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- 34:14: Could you please tell us a little bit about any plans to create a MOGAD biorepository? Why would this be different than say blood collections made at various research laboratories like the Mayo Clinic or Johns Hopkins where many of us have donated tubes of blood - you know - probably yearly?
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- 47:17: Are there any potential for targeting the MOG antibody specifically in treatments?
- 48:39: I want to kind of have you comment on your recent study in nutrition. Did you come to any conclusions about the link between any nutritional changes you might want to do and MOGAD.
- 50:13: So, those that get on the trial and have success, will they have to stop the medication until it gets cleared by FDA or would they be able to continue the drug until FDA cleared?
- 50:56: How can patients get away from using steroids for their MOGAD especially in the acute stage? Is there any research besides - you know - in this acute stage - going on to replace those medicines or I guess the steroids used for the acute attack?
- 53:18: We wanted to know if a patient has - thinks they are having an acute attack in there. They have a negative MRI - you know - and yet they have seemed to have clinical findings. Is there any research going on on better imaging to detect disease activity?
- 55:36: How can I participate in the clinical trial when it starts?

## Introduction

0:00 Introduction [Music]

The MOG Project Logo zooming in. The MOG Project Presents a MOG Project MOGCast, The Latest From The MOG Initiative, with Dr. Michael Levy from the NMO Clinic and Research Laboratory, Massachusetts General Hospital

0:33

Julia Lefelar: All right everybody I'm here with Dr Michael Levy. Hii doctor!

Welcome to our second MOGCast Series entitled The Latest From The MOG Initiative. Today we are speaking with Dr. Michael Levy from Massachusetts General Hospital. My name is Julia Lefelar, Executive Director and Co-founder of The MOG Project. The MOG Project is a US-based on-profit organization devoted to raising awareness advancing research and providing support and advocacy for the MOGAD community in hopes of finding a cure. We would like to thank Dr. Levy and The MOG Project members for their contributions to this MOGCast. This MOGCast is being recorded and will be available on our website, Facebook page and YouTube channel. If you want to submit questions please feel free to do so by commenting on our Facebook live video. We will be answering community questions time permitting so any questions left over will be answered in a follow-up MOG Blog or future podcast so stay tuned.

1:40

Julia Lefelar: Dr. Michael Levy is an associate professor of neurology who is recruited to lead the research unit in the new Division of Neuroimmunology at the Massachusetts General Hospital. His mission is to build a combined clinical and research neuroimmunology program to develop therapies for patients with autoimmune diseases the central nervous system. Dr. Levy moved from Baltimore, Maryland where he was on the faculty at Johns Hopkins University since 2009 and Director of the Neuromyelitis Optica Clinic. Clinically Dr. Levy specializes in taking care of children and adults with rare neuroimmunological diseases

including neuromyelitis optica, transverse myelitis, MOG antibody disease and acute disseminated encephalomyelitis. In addition to four monthly clinics, Dr. Levy is the principal investigator on several clinical studies and drug trials for these conditions.

2:37

Julia Lefelar: We're here today to talk about Dr. Levy's laboratory work specifically related to the work he does in MOGAD. Welcome Dr. Levy! We're thrilled to have you here with us today!

2:49

Michael Levy: Thank you Julia.

2:50

Julia Lefelar: Well, I want to jump right into the first question, and these questions are about the clinical trials. So, I'm not sure if you're aware but this new clinical trial that's come out is basically all the buzz in the MOG community. Can you tell us a little bit about that - you know the history of the drug and what it's currently used for and how it conceptually is going to work in MOGAD?

3:18

Michael Levy: Sure! Well the reason...the way this came about is because of our interest in using IVIG for MOG which we recognized fairly early on as a really good option in the sense that patients would go into remission fairly quickly but it was very logistically difficult - all the IV's and the headaches and insurance coverage, dosing strategies - They were all - it was all logistically difficult but biologically effective so we wanted to see if we can kind of shortcut the process, go directly to the mechanism that IVIG was acting on and see if we could get rid of all the logistical problems but still get that biological effect that we want. And for a lot of diseases for which IVIG is useful, this shortcut approach is being developed including myasthenia gravis, chronic inflammatory demyelinating polyneuropathy, or cidp, guillain-barre disease, many others for which IVIG is being used they're now developing this other drug that'll shortcut all of those problems and go directly to the problem activating the biological pathway that IVIG uses and just making it a lot easier like in a patch form or a subcutaneous injection, things like that. So I thought this would be a great idea for MOG. I contacted two companies that were developing this product and I told them about MOG antibody disease, and I just got kind of some blank looks. And I just didn't stop there. I went on and I called the next company on the list and that was UCB in London and I talked to a high-up person there who thought this was particularly interesting and said, "Why don't you come to London, talk to the team see if you can convince them?" So that was probably in 2017 maybe 2018 - I can't remember now that was a while ago. But I went out there, we had great meetings I think I got some excitement around it and fast forward now we're three or four years later and we're finally getting the trial off the ground so that's the long back story to how this finally got started. But I've been involved the whole way along and I'm just really excited to finally get this going.

