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<https://reachmd.com/programs/cme/additional-treatments-for-alzheimers-disease/14656/>

Released: 12/30/2022

Valid until: 12/30/2023

Time needed to complete: 1h 02m

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### Additional Treatments for Alzheimer's Disease

#### Announcer:

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#### Dr. Agronin:

This is CME on ReachMD, and I'm Dr. Marc Agronin. I'm here today with my colleague Dr. Richard Isaacson.

Dr. Isaacson, we know that Alzheimer's disease is a really difficult disease to treat. There's no magic formula, despite what a lot of people would like to think. A lot of talk about immunotherapy in terms of treating Alzheimer's disease. But there are other treatments that have been out there, other ones that are being studied now. I thought it'd be good to have a discussion about that space and how to guide people who are looking for something beyond just the standard of care. Any thoughts about this?

#### Dr. Isaacson:

Sure. So I think in terms of clinical trials, there are so many mechanisms. As the saying goes, there's a lot more shots on goal nowadays than in the past when we were just kind of hyper-focused on amyloid. So there's anti-tau agents that are being studied, there are agents related to glucose hypometabolism, there's neuroinflammation which is really important. Another mechanism, there's antibodies against galectin-3 and other types of immunotherapy. So I think the take-home point here is that there's different potential pathological factors, and the different studies that are ongoing now are going to try to tease those out.

The other thing is there's also non-drug approaches, for example, different lifestyle interventions may be more effective in different people, different nutritional interventions, omega-3 fatty acids probably don't work at all if you don't have an APOE ε4 variant and don't work at all if you have dementia. But what about in someone pre-Alzheimer's disease that has the APOE ε4 variant? Maybe the omega-3s, DHA specifically, is right for them.

So I think the take-home point with where the field is going and additional treatments, we still have a lot to learn. We still have a lot more studies to be completed. But I'm pretty excited about it.

Marc, what are some of the treatments that you're most excited about?

#### Dr. Agronin:

Sure. There's so many different active clinical trials going on. In terms of symptomatic improvement, there's studies going on of something called piromelatine, which is a melatonin and serotonin receptor agonist. And the focus is can this improve cognition? We have our standard acetylcholinesterase inhibitors, we have memantine, other agents that we could either substitute or add to those that could further improve cognition.

In terms of disease modification, there are some variations in immunotherapy which are being looked at. So for instance, there's semorinemab, which is an anti-tau immunotherapy, and other immunotherapies that have been looked at. TB006 is interesting. It's immunotherapy against something called galectin-3. And the theory here is that if we can interrupt the buildup, the actual aggregation of

either amyloid or tau into the really toxic species of it, can we either stop or slow down the disease in its tracks? Another medication ALZ-801, also known as valiltramiprosate, is focused on anti-aggregation of the amyloid oligomers. And if we look at the amyloid hypothesis, as an example, we know that it evolves from monomers to oligomers and then gets bound up in plaque. And so we're trying to figure out at which point along the way does it make most sense to intervene to make a difference?

Now, you also talked about neuroinflammation. I think that's a good point. And do you find that approaches like diet, other supplements may be perhaps the best approaches to that aspect of this disease?

**Dr. Isaacson:**

Yeah, I think in theory, maybe, but the problem is we don't have the best biomarkers for neuroinflammation. We don't know what to track over time to understand if we're truly having target engagement. You know, we can track amyloid; we can track tau. So I think with some of these other targets, we don't have biomarkers; we can't follow them. But I still believe that multiple shots on goal is critical. And I also believe that the way that our treatment mechanism will evolve is to personalize care, because different people may need different specific cocktails of treatment. And I think that's what I'm really excited about in the years to come.

**Dr. Agronin:**

I would say the key takeaway here is for someone with especially early Alzheimer's disease, but at any stage, look at what clinical trials are out there. There's an enormous variety of trials; it's important. There could be benefit in terms of just being monitored more closely for the diagnostics and potential benefit if this is what's going to be the next medication on the market.

So, Dr. Isaacson, this has been a brief but great discussion. Unfortunately, our time is up. To everyone, thank you for listening.

**Announcer:**

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