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Clinical Conundrums in ARIA: Evolving Approaches to Mitigate ARIA Risk in Patients Prescribed Anti-Aβ mAbs

Announcer:
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Dr. Bateman:
Welcome to Clinical Conundrums: Navigating Case Scenarios in Your Own Practice Setting, where we will cover quick and challenging cases related to amyloid-related imaging abnormalities, or ARIA, management. I'm Dr. Trey Bateman, and here with me today is Dr. Joy Snider. Let's dive into our case.

Dr. Snider:
Well, this case is Edward, who's a 75-year-old patient who has mild impairment due to Alzheimer disease, and he's interested in starting donanemab. He is concerned about the side effects, and has asked whether there are alternative strategies to reduce the risk of side effects.

Dr. Bateman:
That’s a valid concern. So Joy, could you explain the recent data from TRAILBLAZER-ALZ 6 and how the modified titration regimen compares to the standard dosing regimen with donanemab for reducing ARIA risk?

Dr. Snider:
Sure. TRAILBLAZER-ALZ 6 is a study that explores different dosing regimens in using donanemab. And the regimen that seemed to really be beneficial was a regimen where, basically the titration, instead of being two doses of 700 mg and then going to the full dose of, let's see, 1,400 mg, is to take the first dose and reduce it from 700 to 350 mg, do the second dose at that 700-mg dose, then add the 350 from the first dose to the third one, so it's 1050 and then you hit the full dose by the fourth treatment. So this is actually the same amount of dosing over that first 4 months, it just has a more gentle titration up to that full dose that you get after 4 months.

And this, at least in the study provided, and it wasn't a huge study, there were several hundred participants, not 1,000 but did dramatically reduce the UH risk of ARIA-E in these patients, and particularly also reduce it in the APOE4 homozygotes, which is an area of big concern. So this dosing regimen seems to reduce the amount of ARIA-E. It did not, as best they could tell, again in a study with small numbers, reduce the clearance of amyloid. It didn't reduce the overall dose of the drug. Really didn't change the pharmacokinetics after that fourth dose. So seems to offer similar reduction of amyloid. We would assume similar efficacy, although that wasn't tested in this study as yet, with lower risk of side effects. I think many of us, as we start treating with donanemab, are planning to use this altered dosing strategy, because it seems to be a win-win. Even if the numbers in the long-term aren't as robust as they were in this small study, it still seemed to offer, based on looking at the confidence intervals of the data, it'll offer some reduction in risk. So seems to offer reduction in risk, no change in efficacy. So it is a great idea.

Dr. Bateman:
Yeah, this seems like really a win-win, as you said, based on a small number of patients, but similar efficacy in target engagement with a reduction in ARIA is really a good goal. So this is not something that we've started doing in our practice yet, but I think it's something that everyone I've spoken with who is using donanemab is interested in doing. One of the challenges that some people have expressed is that, technically, this could be considered off label, because you're not dosing it in the way that it's in the package insert. So is this a concern there at your practice, or something that's come up?

Dr. Snider:
It is. Absolutely concerned, and I answered emails about it this morning. So our accounting department is certainly very interested in if insurers will cover this modified dosing. And full disclosure, we are dosing our first patient, I think tomorrow. So we are working on ways to order the modified dosing in our EMR, and are hopeful that it will be reimbursed. But that is something that we will all have to explore over the next few weeks. Certainly, it doesn't change the overall cost. Doesn't change the number of infusions, even the number of vials. But in the current environment, where it is hard to get these drugs covered, it does offer an additional challenge.

Dr. Bateman:
Yeah, this really speaks to the fact that it's a changing landscape. Every few weeks or months, we are learning more about the best way to logistically approach and handle this. So really great discussion, and hopefully an important future where we're coming up with even more ways that we can reduce the risk of ARIA while still maintaining the same benefit from these infusion therapies.

Thank you for this insightful discussion. To our viewers, be sure to explore our other episodes for more in-depth insights into the nuances of ARIA management. Thank you for joining us.

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