Guidance on new treatments for early Alzheimer's disease issued

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New therapies for early Alzheimer's disease, monoclonal antibodies that remove amyloid-β plaques in the brain, are bringing hope to people whose lives have been affected by the disease. To help neurologists

discuss these therapies with patients and caregivers, the American Academy of Neurology has developed an Emerging Issues in Neurology article, published online on July 26, 2023, in *Neurology*.

Emerging Issues in Neurology articles are designed to provide timely guidance to neurologists and other clinicians, derived from expert consensus about new or emerging issues, that have immediate implications for patient care but for which a formal evidence base is still evolving.

"Neurologists care for millions of people with Alzheimer's disease and many people with early forms of dementia are eager to learn if these new therapies could help them," said American Academy of Neurology President Carlayne E. Jackson, MD, FAAN. "To help neurologists provide the highest quality care, experts with the American Academy of Neurology have summarized the available evidence on anti-amyloid monoclonal antibodies so that neurologists, patients and their caregivers can make informed decisions together about possible treatment with these therapies."

The Emerging Issues in Neurology article was written using available information on lecanemab, aducanumab and donanemab. It is important to note that this article is not a clinical practice guideline.

"Recent data on lecanemab and other monoclonal antibody infusions targeting amyloid-β protein make clear that new agents are highly likely to be part of the toolkit for neurologists caring for people with Alzheimer's disease," said article author Vijay K. Ramanan, MD, Ph.D., of the Mayo Clinic in Rochester, Minnesota. "While the formal evidence base is still evolving, this article was created with expert consensus until there is enough evidence on these therapies to inform evidence-based recommendations."

Lecanemab received traditional FDA approval on July 6, 2023. Aducanumab received accelerated approval from the FDA in June 2021 but has not yet received traditional approval. Aducanumab is currently available only to people participating in a clinical trial. Donanemab is not yet approved, but a decision on traditional FDA approval is expected later in 2023.

The article explains who is eligible to receive these therapies. Currently only people with early symptomatic forms of the disease, mild cognitive impairment or mild dementia due to Alzheimer's disease, may qualify to receive lecanemab. In addition, the article says people should be counseled about certain genetic risk factors and must not have a history of certain types of strokes. This is due to the risk of a serious side effect called amyloid-related imaging abnormalities, or ARIA, which is brain swelling and bleeding in the brain that can lead to death.

For this reason, people taking certain anticoagulant medications that are commonly prescribed to older adults may also not be eligible. There have been three deaths linked to lecanemab. The article notes that at least two of those people were given anticoagulants while on the therapy.

While the goal of using these therapies is to remove amyloid-β plaques to slow cognitive decline, the article notes the therapies are not a cure for the disease. It also explains that the reduction in the rate of cognitive decline seen over 18 months in some studies may not be evident to the people receiving these therapies.

The article discusses the high cost of these therapies and notes that additional costs will come with diagnostic testing, administration and safety monitoring. The drugs are administered through regular infusions and monitoring requires multiple brain scans. Plus, there is a shortage of neurologists and medical professionals needed to provide this care and meet the anticipated demand.

The article expresses concern that study participants so far have primarily been white, while Black and Hispanic people have been underrepresented. It says steps must be taken to ensure that future studies include a diverse range of participants, especially since the incidence of dementia has been shown to be higher in Black and Hispanic populations compared with white populations.

"There is much optimism that anti-amyloid monoclonal antibodies may facilitate slowing of the disease process in some people with Alzheimer's disease," said Ramanan. "Additional research is needed to further determine who may be most likely to benefit from these therapies, as well as to find ways to improve outcomes for people using them and enable future advances in this new era of Alzheimer's disease care."

More information: Vijay K Ramanan et al, Antiamyloid Monoclonal Antibody Therapy for Alzheimer Disease: Emerging Issues in Neurology, *Neurology* (2023). DOI: 10.1212/WNL.0000000000207757

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