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Advancing MOGAD Care: Insights from the METEOROID Trial

**Narrator:** Welcome to Neuro Frontiers, a series in which Practical Neurology partners with Reach MD to bring you clinical research and advancement that further clinicians' ability to diagnose and treat neurologic conditions. What do the latest meteoroid trial results mean for neurologists treating MOGAD? In this episode, Dr. Michael Levy from Massachusetts General Hospital discusses relapse prevention, diagnostic challenges, and the future of MOGAD management with Dr. Peter Sguigna from UT Southwestern Medical Center.

**Dr. Peter Sguigna:** Hello, I am Peter Sguigna with the University of Texas Southwestern. I'm joined today for our "Practical Neurology" podcast by the one and only Michael Levy, world-renowned MOGAD expert. Thanks for joining the podcast. Happy to be here. Dr. Levy, Practical Neurology has written a few review articles that I would refer the listeners to for some background, but as a very quick introduction, can you give a brief outline of what MOGAD is?

**Dr. Michael Levy:** Yeah. MOGAD is an autoimmune demyelinating disease mediated by immune attacks of the optic nerve, spinal cord, and brain. The attacks cause vision loss if it's in the optic nerve, weakness and numbness and bowel/bladder dysfunction in the spinal cord, and usually ADEM or seizures and cortical attacks in the brain.

**Dr. Peter Sguigna:** And these can be recurrent in about half the time or about monophasic about half the time

**Dr. Michael Levy:** And as a rare disease, it's been incredible to see the formal diagnostic criteria being published in recent years and to the first phase 3 clinical trial being recently published. Can you tell us a little bit of what was called METEROID? Well, first, you referenced the criteria. The criteria were really critical because up to now, up to around 2017 or so, I would say, MS and MOGAD were not easily distinguishable.

And then we got a great MOG blood test and the criteria in 2023 that really helped distinguish MOG from MS, and we recognized that MS treatments do not necessarily help prevent MOG attacks. So we launched into new trials based on good science about the immunopathogenesis of MOG, and went towards two different types of therapies that are not used in MS, and we're developing them for MOG now, and one of them is METEROID.

And so this was a phase 3 clinical trial, and again, this is a rare disease, so there's been a lot of regulatory attention to conditions that are like this and are similar to this. And was this a clinical trial only for adults? So the inclusion criteria required people to be at least 12 years of age, and we really tried hard to enroll adolescents, but unfortunately, we only got, I believe, like seven total, and most of them ended up in the placebo arm.

**Dr. Peter Sguigna:** So most of the cases were adults, 132 people total, out of which the vast majority were adults. And it was international, 65 sites, I believe, all across the world And so it's great to see the community come together in engagement with, pediatric neurology colleagues. Now, this agent, the satralizumab, is an FDA-approved drug for other conditions, but were there any new safety concerns when it was studied in this population?

**Dr. Michael Levy:** Yeah. The drug is satralizumab, which is an interleukin-6 receptor blocker. It is approved for aquaporin-4 seropositive neuromyelitis optica spectrum disorder. People may recognize the older version of satralizumab, which is called tocilizumab, which is approved for arthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, and vasculitis.

The newer version, satralizumab, which is approved for NMOSD, is monthly, and it's a subcutaneous injection. In the trial for NMOSD, and now we have over five years of safety data, the side effects have been relatively mild. We notice fibrinogen goes down and lipid levels go up a little bit. There's some neutropenia early on in the treatment.

**Dr. Peter Sguigna:** But the side effects that patients feel, generally injection site reactions and occasional headaches, and that's pretty


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much it. And you had kind of alluded to an interesting challenge earlier in the talk. MOGAD as a condition is very much dependent on this antibody assay, and I know you were very involved with its development.

**Dr. Michael Levy:** It was a very technically challenging assay to conduct, and one of the concerns is, are the right people getting access to this advanced testing? Yeah, you're right. The test is called a cell-based assay, and there are two different types. There's the fixed, which comes as a convenient kit from Euroimmun, or there's the live cell-based assay, which I think is only available in the US at the Mayo Clinic.

The live cell-based assay is much better. It's much more sensitive. And as far as access goes, I guess anyone could send it there, but obviously there are contracts and costs, and worldwide, it's also a struggle to get live cell-based assays anywhere outside of the US, UK, and other parts of Europe. There are problems getting the test.

**Dr. Peter Sguigna:** The fixed cell-based assay, as I said, is just a little bit less sensitive, but it's fairly widely used throughout the world. Exactly. And in the setting of now what sounds like a positive Phase 3 study, should this reshape how neurologists across the United States approach these patients who may be coming in with their first event of optic neuritis or transverse myelitis?

**Dr. Michael Levy:** So, that's a trick question, 'cause you said for their first event. This trial only enrolled people who had relapsing disease. So, if you have your first event of MOG, you're not guaranteed to have a second. You're only 50/50 chance of having a second event. There's still a lot of debate about what to do for those people and how to make sure that people who have their first event don't have a second event.

**Dr. Peter Sguigna:** But if you do have a second event and you're in the relapsing group, this treatment helps doctors to treat those patients and make sure they don't have a third, fourth, and fifth event. No trick intended. Thank you for that response. I would entirely agree with that assessment. We're very much looking forward to more data and possibly even regulatory decisions.

**Dr. Michael Levy:** Is there anything else you would like to share with our listeners today? Well, yeah, let me tell you the results of the study. So we had-- We'd enrolled 132 people. They were randomly assigned to either weight-based dosing of satralizumab or placebo. If you were on a background immunosuppressant like mycophenolate or azathioprine, you were allowed to stay on that stable dose.

And it-- the two arms were stratified by those people who were using background immunosuppressive therapies to be equal in each arm. They were treated monthly and followed for two years. The primary outcome measure was time to first attack. What we found is that by as early as about eight weeks, the placebo curve and the satralizumab curve began to diverge.

And by one year, there were only 13% of people who relapsed in the treatment arm, whereas 33% of the placebo arm had relapsed. Over the course of the whole study, there were 24 relapses in the placebo arm and only nine in the satralizumab arm. So the overall hazard ratio was 0.32, which translates to a risk reduction of 68%.

And remember, that's on top of background therapy. So what we can confidently say in this scientific, rigorously conducted, blinded, randomized, placebo-controlled trial is that satralizumab reduces the risk of relapse by 68%.

**Dr. Peter Sguigna:** Those are impressive numbers. Any other highlights from the trial? There were some secondary outcome measures. There were fewer MRI lesions. The annualized relapse rate was lower. The number of  treated patients in the satralizumab arm was lower. So everything correlated with satralizumab being more effective.

**Narrator:** And then on the safety side, as I mentioned, there were no new safety signals. We are planning to submit to New England Journal of Medicine in the next couple of weeks, and FDA filings are gonna go in May. Thanks again for joining us, Dr. Levy.

Thank you, doctors, for sharing your knowledge in this episode of NeuroFrontiers, and thanks to you, our listeners.

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