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/lipids-and-the-brain-extending-cardiovascular-risk-reduction-to-neurodegenerative-disease/85305/

Released: 10/28/2026
Valid until: 10/28/2027
Time needed to complete: 1h 03m

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

Lipids and the Brain: Extending Cardiovascular Risk Reduction to Neurodegenerative Disease

Announcer:
You're listening to GLC on ReachMD. This activity is provided by Global Learning Collaborative and 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. Ballantyne:
Welcome to CE with GLC. I'm Dr. Christie Ballantyne. Here with me today is Dr. Philip Scheltens. Our discussion today will focus on cardiovascular risk reduction and neurodegenerative disease. So this is, I think, a really exciting area. There have been some emerging data regarding the mechanistic link between lipid biology, HDL-mediated transport, and neurodegeneration. Philip, can you elaborate on this for us?

Dr. Scheltens:
Yeah. Thank you, Kristi. It's a very exciting time actually in the Alzheimer field in many ways. Cholesterol plays an important role in Alzheimer's disease, and we know that actually because APOE4 is the biggest risk factor for Alzheimer's disease. If you have one allele, you have 8 times the chance to get it, and 2 alleles, you have 16 times.

And APOE4 is known to carry cholesterol in the blood, to the brain actually over the blood-brain barrier. So cholesterol in itself actually plays an important role in the neurons, in the pathophysiology of Alzheimer's disease. So we know that cholesterol is in the neurons. It has a connection to Alzheimer's disease.

It has a connection to APOE4. But thus far, any sort of intervention, targeting lowering cholesterol, for instance, has failed.

Dr. Ballantyne:
So it's really fascinating. I started off as a basic researcher working in mice, but we looked at a lot of tissues, but it's really quite clear that the brain has the highest cholesterol content of any organ. It has its own cholesterol metabolism, which is mostly HDL particles, which is quite interesting.

There's some phase 3 data on obeticholic acid, which has, I think, some very interesting implications in terms of Alzheimer's disease and what's going on in the field with biomarkers. Can you summarize this for us?

Dr. Scheltens:
So obeticholic acid is a CETP inhibitor. So what it does actually, it lowers your LDL cholesterol, but it increases your HDL cholesterol. And the latter part is really very important. This HDL component of obeticholic acid, it could play a role in Alzheimer's disease exactly for the reason you mentioned, because cholesterol in the neurons is related to HDL.

© 2026 ReachMD

HDL particles can actually cross the blood-brain barrier, can actually try to remove cholesterol from neurons.

So now with the advent of blood-based biomarkers, you can actually get a sense of the Alzheimer's disease pathology by doing a blood test. And notably p-tau217, for instance, gives you a very good indication of the amount of amyloid and tau in the brain. Very exciting. In the blood, you know?

So it's very far from the brain, but it does give you a very good indication. It's actually now also officially approved by the FDA as a diagnostic test. Now we knew this test was there already, and in the Broadway trial, we tagged on that trial from baseline, and at 12 months we measured the blood-based biomarkers.

And this was a placebo-controlled trial, and we looked at the changes in the blood-based biomarkers over 12 months as a result of the obeticholic acid intervention. And lo and behold, we saw actually that especially in APOE4 carriers, 1 or 2 alleles, you saw a decrease in p-tau217 as opposed to placebo, over a year time.

And this has never been seen before, so it's a cholesterol-lowering drug, lowering LDL, increasing HDL. This has actually a huge influence on Alzheimer's disease pathology as measured with the blood-based biomarkers, and that is actually quite striking. We presented this last year at the AIC, at the Alzheimer's World Conference.

Dr. Ballantyne:
So in summary, what we have is a secondary analysis of a trial done in high-risk individuals for cardiovascular disease or with cardiovascular disease, Broadway. and looking at, at, at, the most promising biomarker for Alzheimer's, p-tau217, you saw a reduction and it was in those individuals with APOE4, who, as you mentioned, are at the greatest risk for Alzheimer's.

For those of you who are more cardiology or internal medicine oriented, I'm the PI of a laboratory for the atherosclerosis risk in community study. At age 75 on the fifth visit, if you looked at people with cardiovascular disease you follow them for 5 to 10 years, they were more likely to end up with dementia than to have a recurrent heart attack or stroke.

I think that we don't think enough about the cognitive risk, and there's this issue interplay between vascular dementia and then also neurodegenerative disorders related to Alzheimer's. So having a drug that might be beneficial, we'll find out, for both the vascular and the neurodegenerative would really be...I mean, that's exciting.

Dr. Scheltens:
Yeah. It's interesting that you mention this, Dr. Valentine, because I think for cardiologists, it's really very interesting to know that if you look at the Broadway baseline, a third of the individuals at baseline, and these were recruited because of their cardiovascular disease, and they were hypertension, diabetes, et cetera.

A third of them had already increased p-tau levels. So basically, they had the disease already at baseline, and this has been replicated in other sort of natural history studies. And it's a common fact, as you say, that a large proportion of patients you see, you treat them for the cardiovascular disease, but underlying they may also have Alzheimer's disease.

And now we can tackle that with these broad-based biomarkers, and obicetrapib may be an ideal drug to tackle both of the things to lower your risk, cardiovascular risk, but also lower your Alzheimer risk. But that, of course, has to be proven.

Dr. Ballantyne:
Has to be proven. It's very exciting about this, this data. So this has been a great, we call it a bite-sized conversation. It's a large topic, very important, but our time is up, and thanks for listening.

Dr. Scheltens:
Thank you.

Announcer:
You have been listening to GLC on ReachMD. This activity is provided by Global Learning Collaborative and is part of our MinuteCE

© 2026 ReachMD

curriculum.

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

© 2026 ReachMD