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### Future Frontiers: The Future Landscape of Alzheimer's Therapeutics

#### Announcer:

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#### Dr. Hardy:

This is CME on ReachMD and I'm Dr. John Hardy, and today we're going to discuss the future landscape of Alzheimer's therapeutics, which I think is a very exciting and challenging area of research and clinical research, right now.

What could those future improvements be? The first future improvement would be to be able to make earlier diagnosis. Earlier diagnosis, if accurate that is, would mean that one could, if you like, save more of one's cognitive ability. But also, earlier diagnosis, if one could start making diagnoses before amyloid build up in the blood vessels, one could perhaps reduce the ARIA complication of the use of these therapies.

The second way we can think of making improvements is through easier administration, and through the use, perhaps, of drug holidays. Can we move from intrathecal to subcutaneous, administration? I think that's a very likely improvement, which is being tested right now by several drug companies. And drug holidays, can we, once we've removed amyloid from the brain, can we then, not give the drug for a period until amyloid starts to build up again? That would both reduce the cost and the caregiver and medical burden, also.

Avoidance of ARIA. As ARIA is caused by the antibody hitting the blood vessel, amyloid. And if one could get through the blood-brain barrier and get higher concentrations of the antibody in the brain parenchyma, then one could reduce the, amount of antibody given and increase its effectiveness, and therefore perhaps reduce the complication of ARIA.

The next way is, can we think of ways of, other amyloid-based therapies? There have been failed therapeutic trials of the enzymes, inhibiting the enzymes which produce amyloid, that's beta secretase and gamma secretase. One could imagine, although those trials failed, now we have got a way of removing amyloid from the brain. Perhaps in that context, these usually pill-based therapies might have a second life, if you like, in the context of amyloid antibodies. So, we might, be able to move back to these failed trials and revisit these chemicals and revisit them in the context of amyloid anti-amyloid antibodies.

And finally, can we use non-amyloid therapies? Can we use anti-tau therapies? Dealing with these quickly, yes, we can, get better at diagnosing earlier. We can use genetics, as we and others have shown, using polygenic risk score analysis, that's shown in this paper here. We can, use genetics to identify people who were at high risk of disease and concentrate our clinical efforts on those. And the, in terms of drug holidays, subcutaneous versions are now under development of testing, and current self-administrative, like current self-administered insulin injections. And the advantage of this is that no medical supervision would be required.

So, now we know what amyloid therapies need to achieve. We now have a much better, notion of what our goal has to be in other anti-amyloid therapies. And so, for that reason, I'm very excited and enthusiastic and believe that we will get better therapies in quite a short order from now.

**Announcer:**

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