5:51

Michael Levy: You're, you're muted Julia. (Smiling) I know, I know you haven't used Zoom that much, but you know.

6:04

Julia Lefelar: (laughing) I know that's all we do. You'd think I'd be able to do that. I appreciate that response. I mean that's amazing because I definitely remember you talking about it early on - you are mentioning it but I didn't realize...

6:15

Michael Levy: I've been waiting for a long time for this.

6:17

Julia Lefelar: Yeah very exciting! So I guess I would like to know - it's called Rozanolixizumab or Rozimab, right? So, we wanted to know how that's created and is it donor based like IVIG or created in a different way?

6:36

Michael Levy: It's created in a different way. It's synthetic. It's an antibody and just like rituximab is an antibody and all the biologicals that are used for neuromyelitis optica - they're all antibodies - Rozanolixizumab is just another antibody. In this case I believe it's produced in cells and then purified. So cells in a dish and then purified. So it's not raised in animals. That's how we used to make them but now we just use cells in a dish. We can get the same product without harming any animals. But the idea is that this antibody, this Rozanolixizumab antibody, it is trying to do the same thing that IVIG does so the benefit that we see with IVIG is the idea that you're diluting all of your antibodies with donor antibody. So, you collect in in one bottle of IVIG, you get between ten thousand and fifty thousand people's antibodies all concentrated into one bottle. And when you infuse that into a person you're basically just totally diluting the patient's own antibodies. And then as the body gets all these antibodies, these donor antibodies, it recycles all of it back to a normal level. But most of the patient's antibodies are now gone. They're recycled and destroyed, and the patient now has antibodies from other people. Eventually though the patient will make all of their own antibodies back and probably at the end of four or five weeks or so it's back to how it was before. So that's why IVIG has to be dosed monthly. The way Rozanolixizumab works is a little bit different. Instead of diluting antibodies it just triggers the recycling of your own antibodies. So, what happens is you get this Rozanolixizumab drug and your antibody levels drop by 70 percent in a day and then they all get recycled and your body will just start making more again. So, it's instead of diluting the antibody you're just reducing the antibodies that the patient's making.

8:53

Julia Lefelar: That's pretty interesting. You know, I guess, so that's every antibody that you have then, correct?

9:02

Michael Levy: Correct, not just MOG, but it is all of the antibodies and that has a quieting effect on the immune system.

9:12

Julia Lefelar: Wow, okay that's it that's interesting. I think a lot of people would want to know that distinction. So, I'm glad that you said that. So, as far as the trial, could you tell us a little bit about eligibility. For instance, who are you looking for, what criteria, what eliminates people and so on.

9:35

Michael Levy: Well this is a preventive study we're trying to prevent the next attack of MOG, so you have to you know there are a lot of MOG people who never have a second attack. We obviously don't want to include those patients in the trial because we're trying to prevent the next attack and we want to try to impact

the disease process. So we're only enrolling people who've proven that they have a relapsing MOG so that's at least two attacks and then one of those attacks has to be in the past year because we don't want people who've been in long remissions, because if we're trying to prevent attacks in the next year or two we don't want people who've been in a prolonged remission because that could just be the chance of the disease just not relapsing again. So you have to have two attacks in your life and one has to be in the past year. You have to test positive for the MOG antibody and you have to be an adult for this study. I think we're going to get into kids later on but the - I really did push for enrollment of kids in the study. The problem is that you have to redo all the dosing if you're going to enroll kids. You can't just give them one dose because kids are not just small humans, but they also metabolize antibodies differently and you have to do all of the antibody dosing tests to be able to enroll kids. And I think the compromise we got to was, well perhaps we'll enroll large kids you know 14, 15 year olds at least who are 40 or 45 kilograms of body weight so that they metabolize and handle the drug in much the same way as grown-ups do. Now we don't have that commitment yet from the company so right now we're just going to be doing adults but we're hoping to add on kids after we demonstrate that adults respond safely.

11:33

Julia Lefelar: Okay so their's just a quick follow-up. So, I've seen some comments from people on this that said that you couldn't - you were - you would be eliminated if you've had an attack within six months, That's not true correct?

11:50

Michael Levy: It's not true we don't want people who are still in the midst of their most recent attack we want them to be in remission we want that last attack to be treated and then to be stabilized. I don't remember what the time is from the onset of that last attack. I believe it's three months. I like even one month. I can't remember but basically that last relapse has to be done.

12:15

Julia Lefelar: Okay so we would encourage people to, you know, at least inquire.

