EDITORIAL ARTICLE

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The Recent Monoclonal Antibodies Treatment for Alzheimer's Disease: A New Era of Hope and Caution

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According to world health organization (WHO) classifications, dementia represents a progressive syndrome impacting neurological function. The Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) categorizes it as a significant neurocognitive condition affecting various cognitive spheres, eventually leading to functional deterioration [1]. This condition predominantly correlates with advanced age. WHO data indicates approximately 55 million individuals worldwide were affected by dementia in 2021. As populations aged 65 and above continue expanding, projections suggest dementia cases will reach 152.8 million by 2050 [2]. Alzheimer's disease (AD) represents a dementia variant named for German psychiatrist Alois Alzheimer, who initially characterized this clinical condition featuring distinctive histopathological markers including abnormal amyloid protein accumulations forming plaques. Additional fundamental histopathological characteristics of AD include neurofibrillary tangles predominantly comprising paired helical filaments with hyperphosphorylated tau proteins [3]. This dementia subtype predominates among cases, representing 75% of diagnoses, with age-standardized prevalence reaching 4.4% among Europeans over 65 years in population studies. Within Arab regions, dementia prevalence among those over 60 peaked in Lebanon (4.88%) and Iraq (3.93%), with regional care expenses projected at $12.7 billion [4].

Alzheimer's disease has historically resisted effective disease-altering interventions. Contemporary developments in monoclonal antibody (mAb) treatments targeting amyloid-beta (Aβ) have initiated a transformative period, presenting opportunities for modifying disease progression. Nevertheless, these innovations introduce complexities regarding effectiveness, safety profiles, availability, and healthcare system capacity [5].

The authorization of mAbs including aducanumab, lecanemab, and donanemab represents a crucial advancement in AD therapeutics. These interventions target cerebral Aβ plaque reduction, representing a primary AD pathological feature. Lecanemab obtained complete FDA authorization in 2023 following demonstration of 27% cognitive decline reduction across 18 months in early-stage AD participants [6]. Donanemab, receiving FDA approval in 2024 and Australia's Therapeutic Goods Administration (TGA) approval in May 2025, demonstrated 35% cognitive decline reduction in similar patient populations [7]. Although these mAbs have demonstrated potential in decelerating cognitive deterioration rates, benefit magnitudes differ. Recent meta-analytical findings indicated that lecanemab and donanemab substantially enhanced cognitive and functional parameters, though clinical significance of these enhancements continues generating debate [8]. Within the TRAILBLAZER-ALZ 2 study, donanemab reduced clinical deterioration by up to 40% among participants exhibiting low-to-moderate tau pathology [9].

Safety considerations persist, especially regarding amyloid-related imaging abnormalities (ARIA) risks, encompassing cerebral edema (ARIA-E) and microhemorrhages (ARIA-H) [10]. Donanemab studies reported ARIA-E occurrence rates reaching 24% of participants, emphasizing requirements for consistent magnetic resonance imaging monitoring. Although numerous ARIA instances remain asymptomatic, serious complications including fatalities have emerged, requiring careful patient screening and surveillance protocols [11].

Monoclonal antibodies present logistical and financial obstacles. Donanemab's annual expense, estimated at USD 26,500, creates substantial affordability concerns [12]. These interventions demand sophisticated infrastructure including positron emission tomography (PET) imaging capabilities and infusion facilities, which remain inconsistently accessible. Australian memory clinic surveys revealed only 38% possessed

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PET scan access, with fewer than half maintaining infusion capabilities. This resource availability variation may worsen healthcare disparities, particularly affecting rural or under-resourced areas [13].

Furthermore, workforce requirements for treatment delivery, encompassing neurologists, nursing staff, and radiologists, necessitate considerable investment in educational and retention initiatives [14]. Resolving these operational constraints remains essential for ensuring equitable therapy distribution. Anti-Aβ therapy advancement may involve subcutaneous formulations, such as lecanemab preparations, potentially reducing logistical challenges and enhancing patient compliance [15]. Growing interest exists in combinatorial strategies targeting tau pathology and neuroinflammation, possibly yielding more comprehensive disease modification [16].

Extended follow-up data remains necessary for evaluating persistent benefits and cumulative adverse effects. Regulatory agencies and healthcare networks must collaborate ensuring access remains evidence-driven and fair. Pharmacoeconomic evaluations will critically influence reimbursement and funding determinations.

In conclusion, mAbs constitute an encouraging advancement in early-stage AD management. While clinical studies demonstrate positive trends in disease progression deceleration, these advantages require careful consideration against safety concerns, elevated costs, and system preparedness. Future achievements will depend not solely on scientific breakthroughs but also on strategic health policy development and equitable implementation approaches. A careful and comprehensive strategy remains vital for genuinely transforming the AD therapeutic environment.

ETHICAL DECLARATIONS

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Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Availability of data and material

None.

Competing interests

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Use of Artificial Intelligence

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Authors' Contributions

Salih SA was responsible for conceptualization, design, and writing the manuscript. Salih SA read and approved the final version of the manuscript.

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