factors can contribute to the development of Alzheimer's and are also considered concurrent symptoms of Alzheimer's. The social and familial burden of caring for an Alzheimer's population would be enormous and unsustainable. Therefore, treatment for Alzheimer's dementia is very important because it can help inhibit or slow the progression of the disease, improve the sufferer's quality of life, and provide support and well-being to the family [2].

3.2. Pathogenesis of Alzheimer ' s Dementia

Alzheimer's dementia is a disease characterized by synapse loss, leading to neuronal atrophy throughout the cerebral cortex. This process starts in the hippocampus and entorhinal region and extends to the entire frontotemporal cortex. The main pathophysiology of Alzheimer's dementia involves two processes, which are the formation of neuritic plaques and NFTs that reduce the neurotransmitter acetylcholine [3].

Neuritic plaques are a type of lesion with core accumulation of β-amyloid peptides deposited extracellularly and surrounded by swollen axon terminals. β-amyloid accumulation occurs around meningeal blood vessels, cerebral and cortical gray matter [11]. The formation of β-amyloid is initiated by proteolysis of β-amyloid precursor protein (APP) by β and γ-secretase enzymes resulting in the release of peptides into the cytosol. This results in disruption of signal transduction that plays a role in the development, growth and survival of neurons [3]

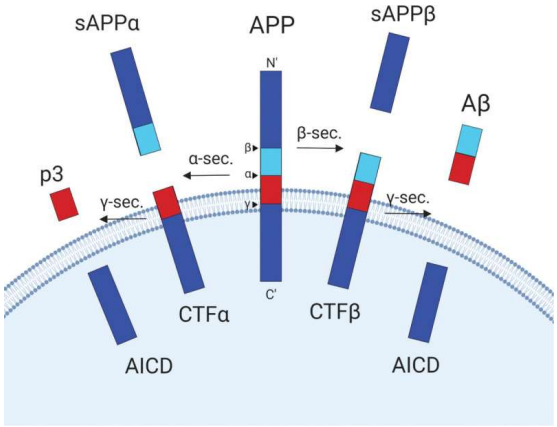

Figure 1. Proteolysis of APP by β- and γ-secretase enzymes [3]

Furthermore, β-amyloid aggregation triggers the hyperphosphorylation of tau protein, which plays a role in stabilizing microtubules along neuronal axons to support intracellular transport. The hyperphosphorylated condition causes tau protein to misfold and form aggregates of paired helical filaments known as NFTs. These NFTs accumulate within neurons, disrupting microtubule function and impairing axonal transport, which is essential for neuronal communication and survival [11].

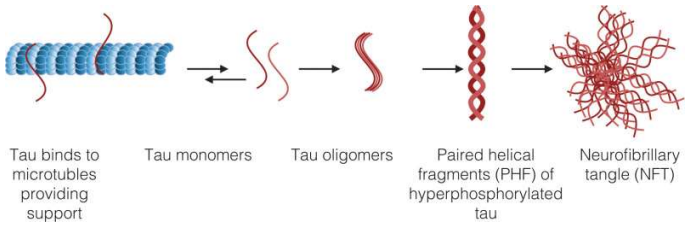

Figure 2. Aggregation of tau proteins to form NFTs [3]

This buildup of protein aggregates activates a complex molecular and cellular response of synaptic dysfunction, neuroinflammatory activation, and progressive neuronal death [12]. Genetic and environmental factors contribute to the development of Alzheimer's dementia through mitochondrial dysfunction and oxidative stress. Mitochondria accumulated at synapses supply energy for the metabolic processes of neurons. However, APP can cause mitochondrial deficits and increase the production of reactive oxygen species (ROS) at synapses. This condition is exacerbated by low antioxidant levels due to insufficient ATP and high brain lipid concentrations, leading to oxidative stress. As a result, oxidative stress will affect β-secretase activity, which may eventually alter β-amyloid production [3].

