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https://reachmd.com/programs/cme/evolving-treatment-paradigms-for-mild-cognitive-impairment-and-dementia-how-new-dmts-will-fit-into-clinical-practice/16056/

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

Evolving Treatment Paradigms For Mild Cognitive Impairment and Dementia: How New DMTs Will Fit Into Clinical Practice

Announcer:
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Dr. Cohen:
Hi. I'm Sharon Cohen. I'm a Behavioral Neurologist in Toronto, Canada. And it's my pleasure to talk with you about Evolving Treatment Paradigms for Mild Cognitive Impairment and Dementia, and How Will New Disease-Modifying Therapies Fit into Clinical Practice?

This is a big question. And it's a question because the treatment landscape for mild cognitive impairment has changed. Number one, we haven't had treatments specifically for mild cognitive impairment due to Alzheimer's disease. And number two, the treatments we've had for dementia have been oral therapies, they hadn't required any specific monitoring, they don't cause ARIA. So they're very different from disease-modifying biologic therapy.

So because we haven't had therapies for MCI until recently, many individuals with mild cognitive impairment don't get properly diagnosed. They tend to be underdiagnosed, told that what they have is, you know, normal forgetfulness, or aging, and it may well not be, or that they're stressed, or you know, they haven't slept well. So now we really need to take an interest in this population so that people don't miss a treatment opportunity. And this is particularly the case with the full approval of lecanemab for MCI and mild dementia. And that full approval came in July of 2023. So making sure that we diagnose early and accurately has become an important consideration.

Biomarker confirmation of Alzheimer's pathology, either through cerebral spinal fluid analysis or PET amyloid imaging is currently needed in order for someone to be eligible. It's not enough to have the MCI syndrome, we also have to have the pathobiology of Alzheimer's disease. So that's a challenge, but also rewarding in that you can be sure now of what's going on with your patient rather than just guess at an underlying pathology. And it will also be important to, you know, look at additional criteria for eligibility for these new therapies. And we'll talk a little bit about that.

So healthcare providers are going to need to understand mild cognitive impairment better. This is a syndrome where people are still functioning independently, maybe not as efficiently as they did before, but they're performing all of their day-to-day activities independently. But they do have either an amnestic deficit or some cognitive impairment that they notice and that we can see on objective testing. So you know, if they have memory complaints, but their test scores are normal, they don't have mild cognitive impairment. And so we need to do cognitive testing, and then we need to consider what's the etiology, because it's not all Alzheimer's. People can have adverse effects from drugs, they could have had a stroke or head injury or another neurodegenerative disease, Parkinson's disease, for example, causing mild cognitive impairment. So we need to diagnose the syndrome, and then look at the underlying etiology with, as I mentioned, CSF or PET imaging.

And then for monoclonal antibodies that cause ARIA, such as lecanemab, we need to know that patients can undergo MRIs. So people

who may have mild cognitive impairment due to Alzheimer's, but if they have a pacemaker, or severe claustrophobia, they're not going to be candidates for lecanemab, unfortunately. That'll be true for donanemab if that drug is approved, and for other monoclonal antibodies targeting amyloid.

Access to apoE genotyping is also highly recommended in this case, not 100% required but highly recommended to inform risk-benefit analysis when speaking with patients about trying one of these monoclonal antibodies. Then, so individuals will need to think about, physicians will need to think about, number one, how do they perform apoE genotyping on their patients? And who's going to do the counseling?

Now we need to make sure our healthcare system is ready. We need more dementia specialists or wait times don't keep growing. Availability of blood-based biomarkers may help us a lot in terms of narrowing the funnel of who goes on to confirmatory PET or CSF testing. We're going to need to educate, not just ourselves about ARIA, but a broad range of healthcare workers, including emergency room physicians and radiologists so that if patients show up in these different healthcare locations, they are being told the right thing or having the right kinds of scans. And we're going to need to access infusion centers to monitor patients and to deliver medications.

There are appropriate use recommendations that were published by Cummings group, and these were published for aducanumab and then updated for lecanemab based on the accelerated pathway approval. And it is likely that there will be appropriate use recommendations that will be drug specific. So if donanemab is approved, there will likely be one for that drug. And these appropriate use guidelines are meant to assist treating physicians but not to replace the FDA prescribing information.

So I trust this has been of interest and helpful. Thank you very much for your attention.

Announcer:
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