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Therapeutic Insights: Navigating the Use and Challenges of Disease-Modifying Therapies

Announcer:
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Dr. Hardy:
Hello, this is CME ReachMD and I'm Dr. John Hardy. Today, we're going to discuss the use and challenges of disease-modifying therapies in Alzheimer's disease.

So, there are two major issues in the use of disease-modifying therapies in Alzheimer's disease. The first is early and accurate diagnosis. We need, if we're going to give an anti-amyloid therapy, we need the patient that we're giving that therapy to has amyloid pathology. Obviously, one doesn't want to give an anti-amyloid therapy to somebody without amyloid pathology. And so, this is absolutely key in the use of anti-amyloid therapies. And so, to use these therapies, one needs to have done either a PET scan or a CSF assessment of amyloid pathology, or as they come on board, a blood marker test, for amyloid pathology, though that is clearly, required for therapies.

The second issue, equally important, is safety monitoring, especially with respect to ARIA. ARIA, the word ARIA stands for amyloid related imaging abnormality. Now, what ARIA is, is it's caused by the antibody you're giving coming into contact with the cerebrovascular amyloid at high concentration. Remember, the cerebral vascular amyloid is outside of your blood-brain barrier, and so when you give an amyloid antibody, this is the first thing it hits, and it hits this, cerebrovascular amyloid at a much higher concentration than the antibody gets into the brain. And then, you get and, an inflammatory macrophage attack. This is more of an issue in APOE4 homozygotes than it is in other cases, though it's an important issue in all cases. The reason it's important, particularly important in E4 homozygotes is because E4 homozygotes have more vascular amyloid.

Because of the way I've just told you about the pathogenesis, this ARIA, effect is usually early in the treatment after the first or second dose, and it's believed that this is the case, because after this, first or second dosing, most of the amyloid has been removed from the blood vessel, and so it's no longer an issue. Now, what are the symptoms? Well, the symptoms usually are just a headache, or in fact, often the patient is not, aware of any symptom at all. But the inflammation is seen on an MRI, that's why it's called amyloid-related imaging abnormality. However, although most cases are benign, it's occasionally dangerous and associated with hemorrhage. And because of this, it needs to be carefully monitored, and that there's a need to exclude individuals who are on anticoagulant drugs, because obviously, if you have a hemorrhage and you're on an anticoagulant drug, that hemorrhage can have serious consequences. And so, this requires MRI monitoring at the moment.

Whether as we learn more about the, control of ARIA and how to deal with it, we might be able to slightly relax these monitoring requirements is possible. But at the moment, giving, lecanemab and other amyloid antibodies requires MRI monitoring and listening to the patient, also, to see if ARIA is a problem in that patient. And if ARIA is a problem, then probably at least a drug holiday is requested.

So, thanks for listening to this lecture.

Announcer:

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