3.3. Current Treatment of Alzheimer ' s Dementia

3.2.1. Donepezil

Donepezil is an acetylcholinesterase inhibitor that plays a role in inhibiting acetylcholine metabolism in the postsynaptic cleft in patients with Alzheimer's dementia. This drug has selective, reversible, and non-competitive activity by targeting the peripheral anionic site of acetylcholinesterase in the central nervous system, thus improving cholinergic neurotransmission. Reversibly, donepezil binds to acetylcholinesterase to prevent the hydrolysis of acetylcholine, resulting in increased availability of acetylcholine at the synapse. In addition, donepezil also contributes to increasing nicotinic receptors on cortical neurons, which is neuroprotective [4].

Gastrointestinal absorption of donepezil is quite long, lasting 3-5 hours to reach peak plasma concentration. Donepezil binds to serum proteins such as albumin and alpha-1 acid glycoprotein, and is easily excreted through urine. Hepatic metabolism of donepezil has a long half-life, about 70 hours involving cytochrome P450 enzymes CYP2D6, CYP3A4, CYP3A5 and CYP2C9 [13].

3.2.2. Rivastigmine

Rivastigmine is a cholinesterase inhibitor that reversibly inhibits the activity of acetylcholinesterase (AChE) at the synaptic junction and butyrylcholinesterase (BuChE) in brain glial cells. By preventing the breakdown of acetylcholine, rivastigmine helps enhance cholinergic neurotransmission, which is crucial for cognitive function. It is primarily used to treat mild to moderate Alzheimer's dementia, aiming to improve short-term memory, cognitive abilities, and overall daily functioning. Additionally, rivastigmine has been shown to slow the progression of symptoms, although it does not halt disease progression [5].

Rivastigmine shows higher selectivity for areas of the hippocampus and cortex that have the most significant cholinergic deficiency in people with Alzheimer's dementia. The drug's ability to inhibit acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) leads to higher neurotransmitter gains and better cholinergic receptor function. Orally, rivastigmine has a bioavailability of up to 36% with peak plasma concentration reached within 1 hour. Absorption of this drug with food requires a longer time, of up to 90 minutes and a half-life of up to 10 hours. Side effects that can arise from oral administration of rivastigmine include nausea, vomiting, and abdominal pain caused by muscarinic receptor stimulation [14].

3.2.3. Memantine

Memantine is a drug that acts as an N-methyl-D-aspartate receptor (NMDAR) antagonist of glutamate receptors, aiming to reduce neurotoxicity in patients with Alzheimer's dementia. Memantine is an extra-synaptic N-methyl-D-aspartate receptor (NMDAR) inhibitor that selectively enters ion channels with low affinity and prevents disruption of normal synaptic transmission, thus protecting nerve cells from further death. The mechanism of action of this drug includes blocking NMDAR activity on glutamate receptors so that glutamine receptor activity can be inhibited and physiological activities continue to run optimally. In addition, memantine also increases antagonistic activity at serotonergic type 3 (5-HT3) receptors and receptors nicotinic acetylcholine [6]. Memantine taken orally is absorbed almost completely, taking 3-7 hours to reach peak drug concentration. The drug is excreted via the kidneys, with almost 48% remaining unchanged in the urine [14].

3.4. The Potential of Monoclonal Antibody Drug Lecanemab (Leqembi) in Reducing Beta-Amyloid Plaques and Slowing Alzheimer's Progression

AD is a neurodegenerative disorder characterized by the accumulation of beta-amyloid (Aβ) plaques in the brain, leading to synaptic dysfunction and progressive neurodegeneration [8]. At present, the pharmacological management of Alzheimer's dementia is primarily symptomatic and does not address the underlying pathology of the disease. Several studies have demonstrated that Aβ removal can slow the progression of AD, making anti-amyloid-based therapy a promising therapeutic approach in recent years [7].

A significant advancement in the pharmacological treatment of AD is the approval and clinical application of anti-amyloid monoclonal antibodies. Two monoclonal antibodies that have been approved by the U.S. Food and Drug Administration (FDA) are lecanemab (Leqembi) and aducanumab (Aduhelm). These agents function by targeting Aβ aggregates to reduce amyloid burden, as measured by positron emission tomography (PET), and to slow clinical decline in clinical trials [15].