12:20

Michael Levy: Definitely you don't want to wait too long because if you're out of that one year time window then you can't - you're not eligible anymore.

12:27

Julia Lefelar: Okay thank you for that. So, this is obviously going to put some, you know, something to do in every everybody's daily lives and so could you tell us about how their daily lives are going to be as affected as far as time commitment, the type of treatment delivery any clinical visitation or how anything else like that goes.

12:54

Michael Levy: We're trying to make it convenient and the pandemic has actually helped make it more convenient in that regard because we've convinced the company that most of the visits should be done at home over zoom and only some of the visits in person. So, the first four visits are once per week and those have to be done in person. There's lots of testing that has to be done including - you know - all kinds of different clinical assessments and blood draws. and then we give the first two or three doses in person where we show you how to apply the patch. It goes on the arm or the leg and we want to be there while that happens and just make sure that that you don't have an allergic reaction or something like that. Then after the first four weeks then you can go home and from then on for the next three months you'll just take the patch once every week at home and I think - you know - we're gonna have this set up on zoom so that you can show us where you put the patch and that you responded okay and so on and the patch stays on for about 15 minutes and then afterwards you just take the patch off and there'll be some observation time. And then after three months and you come in once every three months for an assessment blood draws you hearing that your analysis things like that so we're trying to make it as convenient as possible.

14:24

Julia Lefelar: Okay so it sounds like you probably need to live near the clinic since it's every three months unless you wanted to travel up there correct?

14:34

Michael Levy: Yeah you could pick a clinic site. There'll be 20 different countries and something about 50 different sites available. So, Boston will be a site. We're hoping to open sites all across the North America and in Europe so hopefully there won't be - it won't be too far or inaccessible to people. Obviously, they're going to pick population centers. If you don't live in a city you might have to travel to the city but then after those first four weeks - So if you're going to enroll in Boston you have to kind of be in Boston for those first four weeks but then after that then you can just come once every three months for just a one day visit.

15:17

Julia Lefelar: Okay, that's good to know. So, we're basically getting messages from all over about wanting to participate in this clinical trial. Have the locations that you're talking about been determined yet and is there a list somewhere where people can go and see that yet?

15:39

Michael Levy: Not yet we've reached out to all the sites and they all have to go through a contract process to make sure that the institution is supportive of the trial and that the principal investigator at each site is aware of how everything works. But we did have our first investigative meeting it was about two weeks ago or so for both the eastern hemisphere and the western hemisphere. On the western side was at a reasonable hour and I addressed everyone and explained how this all works and I think that there was reasonable excitement and I believe they are about 20 or so investigators. I remember specifically people in Colorado, in California and other places and then we also had a similar investigator meeting for Asia and I had to get up at 2 30 in the morning to give that address which was fine because you know the hours are 12 apart. So - but - we had a nice turnout there as well from representative countries from all over the east and so I'm hopeful that there'll be a lot of options, but they have not yet been publicized.

16:51

Julia Lefelar: Ah well we'll certainly look forward to that. So, I want to just ask a little question that's been, I think, asked of us and I think it's in the literature but I want you to kind of expand on it a little bit. So, what if somebody joins the clinical trial and - you know - they're going on with whether they have the medicine or not and they relapse. What happens then?

17:18

Michael Levy: The whole trial is designed to prevent relapses, but there is a placebo arm. So, the enrollment will include people - it's randomized - you don't - I don't get to pick - you don't get the pick - no one gets to pick - it's randomized where you'll end up. But people are only allowed to have one relapse in the study and once you have what's called an adjudicated relapse meaning it can't just be a relapse that we think happened it has to meet all the criteria there might be MRI criteria imposed or OCT or ophthalmological exam or some other criteria. If you meet that criteria and it's called a relapse, then you're done with the randomized portion of the study. You're going to get treated - you're - everyone usually starts with steroids, but it's site specific so your doctor gets to pick for you and if they use IVIG like we use IVIG heavily that's an option, or plasma exchange or basically wherever in the world you are, your local standards of care will apply. And after you're treated then you're guaranteed the actual drug in the patch from then on until the end of the study. So, if you were in the placebo arm you won't know, right? When you relapse, you won't know if you failed the actual drug or if you were in the placebo arm. But either way from then on you get guaranteed medication in the patch and you can use it for as long as you want. You don't have to accept that, you can then go back to IVIG or some other approach that you were happier with. But if you if you want that definite drug from then on, then you'll get that until the drug - until the trial is done and the local agencies have approved the drug in your country.

19:11

Julia Lefelar: I see so that's pretty comforting especially for people that are worried about being on the placebo and getting a relapse. And is that true if you're - you know - they know at the time that you're actually on the drug, don't they? Or so if you were on the drug and you relapsed, would that be the same thing? You would be given the option to just continue and you definitely get the drug of course still or would they - you know - get you out of the - allow you to get out of the clinical trial?

