CosMOG - Clinical Trial for MOGAD Treatment

You can listen to the audio of this podcast at: youtu.be/2RtSL2hwhU0

[00:00:00] **Krissy Dilger:** Hello and welcome to the SRNA, “Ask the Expert” podcast series, “Research Edition.” This podcast is titled “CosMOG - Clinical Trial for MOGAD Treatment.” My name is Krissy Dilger, and I moderated this podcast. SRNA is a nonprofit focused on support, education, and research of rare neuroimmune disorders. You can learn more about us on our website at wearesrna.org. Our 2023, “Ask the Expert” podcast series is sponsored in part by Horizon Therapeutics, Alexion, AstraZeneca Rare Disease, and Genentech. Horizon is focused on the discovery, development, and commercialization of medicines that address critical needs for people impacted by rare autoimmune and severe inflammatory diseases. They apply scientific expertise and courage to bring clinically meaningful therapies to patients. Horizon believes science and compassion must work together to transform lives.

[00:01:10] Alexion, AstraZeneca Rare Disease is a global biopharmaceutical company focused on serving patients with severe and rare disorders through the innovation, development, and commercialization of life-transforming therapeutic products. Their goal is to deliver medical breakthroughs where none currently exist, and they are committed to ensuring that patient perspective and community engagement is always at the forefront of their work. Founded more than 40 years ago, Genentech is a leading biotechnology company that discovers, develops, manufactures, and commercializes medicines to treat patients with serious and life-threatening medical conditions. The company, a member of the Roche Group has headquarters in South San Francisco, California. For additional information about the company, please visit www.gene.com.

[00:02:04] For today's podcast, we are pleased to be joined by Dr. Michael Levy. Dr. Michael Levy is an Associate Professor of Neurology at Massachusetts General Hospital and Research Director of the Division of Neuroimmunology & Neuroinfectious Disease. He completed the MD/PhD program at Baylor College of Medicine with a focus on neuroscience. In 2009, Dr. Levy was appointed to the faculty as Assistant Professor at Johns Hopkins where he started the Neuromyelitis Optica Clinic and Research Laboratory and in 2019 he moved to the Massachusetts General Hospital and Harvard Medical School to develop the research program in neuroimmunology.

[00:02:47] Clinically, Dr. Levy specializes in taking care of patients with rare neuroimmunological diseases including neuromyelitis optica, transverse myelitis, MOG antibody disease, acute disseminated encephalomyelitis, and optic neuritis. In addition to neuroimmunology clinics, Dr. Levy has a special interest in patients with superficial siderosis of the central nervous system. Dr. Levy is the principal investigator on several clinical studies and drug trials for all of these conditions. In the laboratory, Dr. Levy’s research focuses on the development of animal models of neuromyelitis optica and transverse myelitis with the goal of tolerization as a sustainable long-term treatment.

[00:03:34] Welcome, Dr. Levy and thank you for joining me today.

[00:03:39] **Dr. Michael Levy:** Glad to be here.

[00:03:40] **Krissy Dilger:** Can you just start off by providing a brief explanation of what MOG antibody disease is?

[00:03:47] **Dr. Michael Levy:** MOG antibody disease is an autoimmune disease in which the immune system is attacking the MOG protein, which is expressed on the myelin in your brain, optic nerves, and spinal cord. It's a disease that we used to think was bundled up with multiple sclerosis, and then it was recognized to be a part of the ADEM spectrum in kids and now more recently, part of neuromyelitis optica. And now, since we have a good blood test for it, we recognize that it's really different from all three of those conditions. Now we separate it out. It's its own thing. It's called MOG antibody disease or MOG antibody-associated disease. And there are trials being developed specifically for that disease.

[00:04:36] **Krissy Dilger:** Thank you. And so, speaking of trials, can you tell us how the CosMOG-Clinical Trial came to be? What is the background of how this drug Rozanolixizumab?