Lecanemab (BAN2401) is a humanized IgG1 monoclonal antibody that specifically targets Aβ protofibrils, which are soluble Aβ aggregates that contribute to neurotoxicity by disrupting electrophysiological systems involved in memory function. Compared with aducanumab, lecanemab exhibits significantly higher affinity, 100 times greater for small protofibrils and 25 times greater for large protofibrils. It is administered intravenously at a fixed dose of 10 mg/kg every two weeks without the need for dose titration [16].

Preclinical studies in animal models have demonstrated that lecanemab effectively reduces Aβ protofibrils and amyloid plaques. A phase I clinical trial involving 80 participants confirmed an acceptable pharmacokinetic profile with no serious adverse events, such as ARIA-E, although amyloid-related imaging abnormalities with hemosiderin deposits (ARIA-H) were observed in some cases. A subsequent phase IIb trial (NCT01767311) involving 856 participants aimed to determine the optimal dose and efficacy of lecanemab. Although the trial did not meet its primary endpoint at 12 months, a follow-up analysis at 18 months revealed a slowing of cognitive decline and a reduction in Aβ plaque levels. However, the risk of ARIA was higher in individuals carrying the APOE ε4 allele [17].

A phase III trial (CLARITY AD), involving 1,795 participants, further demonstrated that lecanemab significantly slowed cognitive decline compared with placebo, reduced Aβ plaque accumulation, and improved AD biomarkers. The primary adverse events reported included infusion-related reactions, ARIA-E (12.6%), and ARIA-H (17.3%), with a higher incidence in individuals homozygous for the APOE ε4 allele. Based on robust clinical evidence supporting its efficacy in reducing Aβ burden and slowing disease progression, the FDA approved lecanemab for the treatment of AD [17]

Furthermore, a study by Teli and Dhande reported that lecanemab significantly improved secondary clinical outcomes, including the ADAS-Cog, the AD Cooperative Study-Activities of Daily Living (ADCS-ADL), and the MMSE. These findings suggest that lecanemab not only mitigates cognitive decline but also enhances daily functioning in patients with AD [8].

3.5. The Effectiveness of Lecanemab in Reducing Beta-amyloid Plaques in Alzheimer's Dementia

There are limited treatment options for AD, with current therapies like memantine and cholinesterase inhibitors only providing temporary symptom relief without addressing the disease itself. In contrast, lecanemab, an FDA-approved treatment, targets amyloid pathology in the brain, slowing disease progression and delaying cognitive decline, potentially offering long-term benefits and addressing the root cause of the condition [8].

Lecanemab′s effectiveness and safety have been evaluated in several clinical studies. In a study measuring the Clinical Dementia Rating-Sum of Boxes (CDR-SOB) score, lecanemab-treated patients showed a slower decline in cognitive function compared to those on a placebo, with scores of 1.21 and 1.66, respectively [7]. The CDR-SOB, which assesses dementia severity by evaluating cognitive and functional abilities, supported the conclusion that lecanemab slows cognitive decline. Additionally, lecanemab significantly improved secondary endpoints, including the ADAS-Cog, the AD Cooperative Study-Activities of Daily Living (ADCS-ADL), and MMSE [8].

Further studies found that lecanemab reduced amyloid levels in the brain, with a mean level of 22.99 centiloids, below the amyloid positivity threshold of 30 centiloids [7], suggesting the drug′s potential to slow amyloid buildup and, by extension, AD progression [18]. As of March 2023, three randomized controlled trials involving 2,729 participants have been conducted to assess lecanemab′s efficacy. These trials, including an initial double-blind trial and the Phase 2b clinical trial (NCT01767311), showed that

lecanemab was well-tolerated and provided significant therapeutic benefits in mild to moderate AD patients [19, 20].

The CLARITY AD trial, a Phase III randomized controlled study, enrolled 1,795 individuals with mild cognitive impairment (MCI) or mild AD dementia. It found that lecanemab significantly improved cognitive function and reduced amyloid burden over 18 month [7]. Additionally, a meta-analysis of four RCTs involving 3,108 participants concluded that lecanemab improved cognition and reduced amyloid burden, confirmed by PET imaging [21].

