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Mini Review

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Literature Review: Anti-Amyloid Antibody Infusions in Alzheimer's Disease

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At the heart of the current debate is a pressing question: Do anti-amyloid antibodies deliver meaningful clinical value for patients, or do they represent biological progress with limited real-world impact?

Introduction

The introduction of anti-amyloid antibodies such as Leqembi and Kisunla represents a new therapeutic option for early Alzheimer's disease, offering only modest clinical benefit while introducing high cost and safety considerations. These newly approved agents provide limited clinical improvement at substantial financial and safety risk. The recent FDA approval of Leqembi and Kisunla marks a pivotal development in the therapeutic management of Alzheimer's disease. Anti-amyloid antibodies are the first agents to demonstrate consistent large-scale biological effects on amyloid pathology in randomized controlled trials (Huang et al., 2023). Their introduction has generated both controversy and optimism. Consequently, clinicians must carefully weigh modest clinical benefits, economic implications, and safety concerns against the demonstrated biological effects. Appropriate patient selection is essential: eligible candidates typically have early symptomatic Alzheimer's disease, confirmed by biomarker evidence of amyloid pathology, and no significant comorbidities that would increase the risk of adverse events. Patients must be able to tolerate regular MRI scans and intravenous infusions, and should not have medical contraindications such as a history of severe hypersensitivity to monoclonal antibodies or recent intracerebral hemorrhage. APOE ε4 carrier status, history of anticoagulant use, and the presence of microhemorrhages on MRI should also be considered when identifying suitable patients for these therapies.

Mechanism of Action

Leqembi, a humanized IgG1 monoclonal antibody, binds selectively to soluble amyloid-β. This binding enhances the clearance of accumulated amyloid-β protofibrils and reduces plaque burden. Its

mechanism of action is consistent with its classification as a monoclonal antibody. Kisunla, by contrast, targets pyroglutamate-modified amyloid-β (N3pG), particularly pathogenic species. Kisunla facilitates microglial-mediated clearance of these pathogenic amyloid-β species. Both agents require intravenous infusion: Leqembi is administered biweekly, and Kisunla is administered monthly. Each infusion typically lasts about one hour and is conducted in an infusion center under the supervision of trained personnel. Patients are monitored during and after the infusion for potential reactions. According to Kim et al. (2025), intravenous administration requires routine MRI monitoring to detect amyloid-related imaging abnormalities. As noted by Saido and Iwata (2025), Leqembi and Kisunla have therapeutic limitations, particularly as efficacy has not been established in moderate or advanced stages of Alzheimer's disease.

Statistical Significance Versus Clinical Reality

Neurologists and other stakeholders have evaluated the effectiveness of these drugs. In phase III trials, both Leqembi and Kisunla demonstrated statistically significant results. For instance, Leqembi was associated with a 27% reduction in decline over 18 months (Levien & Baker, 2024). Placebo patients declined by 1.66 points on the Clinical Dementia Rating, while the treatment group declined by 1.21 points, a difference often undetectable to most caregivers and patients. This 0.45-point difference over 18 months is roughly equivalent to remembering one or two extra appointments or maintaining independence with a simple daily task for a few additional weeks. In practical terms, these changes are subtle, and many caregivers report no clear improvement in daily life. Qualitative data, including caregiver-reported outcomes and daily-function diaries, highlight this disconnect: many caregivers report minimal changes in daily cognitive or functional abilities despite the statistical benefit. Standardized caregiver burden scales, such as the Zarit Burden Interview, frequently reveal persistently high levels of stress and responsibility, indicating that modest numerical gains do not readily translate into improved lived experiences. Families consistently observe a pattern of progressive decline, with little perceptible difference in daily functioning (Hunter, 2024). While pharmaceutical narratives emphasize a 27% slower decline, clinical reality demonstrates that patients continue to decline, albeit at a marginally reduced rate. Ongoing and planned long-term studies aim to clarify whether clinical benefits are sustained beyond the 18-month trial period, and data on the durability of effect are being collected. Many clinicians are closely monitoring these extended trials to better understand the longer-term value of anti-amyloid therapy.

