

### Transcript Details

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## Unraveling the Mechanism: How Ocrelizumab Impacts Cortical Lesions in MS

### Announcer:

Welcome to *NeuroFrontiers* on ReachMD. On this episode, we'll explore the possible mechanisms behind ocrelizumab's effect on cortical lesions in multiple sclerosis with Dr. Michael G. Dwyer. He's an Associate Professor of Neurology and Biomedical Informatics with the University at Buffalo in New York. Let's hear from Dr. Dwyer now.

### Dr. Dwyer:

So essentially, one of the ways that many people think these lesions are progressing is that there are B-cell follicles that are resident in the meninges of the brain that are essentially contributing to these cortical lesions. And there are a couple of imaging techniques to look at that specific mechanism of these B-cell follicles. And what's interesting is the studies that looked at that with ocrelizumab were a little bit mixed, so it didn't seem to be having a huge impact on these B-cell follicles.

So we were a little bit curious as to whether it would have this effect on cortical lesions. And so the fact that we do see this effect on cortical lesions, despite it not having as much of a potential effect on the B-cell follicles, tells us potentially that there is some other mechanism for these lesions themselves and that some sort of interaction—I would guess in a B-cell mediated way—is impacting these lesions. And that really interestingly actually dovetails with another presentation that was also given at the recent ACTRIMS meeting looking at a marmoset model of MS, where they actually unveiled pathology for these cortical lesions. So from a completely different angle, they were also saying that there might be a different mechanism for these lesions. I can't speculate too much further than how the drug is doing it, but it's modifying something that is contributing to the growth of these lesions. Is it just a downstream effect? Is it slowing down the white matter lesions and somehow that's slowing down the cortical lesions? But what we saw was that the correlation between white matter lesion accrual and cortical lesion accrual was very modest—about 0.3. So it doesn't appear to be just mediated through the white matter lesions. There's something else going on here.

So the first question was whether these lesions are affected by the therapy. And now that we know, yes, I think we should spend some more time and effort to understand how and why. What is the root mechanism by which it's reducing these lesions? And if we can find and pull on those threads, maybe we can even improve it. We can go from 75, which is already great, to 95 or a hundred percent knocked down. And to do that, we need to understand exactly how it's working; we don't have a perfect understanding of the mechanism because we don't know exactly how it's impacting these B cells, especially the ones within the blood-brain barrier. But it's unquestionably doing something.

### Announcer:

That was Dr. Michael G. Dwyer discussing the potential mechanisms driving ocrelizumab's impact on cortical lesions in multiple sclerosis. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!