Lecanemab has also proven to be cost-effective. Modeling analyses show that when combined with standard of care (SoC), lecanemab improves quality-adjusted life years (QALYs) and reduces costs, particularly in amyloid-positive patients with MCI or mild AD dementia [22]. Other studies confirm that, despite additional treatment costs, lecanemab improves QALYs, equal-value life years (evLYs), and years living outside long-term care compared to supportive care alone [23]. This evidence supports the potential of lecanemab not only as a therapeutic option but also as a cost-effective intervention for AD.

3.6. The Safety of Lecanemab in Alzheimer's Dementia

The safety profile of lecanemab has been evaluated in multiple clinical studies. The most frequently reported treatment-emergent adverse events (TEAEs) were mild to moderate, including dizziness, fatigue, sinusitis, upper respiratory tract infections, headaches, and orthostatic hypotension (Logovinsky, NCT01230853). In general, intravenous lecanemab at a dose of 10 mg/kg was well tolerated, with adverse reactions similar to those seen with other monoclonal antibody treatments. Importantly, no symptomatic ARIA-E or ARIA-H were observed in participants receiving either single or multiple doses of BAN2401, and the incidence of ARIA-E/H on MRI was comparable between those treated with lecanemab and those receiving a placebo [24]. Additionally, there was no evidence of a dose-dependent increase in TEAEs, indicating a consistent safety profile across different dosage levels [16].

A clinical trial by Riederer (2021) involving 1,795 participants, with 898 receiving lecanemab and 897 receiving a placebo, showed similar mortality rates between the lecanemab (0.7%) and placebo (0.8%) groups. Adverse events were reported in 88.9% of participants in the lecanemab group and 81.9% in the placebo group, with a higher incidence of serious adverse events in the lecanemab group (14.0% vs. 11.3%), including infusion reactions, ARIA-E, atrial fibrillation, syncope, and angina pectoris. Common adverse events included infusion reactions (26.4% vs. 7.4%), ARIA-H (17.3% vs. 9.0%), ARIA-E (12.6% vs. 1.7%), headache (11.1% vs. 8.1%), and falls (10.4% vs. 9.6%). Most infusion reactions were mild to moderate and occurred with the first dose [7].

The CLARITY AD study further supports these safety observations. ARIA-E was detected in 12.6% of patients receiving lecanemab, compared to 1.7% in the placebo group. All symptomatic cases of ARIA-E (2.8%) occurred exclusively in the lecanemab-treated group [7]. ARIA-E was frequently associated with brain microhemorrhages or localized superficial siderosis, suggesting a potential link to antecedent ARIA-H. ARIA-H was observed in 17.3% of lecanemab-treated patients compared to 9% in the placebo group, although symptomatic cases remained rare [23].

ARIA-E in the lecanemab group was generally mild to moderate (91%), asymptomatic (78%), occurred within the first three months (71%), and resolved within four months (81%). Symptomatic ARIA-E occurred in 2.8% of cases, with headache and visual disturbances as the most common symptoms. ARIA-H without ARIA-E was observed in 8.9% of participants in the lecanemab group and 7.8% in the placebo group, with dizziness as the most common symptom Macrohemorrhage occurred in 0.6% of lecanemab participants and 0.1% of placebo participants. ARIA-H with ARIA-E generally occurred within the first six months, whereas ARIA-H without ARIA-E could occur throughout the study. The risk of ARIA was lower in individuals without the ApoE ε4 allele, with the highest incidence observed in ApoE ε4 homozygotes [7].

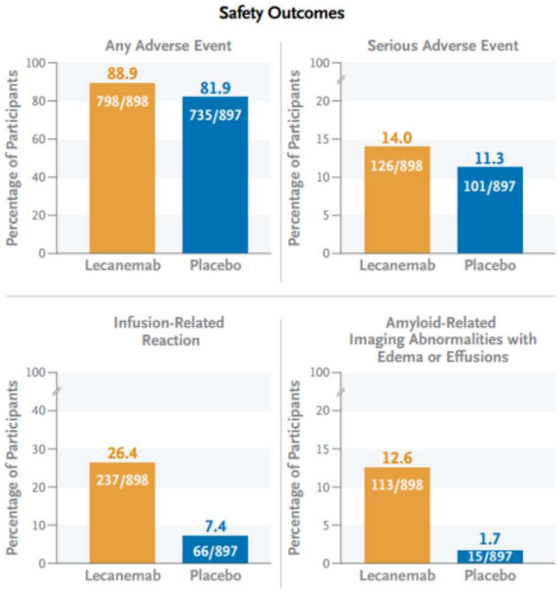

Figure 3. Safety outcomes of lecanemab compared with placebo [7]

