06. Precision Medicine Approaches in Alzheimer's Disease: Clinical Perspective on ALZ-801.

Tanishka Muraleedharan[1], Aditi Balan[1].

[1]ACS Medical College and Hospital, Chennai, Tamil Nadu, India.

Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by abnormal amyloid-β protein accumulation and progressive cognitive decline. The global burden of AD continues to rise, with approximately 9.8 million new cases reported annually. The Apolipoprotein ε4 (APOE ε4) allele is a major genetic risk factor associated with accelerated amyloid-β aggregation and earlier disease onset. ALZ-801 (Valiltramiprosate), an oral anti-amyloid agent targeting toxic amyloid-β oligomer formation, has emerged as a potential disease-modifying therapy in APOE4-associated AD. **Objective:** To systematically evaluate the efficacy and safety of ALZ-801 in patients with early Alzheimer's disease, with emphasis on cognitive outcomes, functional performance, neuroimaging changes, and APOE4-associated therapeutic responses. **Methodology:** A systematic review and meta-analysis was conducted according to PRISMA guidelines using PubMed-indexed studies published from inception to March 2026. Randomized controlled trials evaluating ALZ-801 in adult patients with early Alzheimer's disease, mild cognitive impairment, or APOE ε4-associated AD were included. Outcomes assessed included AD Assessment Scale-Cognitive Subscale (ADAS-Cog13), Clinical Dementia Rating–Sum of Boxes (CDR-SB), Disability Assessment for Dementia (DAD), hippocampal atrophy progression, amyloid-related imaging abnormalities (ARIA), and adverse events. Studies lacking clinical outcome data, duplicate publications, and non-human studies were excluded. Data from eligible studies, including findings from the APOLLOE4 trial, were qualitatively synthesized to assess therapeutic efficacy and safety. **Result:** Treatment with ALZ-801 demonstrated slowing of hippocampal atrophy progression in patients with early Alzheimer's disease, with greater benefits observed among individuals with mild cognitive impairment (MCI). Improvements in cognitive and functional outcomes were reported through ADAS-Cog13, DAD, and CDR-SB assessments, particularly in APOE4-associated subgroups. Neuroimaging findings suggested reductions in neurodegenerative progression without evidence of increased amyloid-related imaging abnormalities. Common adverse effects included nausea, vomiting, and decreased appetite, while no significant increase in serious adverse events, brain edema, or intracranial hemorrhage was observed. **Conclusion:** ALZ-801 demonstrates potential as a precision medicine approach in APOE4-associated Alzheimer's disease by targeting toxic amyloid-β oligomer formation. Although overall clinical efficacy remains variable in broader early AD populations, favorable effects on neurodegenerative progression, functional outcomes, and safety profiles support its potential role as a disease-modifying therapeutic strategy in selected patient subgroups.

Key Words: Alzheimer's Disease; APOE4; ALZ-801; Valiltramiprosate; Amyloid-β Oligomers; Mild Cognitive Impairment; Hippocampal Atrophy; Cognitive Decline; Disease-Modifying Therapy; Neurodegeneration

ISSN 2076-6327

This journal is published by Pitt Open Library Publishing