Monoclonal Antibodies Against Amyloid Beta in the Treatment of Early Alzheimer's Disease - A Literature Review

Sharon Park (parkshar@usc.edu), Tanjia Toma (ttoma@usc.edu), Brian Tran (bdtran@usc.edu), Phitsini Treenate (treenate@usc.edu)

Background/ Purpose

Dementia is a broad term defined as a significant decline in mental status where daily function is affected. As people age, their cognitive ability declines which can lead to dementia. Alzheimer's disease (AD), through widespread brain changes and cellular damage, is the leading cause of dementia, accounting for 60-80% of cases. Accumulation of amyloid beta (Aβ) species in the brain has been studied and linked to the progression of AD. Three major drugs, Aducanumab, Lecanemab, and Donanemab, have gained popularity in recent years for reducing Aβ aggregates and improving cognitive function. Ongoing research has studied the efficacy, safety, and demographics of these drugs to prove their practicality to society.

Methods

A literature review was performed utilizing PubMed. The following terms (aducanumab, lecanemab, donanemab, Alzheimer's) yielded 767 articles. After accounting for article duplication, applied search filters and meaningful data, 4 articles were analyzed due to their significant outcomes.

Results

All of the landmark trials demonstrated a reduction in Aβ plaques, correlating with improvement in cognition. For aducanumab, the EMERGE trial showed 22% reduction from baseline using the Clinical Dementia Rating Sum of Boxes (CDR-SB) while the ENGAGE trial showed 2% increase when patients were given high doses in both trials. Amyloid PET scans showed -.278 and -.232 centiloid reduction in amyloid plaques in EMERGE and ENGAGE respectively. TRAILBLAZER-ALZ2 trial showed CDR-SB scores were lower by 36% and 29% in Donanemab compared to placebo for low/medium tau population and for combined tau population, respectively. Amyloid PET scan showed -87 and -88 centiloid reduction in plaques in low/medium tau population and combined group respectively. CLARITY-AD trial demonstrated a 27% reduction in CDR-SB score with Lecanemab. Amyloid PET scan showed -55.4 centiloid reduction in amyloid plaques in the treatment arm compared to placebo. Secondary endpoints looking at patient demographics found over 70% patients were white.

Conclusion

Although results from clinical trials are statistically significant, they cannot be generalized or accepted in practice due to several limitations. The landmark clinical trials consisted of 80% white population, neglecting Asians, Blacks, Hispanics. Consequently, Biogen removed aducanumab from the market due to pressure from critics who exposed the lack of efficacy and safety from the phase 3 trials. Additionally, there are numerous genetic, social and environmental factors such as diet and access to healthcare that might lead to different response rates amongst other racial groups. Furthermore, the trials consist of a small group of participants with shorter duration of follow-up. Further studies that include a larger and more heterogeneous population are needed in order to evaluate true efficacy and Aβ sensitivity in a general population.