Additionally, a study conducted by Qiau et al. (2023) found no significant difference in side effects between the lecanemab and placebo groups. However, their analysis revealed that the incidence of ARIA-E and ARIA-H was higher in the lecanemab group. Other observed side effects included infusion reactions, headache, and falls, which were also more prevalent in the lecanemab group than in the placebo group. Most of these side effects were mild to moderate [21].

A systematic review and meta-analysis by Abdelazim et al. (2024) which focused on randomized controlled trials (RCTs) published between 2010 and 2023, showed that lecanemab at a dose of 10 mg/kg every two weeks had a positive impact on cognitive outcomes in individuals with Alzheimer's. These results provide critical insights into the potential effectiveness of lecanemab in improving cognitive impairment. However, the meta-analysis also highlighted serious concerns regarding the increased risk of ARIA-E and ARIA-H associated with this dosage compared to placebo [10].

The study by Honig (2024), which used the Clarity AD trial with participants randomized in a 1:1 ratio into placebo and lecanemab (10 mg/kg every two weeks) groups, monitored ARIA incidence through MRI scans. The results showed that lecanemab led to a reduction in brain amyloid, accompanied by consistent improvements in multiple clinical endpoints

in participants with early Alzheimer's. Overall, lecanemab was well tolerated, with the most common side effects being infusion-related reactions, ARIA-H, ARIA-E, and headaches. ARIA-E occurred more frequently in participants receiving lecanemab compared with placebo, but most cases were mild to moderate, radiographically detected, and generally appeared within the first 3–6 months of treatment. ARIA was more frequently observed in carriers of the ApoE ε4 gene, particularly in homozygous ApoE ε4 participants. Infusion-related reactions, ARIA-E, and rare intracranial hemorrhage (ICH) are important side effects associated with lecanemab treatment [25].

Regarding pregnancy, there is currently insufficient evidence to determine whether lecanemab is associated with major birth defects, miscarriage, or other adverse maternal or fetal outcomes [16]. Additionally, lecanemab's safety and efficacy in pediatric populations have not been established, as clinical trials have primarily focused on participants aged 50–90 years [26].

Lecanemab has no known contraindications, but caution is advised when prescribing it to patients with amyloid-related imaging abnormalities (ARIA). In particular, for patients with ARIA-E dema (brain swelling) and ARIA-Hemorrhage (brain bleeding), dosing adjustments should be based on clinical symptoms, type, and radiographic severity [27].

4. Conclusion

AD is a progressive neurodegenerative condition and the primary cause of dementia worldwide. As life expectancy rises, the incidence of AD continues to grow, particularly in low- and middle-income countries, creating significant burdens on healthcare systems and economies. The development of AD is influenced by various factors, including genetic, biological, environmental, and lifestyle aspects. Its key pathological features are the accumulation of amyloid-β plaques and neurofibrillary tangles, which lead to neuronal damage and a gradual decline in cognitive function.

Currently, existing pharmacological treatments, such as acetylcholinesterase inhibitors and NMDA receptor antagonists, only alleviate symptoms without stopping disease progression. However, recent breakthroughs in monoclonal antibody therapies, like lecanemab, offer new hope by targeting amyloid-β accumulation to slow AD progression. Continued research into more effective treatments is essential for enhancing patients' quality of life. With advancements in biotechnology, including antibody-based therapies and improved diagnostic tools, a multidisciplinary approach that integrates pharmacological treatments with technology-driven interventions may provide a more effective solution to addressing AD in the future.