Comparison with Existing Therapies

Anti-amyloid antibodies can be compared to donepezil, an acetylcholinesterase inhibitor approved in 1996. The contrast is notable: donepezil is a $30-per-month oral medication, while anti-amyloid antibodies such as Leqembi cost $26,500 per year and require infusion. According to Saido and Iwata (2025), donepezil provides similar symptomatic benefits and is effective across multiple stages of Alzheimer's disease. Meta-analyses indicate that donepezil slows decline on the Clinical Dementia Rating–Sum of Boxes (CDR-SB) by approximately 1.0 point over 18 months compared to placebo. In contrast, Leqembi demonstrated a CDR-SB slowing

of about 0.45 points over 18 months in pivotal trials, with Kisunla showing comparable effect sizes. Thus, the magnitude of cognitive slowing with donepezil is comparable to, and sometimes exceeds, that observed with anti-amyloid antibodies. Anti-amyloid therapies also necessitate regular MRI monitoring. Neither therapy halts or reverses disease progression, but both slow symptomatic development (Chhabra et al., 2024). As noted by Hunter (2024), the disparity in risks and costs highlights a conflict between patient-centered care and commercial interests. Alongside pharmacological treatments, non-drug interventions such as cognitive training, physical activity, social engagement, and tailored supportive therapies play a vital role in care plans. Evidence suggests that combining lifestyle interventions with pharmacological therapy may enhance quality of life, help maintain daily function for longer, and address individual patient needs more holistically. Consequently, many neurologists advocate for integrating medication with comprehensive lifestyle and supportive strategies to offer a more patient-centered approach.

Safety Profile and Monitoring Burden

Amyloid-related imaging abnormalities are the primary adverse effect associated with these antibodies. Hunter (2024) reports that such effects occur in approximately 12-17% of patients, or about 1 in 8 individuals, experiencing amyloid-related imaging abnormalities (ARIA). These abnormalities typically manifest as cerebral edema and, in some cases, microhemorrhage (Kim et al., 2025). Severe and fatal outcomes have also been documented. According to Saido and Iwata (2025), additional risks include falls, headaches, and infusion reactions. Effective treatment requires consistent MRI surveillance, coordination with infusion center visits, and careful patient selection, particularly for APOE ε4 carriers who are at increased risk of ARIA (Levien & Baker, 2024). The associated monitoring burden further limits accessibility outside specialized centers and increases costs. Access barriers and equity issues are significant concerns: patients in rural or resource-limited settings may find it especially challenging to access these therapies, given the need for frequent travel to infusion centers and ongoing access to MRI technology. These challenges highlight disparities in availability and underline the importance of considering health equity in treatment recommendations.

Limitations of Therapy

When recommending these drugs, neurologists must recognize their limitations. Current clinical guidelines from organizations such as the American Academy of Neurology (AAN) and the National Institute for Health and Care Excellence (NICE) restrict the use of anti-amyloid therapies to early-stage Alzheimer's disease, based on available evidence regarding efficacy and safety. These recommendations reinforce the limited indications for these agents and highlight the need for careful patient selection. For example, Huang et al. (2023) report that these agents are restricted to early-stage disease, excluding patients with moderate Alzheimer's disease and thereby omitting a substantial portion of the clinical population. These therapies do not fully restore lost function or halt disease progression (Kim et al., 2025). Chhabra et al. (2024) similarly note that such therapies only slow decline for a limited period. Consequently, incremental benefits are often offset by logistical, safety, and financial burdens.

Pharmaceutical Spin Versus Clinical Reality

Neurologists play a critical role in safeguarding patients who receive these therapies.

They must advocate for accurate information and critically evaluate the data presented to patients and the public. To increase sales, companies often employ marketing narratives that emphasize breakthroughs, such as a 27% slower decline. However, clinical reality is less optimistic (Huang et al., 2023). The modest slowing is not apparent in daily life, and patients continue to decline. This discrepancy between commercial promotion and lived experience underscores the need for transparent communication (Chhabra et al., 2024). Inexpensive symptomatic therapies, such as exercise, hearing optimization, sleep regulation, and the Mediterranean diet, tend to receive less attention than expensive biologics.

Neurologists are responsible for seeking relevant, up-to-date information and research regarding these therapies. They must maintain a balanced and professional outlook, combining critical appraisal of the evidence with hope and support for patients and their families. Even though current data reveal only modest benefits, neurologists should continue to communicate transparently, advocate for informed decision-making, and encourage optimism about ongoing research and future advancements. The use of these therapies demonstrates that Alzheimer's disease can be modified biologically, providing a foundation for the development of more effective, accessible, and safer agents. Currently, anti-amyloid antibodies such as Leqembi and Kisunla represent incremental rather than transformative advances. While they demonstrate statistical significance in slowing decline during early Alzheimer's disease, their clinical impact remains modest. These therapies require heightened safety monitoring and incur substantial costs. As proof-of-principle agents rather than definitive solutions, they necessitate evidence-based counseling and transparent communication with patients.

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