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What Types of Changes, If Any, Should We Expect with Amyloid-Targeting Therapy?

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Dr. Isaacson:
In this episode of the Frontline of Alzheimer's Care, where we're answering real questions from real clinicians about amyloid-targeting therapies in Alzheimer's disease. I'm Dr. Richard Isaacson, here with Drs. Gayatri Devi and Pierre Tariot. Dr. Chong has an interesting question for us.

Dr. Chong:
So these treatments we're told only slow the progression of Alzheimer's disease. But you know, with donepezil and memantine, sometimes we actually see improvements in patients' clinical functioning. And although it's not to be expected per, you know, what the manufacturer is telling us, I'm wondering if you have ever seen clinical improvement in your treated cases? And how do you counsel patients and families who ask if there is the potential for actual improvements?

Dr. Isaacson:
Well, I look forward to this discussion, because I think getting to know both of you over the years, and also comanaging patients, I think we're all very conservative and we're very cautious about kind of the motto of promising not to overpromise and that, you know, people will get less worse, but they won't get better, and really caveating things, and whether they sign that in the consent form when it's phrased that way, I think we're all very cautious, and we're not kind of over promisers by nature.

Dr. Tariot, what are your thoughts here? You know, aside from philosophically, how do you approach this question? What have you seen? What have you felt? And what are some best practices?

Dr. Tariot:
The first point would be to remember that you can't extrapolate from between-group differences in a large clinical trial, to what will happen to the individual in front of you. You know, Richard, if I start you on a statin, I can't tell you if you will or won't get a heart attack. I can talk about probabilities only. And certainly, the evidence suggests that, as you just said, at a group level, reduced rate of decline is what's to be expected. We don't know if that continues to increase over time. It's beginning to look that way. That would be a big win, in my opinion. There's also discussion about, instead of saying, oh, this slope changed this amount, this line slope changed that amount, that's a between-group difference of 30%. Trying to translate that into time. So how many months over 18 months am I likely to not progress at all? That I think is the way we're beginning to have these kinds of conversations to the exact question, have we seen improvement? Not that we would hang our hats on it.

Dr. Isaacson:
Dr. Devi, what are your thoughts?

Dr. Devi:
So I would say unequivocally in two patients, there has been what I would consider improvement. One is the patient that you and I share, Richard, who we caught very, very, very early in the disease condition, who was mildly impaired, that I started on aducanumab, and who cleared plaque within the 18 months on a very slow titration and currently it plaque negative. Who's shown objective evidence of improvement on his neurocognitive assessment. Again, as Richard pointed out, I'm not sure how much of this was from the clearing of the plaque and any direct benefit from aducanumab, and how much of it was from all the other ancillary treatments that we were deploying with this particular patient.

Another patient where I found there was significant benefit unequivocally, was a woman who was 74 years old, who came in with a very strong family history of early-onset Alzheimer's, who was fairly significantly impaired on cognitive stress testing who I started on aducanumab in July of 2021, and had a very slow titration. She was homozygous for the APOE4 allele, and 18 months later she was just on 6 or perhaps 7 mg/kg of aducanumab, and she had cleared all plaque on repeat imaging of her amyloid. And she had significant improvement on her neurocognitive testing. So that was a patient who likely benefited from the amyloid treatment, although again, I can't 100% say that it wasn't also from the ancillary treatments that she received.

Dr. Isaacson:
Well, I think as we gain more clinical experience as a group and as a scientific community hopefully we'll be able to answer this question with much more objective data.

So thank you, Dr. Chong. Such a great question. Viewers can check out our other episodes for more of what clinicians want to know about the clinical use of anti-amyloid therapies. Thanks for tuning in.

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