ACKNOWLEDGEMENTS

Thank you to Ms. Nafilah Ramadhanti, Ms. Dyah Fatha Istiqomah, Ms. Yolanda Delia Putri, and Ms. Nabila Az-zahra Hasibuan for for their assistance in writing and editing this article. We hope that this article will be beneficial to the readers.

REFERENCES

[1] A. B. Knapskog, K. Engedal, G. Selbæk, and A. R. Øksengård, "Alzheimers sykdom – diagnostikk og behandling," *Tidsskr. den Nor. Laegeforening*, vol. 141, no. 7, 2021, doi: 10.4045/tidsskr.20.0919.

[2] X. X. Zhang, Y. Tian, Z. T. Wang, Y. H. Ma, L. Tan, and J. T. Yu, "The Epidemiology of

Alzheimer's Disease Modifiable Risk Factors and Prevention," *J. Prev. Alzheimer's Dis.*, vol. 8, no. 3, pp. 313–321, 2021, doi: 10.14283/jpad.2021.15.
[3] X. Huang, *Alzheimer's Disease: Drug Discovery*. 2020. doi: 10.36255/exonpublications.alzheimersdisease.2020.
[4] A. Kumar, S. Sandeep, and G. Vikas, "Donepezil," StatPearls Publishing. [Online]. Available: https://www.ncbi.nlm.nih.gov/books/NBK513257/
[5] P. H. Patel and V. Gupta, "Rivastigmine," StatPearls Publishing. [Online]. Available: https://www.ncbi.nlm.nih.gov/books/NBK557438/
[6] B. Kuns, A. Rosani, and D. Varghese, "Memantine," StatPearls Publishing. [Online]. Available: https://www.ncbi.nlm.nih.gov/books/NBK500025/
[7] F. Riederer, "Lecanemab in early Alzheimer's Disease," *J. fur Neurol. Neurochir. und Psychiatr.*, vol. 22, no. 3, pp. 142–143, 2021, doi: 10.1056/nejmoa2212948.
[8] A. Teli and P. Dhande, "Advancing Alzheimer's care: a novel therapy with lecanemab," *Egypt. J. Neurol. Psychiatry Neurosurg.*, vol. 59, no. 1, 2023, doi: 10.1186/s41983-023-00747-y.
[9] M. F. Hossain, A. U. Husna, and M. Kharel, "Use of lecanemab for the treatment of Alzheimer's disease: A systematic review," *Brain Behav.*, vol. 14, no. 6, pp. 1–10, 2024, doi: 10.1002/brb3.3592.
[10] K. Abdelazim, A. A. Allam, B. Afifi, H. Abdulazeem, and A. I. Elbehiry, "The efficacy and safety of lecanemab 10 mg/kg biweekly compared to a placebo in patients with Alzheimer's disease: a systematic review and meta-analysis of randomized controlled trials," *Neurol. Sci.*, vol. 45, pp. 3583–3597, 2024, doi: doi: 10.1007/s10072-024-07477-w.
[11] A. Kumar, J. W. Tsao, J. Sidhu, and G. Amandeep, "Alzheimer Disease," StatPearls Publishing. [Online]. Available: https://www.ncbi.nlm.nih.gov/books/NBK499922/
[12] G. Plascencia-Villa and G. Perry, "Neuropathologic Changes Provide Insights into Key Mechanisms of Alzheimer Disease and Related Dementia," *Am. J. Pathol.*, vol. 192, no. 10, pp. 1340–1346, 2022, doi: 10.1016/j.ajpath.2022.07.002.
[13] P. Pooladgar, M. Sakhabakhsh, A. Taghva, and S. Soleiman-Meigooni, "Donepezil Beyond Alzheimer's Disease? A Narrative Review of Therapeutic Potentials of Donepezil in Different Diseases," *Iran. J. Pharm. Res.*, vol. 21, no. 1, pp. 1–15, 2022, doi: 10.5812/ijpr-12840.
[14] D. C. Miculas, P. A. Negru, S. G. Bungau, T. Behl, S. S. ul Hassan, and D. M. Tit, "Pharmacotherapy Evolution in Alzheimer's Disease: Current Framework and Relevant Directions," *Cells*, vol. 12, no. 1, 2023, doi: 10.3390/cells12010131.
[15] J. Cummings, "Anti-Amyloid Monoclonal Antibodies are Transformative Treatments that Redefine Alzheimer's Disease Therapeutics," *Drugs*, vol. 83, no. 7, pp. 569–576, 2023, doi: 10.1007/s40265-023-01858-9.
[16] S. Chowdhury and N. S. Chowdhury, "Novel anti-amyloid-beta (Aβ) monoclonal antibody lecanemab for Alzheimer's disease: A systematic review," *Int. J. Immunopathol. Pharmacol.*, vol. 37, 2023, doi: 10.1177/03946320231209839.
[17] J. Cummings, A. M. L. Osse, D. Cammann, J. Powell, and J. Chen, "Anti-Amyloid Monoclonal Antibodies for the Treatment of Alzheimer's Disease," *BioDrugs*, vol. 38, no. 1, pp. 5–22, 2024, doi: 10.1007/s40259-023-00633-2.
[18] T. B. Ameen, S. N. Kashif, S. M. I. Abbas, K. Babar, S. M. S. Ali, and A. Raheem, "Unraveling Alzheimer's: the promise of aducanumab, lecanemab, and donanemab," *Egypt. J. Neurol. Psychiatry Neurosurg.*, vol. 60, no. 1, 2024, doi: 10.1186/s41983-024-00845-5.
[19] V. Logovinsky *et al.*, "Safety and tolerability of BAN2401 - A clinical study in Alzheimer's disease with a protofibril selective Aβ antibody," *Alzheimer's Res. Ther.*, vol. 8, no. 1, pp. 1–10, 2016, doi: 10.1186/s13195-016-0181-2.
[20] C. J. Swanson *et al.*, "A randomized, double-blind, phase 2b proof-of-concept clinical trial in early Alzheimer's disease with lecanemab, an anti-Aβ protofibril antibody," *Alzheimer's Res. Ther.*, vol. 13, no. 1, pp. 1–14, 2021, doi: 10.1186/s13195-021-00813-8.
[21] Y. Qiao, Y. Chi, Q. Zhang, and Y. Ma, "Safety and efficacy of lecanemab for Alzheimer's disease: a systematic review and meta-analysis of randomized clinical trials," *Front. Aging Neurosci.*, vol. 15, 2023, doi: 10.3389/fnagi.2023.1169499.

