Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting: https://reachmd.com/programs/cme/novel-and-emerging-disease-modifying-therapies-for-mild-cognitive-impairment-due-to-ad-efficacy-and-safety-of-new-dmts-for-mci/16055/

Released: 09/08/2023
Valid until: 09/08/2024
Time needed to complete: 1h 04m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Novel and Emerging Disease Modifying Therapies for Mild Cognitive Impairment Due to AD: Efficacy and Safety of New DMTs for MCI

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Cohen:
Hi. I'm Sharon Cohen, and I'm a Behavioral Neurologist in Toronto, Canada. It's my pleasure to discuss Novel and Emerging Disease-Modifying Therapies for Mild Cognitive Impairment Due to Alzheimer's Disease. We'll talk about the efficacy and safety of new and emerging therapies.

And first of all, why MCI? Well, we haven't had any drugs to treat MCI until now. And so this is really important. And we've even tried to go earlier in the Alzheimer's disease continuum, to target an earlier stage of disease, a predementia stage when individuals are still functioning well and have a lot of neurons still to preserve. And we're fortunate that we now are able to identify the MCI stage of Alzheimer's disease accurately. And there are therapies to consider.

If we look at the current Alzheimer's Disease Drug Development Pipeline, published by Cummings et al, annually, we see that in the current pipeline, and in the little round circles, that represents every drug that is targeting either mild cognitive impairment or early AD. Early AD defined as MCI due to AD and mild AD dementia. And so lots of different compounds targeting this stage of disease. And these can be found through phase 1, phase 2, and phase 3 of the Drug Development Pipeline. And we also see multiple colors here, which represent the different mechanisms of action and different targets for these drugs. So we've got a lot of breadth here. We are targeting amyloid in different ways, tau in different ways, neuroinflammation, and other mechanisms. So a very rich Drug Development Pipeline, and specifically to our interest today, targeting early AD in so many of these programs.

The anti-amyloid monoclonal antibodies in early AD have been the ones to lead the pack. Now, this is where we are seeing success and we will continue to build on this. Aducanumab was the first drug to be granted FDA accelerated pathway.

Approval, that was in 2021, based on its amyloid lowering, that was felt reasonably likely to lead to critical benefit. A confirmatory trial is currently ongoing and is necessary if aducanumab is going to have full traditional approval. Lecanemab was granted traditional FDA approval in July of 2023, based on a large phase 3 trial, Clarity AD, which showed slowing of decline in the CDR-Sum of Boxes, that's the primary outcome measure, and slowing of decline on all other clinical outcome measures, also on quality of life, and also robust amyloid clearance and impact on downstream markers of neuropathology. Donanemab yielded its phase 3 results which were presented at AAIC in 2023, and it also showed positive results for its primary outcome measure the iADRS, and its secondary clinical outcome measures which included the CDR-Sum of Boxes, the ADCS-iADL, and the ADAS-Cog 13, and biomarker outcome measures. And importantly not to ignore a failed trial, gantenerumab did not meet its clinical outcome measures, primary or secondary, in its Graduate I and II phase 3 studies. And this is felt to be because it did not lower amyloid sufficiently. So the key learning is you need to have robust amyloid lowering of a certain magnitude before you get clinical benefit.

Lecanemab and donanemab have comparable safety profiles in the sense that the most important adverse events to watch out for are infusion-related reactions and ARIA. ARIA stands for amyloid-related imaging abnormality, and occurs in two types, ARIA-E which is edema in the brain, and ARIA-H. And fortunately, although these can occur with lecanemab and donanemab, they are generally asymptomatic when they occur, and they resolve spontaneously. However, ARIA can be serious at times and needs to be monitored so that we can mitigate, either hold dosing or stop dosing. So this creates some complexity with these new drugs.

And there are other anti-amyloid approaches including gene-silencing approaches as with RNA-interfering molecules, there are tau-targeted therapies as well, that are interesting, including antisense oligonucleotides in phase 2, and a whole host of drugs targeting neuroinflammation.

So we can expect to see new players in the Drug Development Pipeline coming to market hopefully in the next years and adding to our clinical trials to treat MCI due to AD.

Thank you so much for your attention.

Announcer:
You have been listening to CME on ReachMD. This activity is jointly provided by Global Learning Collaborative (GLC) and TotalCME, LLC. and is part of our MinuteCE curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.