[00:04:51] **Dr. Michael Levy:** Rozanolixizumab. Yeah.

[00:04:53] **Krissy Dilger:** How did it become considered a potential MOGAD treatment?

[00:04:58] **Dr. Michael Levy:** So, this dates back to our first recognition that MOG antibody disease was its own thing and that these people who came from our NMO clinic were not responding well to rituximab, and we tried to find something better for them. And what we identified is that IVIG was really helpful, which is unusual because IVIG is not that useful for aquaporin-4 NMO. We don't use it for MS, and the fact that these people were MOG people were responding so well to IVIG was really different. Now, IVIG has a lot of problems, blood clots, aseptic meningitis, multiple infusions per month it's not the easiest thing in the world to use. And so, as we started looking for better choices for people with MOG, we found that this new class of drug that Rozanolixizumab belongs to is really targeting the IVIG market. So, we know how IVIG works in MOG, and these new drugs just take a shortcut to that same mechanism of action.

[00:06:07] Rozanolixizumab is a FcRn monoclonal. So FcRn is a part of your blood vessel wall. It's a protein on your blood vessel wall that holds on to proteins and prevents them from being degraded. And if you block that process, then your own antibodies get degraded a lot faster. So that's how these drugs work is they help to degrade your own antibodies. And among them would be the bad antibodies like MOG. Then as you make back your own antibodies, the ones that come back first are your good ones. And so over time, you're going to replace your bad antibodies with only good ones. So that's how the drug works. It's being developed for every disease where IVIG is useful, myasthenia gravis, CIDP, chronic inflammatory demyelinating polyneuropathy. These are other conditions that we use IVIG in and some have already been approved.

[00:06:59] So I approached this company, and they were based in Belgium. They had an office in London. I cold called the office there and I said, "Hi, my name is Mike Levy. I'm a MOG doctor and I have a good idea for you guys with your drug rozanolixizumab." They invited me over to London. We sat in a conference room for eight hours, and we just hashed out the trial design. That was back in 2017 maybe I can't even remember. And it takes some time to get through FDA and everything else. And now the trial is launched, it launched officially last year, I believe, last year and has enrolled a few people in the US and Japan and in Europe. That's how the trial got started.

[00:07:46] **Krissy Dilger:** Great initiative on your part and here we are today. So, that's great. So, what is the broad research question this trial is attempting to answer?

[00:08:00] **Dr. Michael Levy:** What we're trying to understand is can this drug prevent relapses the way IVIG does? So, a lot of MOG people just like NMO, just like TM, they have damage from previous attacks, and they have symptoms from that damage, maybe vision loss, maybe bowel and bladder control. We're not trying to fix that. That requires the spinal cord to heal over time with the optic nerves to heal over time. We don't have good therapies for that. It's still an area of unmet need. But what we are trying to target with this drug is to prevent the next relapse. So, this trial design is placebo controlled. You have a 50-50 chance of either getting nothing or getting the drug. And what we want to know is does getting the drug either delay or stop the chance of having a relapse. And so that's how the trial is designed.

[00:09:02] **Krissy Dilger:** And then have there been safety trials yet in this study?

[00:09:07] **Dr. Michael Levy:** Yeah, there are trials that have used this drug specifically in myasthenia gravis, and that will be approved very soon. And so, we can look at those trials and see that it is safe. We recognize what the safety risks are. They're very, very similar to IVIG. So again, it's all very similar in mechanism and also similar in safety issues. The risk of aseptic meningitis, which is something that happens about 15% of IVIG infusions, and probably not as high with this drug. But what happens is if you give the IVIG too fast, for example, it might trigger an inflammation and the lining around the spinal cord in the brain. It's a horrible headache, fever, and a stiff neck, and you're miserable for two days, and we know what to do in those situations. It's not life-threatening or anything like that, but it's very, very uncomfortable. So, we're trying to understand what causes that side effect with the drug and with IVIG in order to try to minimize it. And so, we already had one case in the trial with aseptic meningitis and have had to revise the consent form to specifically emphasize this side effect. But we've come up with strategies to minimize that including premedication with Benadryl and Tylenol and also reducing the dose depending on your body weight.