[22] A. A. Tahami Monfared, A. Tafazzoli, A. Chavan, W. Ye, and Q. Zhang, "The Potential Economic Value of Lecanemab in Patients with Early Alzheimer's Disease Using Simulation Modeling," *Neurol. Ther.*, vol. 11, no. 3, pp. 1285–1307, 2022, doi: 10.1007/s40120-022-00373-5.
[23] A. C. Wright *et al.*, "The effectiveness and value of lecanemab for early Alzheimer disease: A summary from the Institute for Clinical and Economic Review's California Technology Assessment Forum," *J. Manag. Care Spec. Pharm.*, vol. 29, no. 9, pp. 1078–1083, 2023, doi: 10.18553/jmcp.2023.29.9.1078.
[24] M. J. Hossain *et al.*, "Health-related quality of life among thalassemia patients in Bangladesh using the SF-36 questionnaire," *Sci. Rep.*, vol. 13, no. 1, pp. 1–12, 2023, doi: 10.1038/s41598-023-34205-9.
[25] L. S. Honig *et al.*, "Correction to: Updated safety results from phase 3 lecanemab study in early Alzheimer's disease (Alzheimer's Research & Therapy, (2024), 16, 1, (105), 10.1186/s13195-024-01441-8)," *Alzheimer's Res. Ther.* , vol. 16, no. 1, pp. 1–12, 2024, doi: 10.1186/s13195-024-01507-7.
[26] M. Kane, "Lecanemab Therapy and APOE Genotype Drug : Lecanemab," no. Md, pp. 1–15, 2024.
[27] S. Chowdhury, "Monoclonal Antibody Treatments for Alzheimer's Disease: Aducanumab and Lecanemab," *Discoveries*, vol. 11, no. 3, p. e173, 2023, doi: 10.15190/d.2023.12.