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# How Much Should We Worry About Amyloid-Related Imaging Abnormalities?

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**Dr. Isaacson:**
Welcome to another episode of the Frontline of Alzheimer's Care. I'm Dr. Richard Isaacson. And here with me today to help answer these questions are doctors Gayatri Devi and Pierre Tariot. We have some very important questions from Dr. Paul Stander, and nurse practitioner, Ms. Michele Grigaitis-Reyes, about the safety of anti-amyloid therapies.

**Dr. Stander:**
I'm aware that there are potential bleeding complications with the use of these medications. So I'm just wondering, are you avoiding prescribing these medications in patients who require anticoagulants or antiplatelet medications for other medical conditions they may have?

**Ms. Grigaitis-Reyes:**
The Alzheimer's Disease and Related Dementias Therapeutic Workgroup as well as the American Academy of Neurology guidelines for the use of lecanemab, they both recommend risk discussions regarding those results, whereas the VA criteria for use identifies the E4 homozygous as exclusionary. So I'm interested in what circumstance would you recommend lecanemab to the E4 homozygous patient?

**Dr. Isaacson:**
Well, these are really relevant, and I would also say, really challenging questions. In our practice, we are very cautious

When it comes to anticoagulants, I have not personally put any patients on anticoagulants and we just - actually Dr. Devi and I comanaged a patient who had a stroke, an embolic stroke during their course of the anti-amyloid treatment. And they also had some arrhythmia potentially, that we're actually as we speak, working up. What do we do? Antiplatelets don't treat embolic stroke, but they may be safer, of course, then anticoagulant. And anticoagulants would probably have to stop the anti-amyloid drugs, and the patient doesn't really want to do that, because the patient's doing okay. So these are really complicated questions. And that's a general part of my thoughts.

When it comes to guidelines related to E4 homozygotes being exclusionary for the VA you know that's tricky. I really believe that if you fully follow the FDA label and you titrate as the studies did, sure, there is an increased risk of side effects and adverse events and possibly death. But maybe in E4/4's, that plan should be modified. And that's really what we do with precision medicine. Someone has a specific gene, and you tailor that therapy, you personally tailor the therapy for that person, maybe you start with a lower dose of the drug and you'd have a slower titration and then you'd have more frequent MRI monitoring. So I wouldn't necessarily say that E4/4's would be exclusionary, especially with lecanemab, which is hard to cross compare but lecanemab may be among them more safer, well tolerated anti-amyloid drugs when it comes to these side effects.

Dr. Devi you do this every day, we've worked on this together pretty closely. What are your thoughts about approaches to ARIA risk factors and prescribing strategies?

**Dr. Devi:**
So I actually don't have a hard and fast rule about antiplatelets or anticoagulants, and the use of the anti-amyloid agents. Generally speaking, I avoid them. However, I do have a patient in my practice who we've decided to put on medication and titrate up very slowly.

**Dr. Isaacson:**
Great. Dr. Tariot, any comments?

**Dr. Tariot:**
So I'll add three brief points. Number one, remember that trials conducted to achieve health authority approval for marketing don't fully inform practice. So we need data from the field from people like Dr. Devi, Dr. Isaacson, and phase 4 studies to fill in these gaps. Related to that I like to just note that the donanemab phase 3 program did allow anticoagulants and antiplatelet agents and didn't actually see a relationship between that treatment and adverse events. So we just need more data.

Lastly, the people in our hands who have the greatest risk for ARIA are people who have cerebral amyloid angiopathy at baseline. The trouble is, there's no good biomarker for that, so probably the best you can do these days, is be super careful with you and your neuroradiologists about establishing whether or not there are microhemorrhages at baseline. And if they're more than four, that's probably somebody who shouldn't get this therapy.

**Dr. Isaacson:**
Well, thanks so much. It was a very comprehensive answer to two very important questions. Really appreciate Dr. Stander and Ms. Grigaitis-Reyes for raising these critical considerations. Viewers can check out our other episodes to hear more key questions about the clinical use of amyloid-targeting therapies. Thank you for listening.

**Announcer**:
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