[00:10:38] **Krissy Dilger:** So how is this trial set up? Can you just briefly discuss the design?

[00:10:46] **Dr. Michael Levy:** Yeah, the inclusion criteria require that you have MOG antibody disease but that you also have the relapsing type. So, if you've only had one attack, there's still a 50-50 chance that you're not even going to have a relapse without treatment anyway. So, we don't want you in the trial because we're only trying to prevent the next attacks. We have to know that you have the relapsing form. So, you have to have at least two attacks in your life and one of those attacks has to be in the past year because we want active disease. We don't want to presume that if you don't have a relapse, it's because the drug is working. We need to know that you have active disease and that we're stopping that process. So, two attacks in your life, one in the past year, you have to have MOG, and then there's a 50-50 chance that you're going to be getting placebo. Now, the trial design only allows one attack. If you have one attack, you're done, you're out of the study, you're into a different arm where you're guaranteed drug for not just the duration of the study, but even beyond that until it's FDA approved, assuming that the drug is safe and effective. So, the ethical concern about the placebo arm is mitigated by the fact that you're only allowed one relapse and that's it.

[00:12:02] **Krissy Dilger:** That's very helpful to know. So, you discuss some of the criteria for who can participate. But is there anything else that is required in order to participate in this trial?

[00:12:15] **Dr. Michael Levy:** One thing that I should mention is that the drug is infused weekly. And what does the infusion require? Well, it's a very small volume of medication, but it's not small enough to fit into one syringe. So, you can't just give one shot and be done. It could be four shots. But the way that the company decided to do this is to infuse the medication through this little pump device rather than to do four shots. So, the needle is very small. It's a same size needle that they use for blood draws and they put it under the skin somewhere in the body or in the leg or wherever you want, just right under the skin, put a piece of tape on it

and then there's a pump about two iPhone sizes and you put the medication on one corner of it and it goes to this little tubing right into that needle and then it's infused under the skin for about 15 minutes. And that is an infusion that's required every week. So, you have to be near a trial site. Now, we've had people-- we're in Boston, we have people in Rochester, New York, fly in once a week. It's not a huge problem, but it's better if you're near the study site. Now, after a certain period of time, you can do the infusions at home, but you still have to have a nurse come to your house and do it. So, logistics matter for this study. And so, before you jump to the opportunity, I encourage you to look at the trial map, see if it makes sense for you.

[00:13:42] **Krissy Dilger:** Yeah, that makes sense for sure. Can participants continue on other management therapies while in the trial or will they be required to stay off other therapies?

[00:13:54] **Dr. Michael Levy:** You can't be on any other immune therapy. So, the FDA has to know if this drug is working and not do it to something else like CellCept or prednisone, you can't be on those medications. You can't be on rituximab or anything like that. You have to come off of everything, and then you can participate in the study. Now, if you're on medications for your bladder or for blood pressure or anything else, you can stay on those medications, but it can't be immune suppressive.

[00:14:20] **Krissy Dilger:** What is the status of the trial thus far? Have there been any results you can report or is it too soon?

[00:14:28] **Dr. Michael Levy:** The trial just launched, and it's expected to go through 2025. There are no results that I can report yet. This is a double-blind study. Patients don't know if they're in the placebo arm. I don't know if they're getting drug or not, nobody knows. It's only going to be revealed at the end so that they can plainly see, what the effect of the drug is versus the placebo. So, we have no results to report. I can tell you that trial sites have been opened in, I think 20 countries approximately. I think there are eight in the US, for example, places have begun to enroll as of late last year, and I think there maybe 10 or so who have enrolled already.

[00:15:15] **Krissy Dilger:** Awesome. So, you mentioned the trial is expected to go through 2025. If successful, what is the kind of general timeline to be expected in terms of when this drug might actually become available for people to take if they have a MOGAD?

[00:15:36] **Dr. Michael Levy:** Assuming it finishes in 2025, and assuming that it proves to be effective, then they would file with regulatory agencies in the US and Europe and Japan, and other places for approval. And that process can take anywhere between six months and a year, and then it would become available, and hopefully, it won't be priced too high, and it will become easily accessible to all. So, it's not just a matter of getting approval. It also has a hurdle in terms of the price. Just to emphasize their-- in the aquaporin-4 version of NMO, there are three drugs approved in many countries, but they're not covered or accessible in a lot of those countries. So, makes it essentially unaffordable. So, we need not just approval but also access to this medication.

[00:16:24] **Krissy Dilger:** Yes, that's definitely a big part of access to appropriate treatments that will remain helpful for sure. So, this is all assuming that the trial is successful, how will that be determined if the trial is successful or not?

[00:16:42] **Dr. Michael Levy:** So, what happens is after the trial is done, the data is locked, can't make any other changes. And then there's an unbinding process whereby all the pharmacies will report to us who is on what drug and when and a statistician gets it an unbiased statistician and then they just run the statistics and then they show us what was the result of the drug compared to the placebo. And if the statistics are clear and presentable to the FDA, then the company can turn that in to the FDA for approval. And what we're looking

for is proof positive that this drug prevents attacks better than placebo does. And it has to be meaningful. If it just prevents it a little bit more, it may not be useful. What we're really looking for is something on the order of what we're observing with IVIG. Now, our observation with IVIG is not blinded. I can't be certain that IVIG is that effective, but my experience with it is pretty good. And I think that's the level of expectation for this drug Rozanolixizumab.

[00:17:50] **Krissy Dilger:** So, if successful, who will be potentially eligible for this treatment in the future? For example, will both kids and adults be eligible? Will you have to be MOG positive?

[00:18:04] **Dr. Michael Levy:** The way that the trial is written is that you have to meet the new criteria that were just published for those of you who don't know there's a huge consortium worldwide consortium that put together a diagnostic criterion, a set of rules that basically rule in MOG antibody disease. And the trial is now attached to that criterion. So, it does require a MOG antibody positivity and using certain types of tests. It has to be positive. And all of that is detailed in this large consortium study that I think the SRNA has probably made available to everyone should. And that's going to be the criteria for using this drug as well and for participation in the study. There's one exception, the trial is not enrolling children. We tried, we pushed for it, pushed really hard for enrolling kids, but the FDA insisted that we do all of these pharmacokinetic studies, because the drug is weight based, we would have to do a different dosing for each age group, and it would require all these blood draws in these poor kids, and we just couldn't get that all together. Especially if the kids wanted the infusions at home, we couldn't time the blood draws well enough. And so, kids are excluded unfortunately. But assuming that it is approved for adults, there will be a separate kid study after that, which will be done for approval in children.

[00:19:23] **Krissy Dilger:** So, one last question. How can someone participate in the trial? Is there a website you can direct them to or how does someone find more information?

[00:19:47] **Dr. Michael Levy:** The best is to go to clinicaltrials.gov, put in the MOG antibody disease and the disease blank. You'll see all the studies that come up from MOG, and then you can choose rozanolixizumab or look at the other options. I think there is a nice CosMOG website as well, and you can look at that, that's industry sponsored. So, you have to consider that, and you can also email me and ask your physicians, and if your physicians don't know, they can reach out to us at SRNA or me directly. So, among all those options, there should be at least one way that you can learn more about it.

[00:20:24] **Krissy Dilger:** Awesome. Well, thank you so much for your time. We really appreciate it and I know this is a topic people are really excited about. So, thank you also for all the work you've done on this study.

[00:20:36] **Dr. Michael Levy:** Thank you. Thank you for hosting me.