19:45

Michael Levy: It's tricky because if I peek into the randomization book to see which arm you were in when you relapsed it biases the whole trial. It distorts the way we evaluate patients and the FDA doesn't know how to evaluate the data as a result. So, this is really importantly a double-blind study. You're blinded, everybody's blinded. The only person who's not blinded as a pharmacist who has no idea what this trial is about and is just there to randomize things but everything has to be done in a double-blind manner in order to really minimize any bias that comes out of knowing what you're getting and what you're not getting. That's really the best way that the FDA can evaluate the results, or your country's regulatory agency can really evaluate the signs and determine if the drug is beneficial or not.

20:41

Julia Lefelar: Okay wow! That was a really good peak under the hood, and I think that clears up really how and why this has to work so thank you for that. My next question is just kind of going back to - you know - just the comparison with IVIG and subcutaneous IG. Those don't suppress the immune system. Does the Rozimab's mechanism really cause immune system suppression? It sounded a little bit like you said it did, but is this suppression similar to other treatments that we take for MOGAD that are not IVIG and subcutaneous IG?

21:24

Michael Levy: It's very similar to plasma exchange in the sense that you're just removing antibody and then making it back again. You would imagine plasma exchange would be immune suppressive if given on a regular basis, but we just haven't observed that, and it may be that we're not taking out enough antibody or the patient's producing enough antibody regardless. And the same is true with Rozanolixizumab. You would think taking out 70 percent of your antibody in one day would make you suddenly vulnerable to all kinds of infections. But in fact, that doesn't happen, and their side effect profile doesn't show any increased risk of infection. So, it does make sense in terms of rational explanation of how this drug works that you would think that it should be immune suppressive, but it doesn't seem to work that way. Now with IVIG you also get an immune calming effect. When you flood your system with antibodies there is a negative feedback loop, so the immune system goes "Whoa, whoa, whoa! Hang on! We gotta - you know - redo this!", and everything just kind of calms down and dies down for a second while your antibodies are recycled and that's not really immune suppressive either. People on IVIG don't get weird infections and they're not more likely to get common infections, so, again rationally when you're talking about these medications you can understand that your immune system does get either activated or calmed down, but not to any degree that you would notice and not to any degree that you would get any infections as a result.

23:06

Julia Lefelar: Okay so subcutaneous IG is more of an even distribution over the course of a month. Does it have that effect as well or is that one that isn't quite working like IVIG or this Rozimab?

23:21

Michael Levy: Subcutaneous IG is a easier subcutaneous delivery of the same amount of antibody. You just put it under the skin. It forms a little pouch under your skin and then it dissolves over the course of 48 hours into the body and for a lot of people it's easier to do one injection like that every week than to do four times that amount intravenously that might be divided over two, three or four days. There's never been a direct comparison about which one is more or less effective or immune suppressive. The idea is that whether you're getting it subcutaneously or intravenously you're getting a certain amount of antibody, enough to trigger recycling of the antibodies. And that calming effect you get that whether you use subcutaneous or IV.

24:14

Julia Lefelar: Okay, so that's actually very helpful, thanks. So, could you just tell us a little bit about the possible side effects of Rozimab and what are the - what are some of the possible adverse effects that people may present with during or after treatment?

24:36

Michael Levy: The side effects - the number one side effect, and I'm not sure why, is headache. It's true with almost every biological. That's true with Alexion's drug that was approved for neuromyelitis optica called Eculizumab. It's true with - in almost every disease in which Rozanolixizumab has been tested and many other - it's almost - headache is number one on almost every side effect profile for biological drugs. And someone did an interesting study looking at the reason why and the best explanation is that when people are enrolled in these studies, they tend to not stay hydrated on the day of the infusion. They're nervous or excited or whatever and they don't have their normal cup of coffee or breakfast or whatever, and they come in and in the dehydration process tends to trigger a headache. That is the best explanation we can come up with because it's not like these drugs get into the central nervous system - they really don't. They remain outside in the periphery in the blood in the lymph nodes and everywhere else. So it doesn't really make sense that headache should be number one in almost all of these drug trials but it is. And so that's true with this drug as well. And then upper respiratory infections, urinary tract infections - the things that people commonly get anyway are kind of number two and three on the list.

26:19

Julia Lefelar: Okay thank you. Well, let's say this goes through these clinical trials. What kind of timeline should patients expect for this to be reach FDA approval in the best and the worst case? I know it's not an exact number.

26:37

Michael Levy: Yeah, these trials - this trial is expected to go through 2024 at least and then it would require some analysis and FDA filings and things like that so maybe 2025 I think is best case scenario.

26:58

Julia Lefelar: Okay that's good to hear that's not far away.

Michael Levy: Not anymore. I mean started 2021, so...

Julia Lefelar: Amazing. So, with the recent Solaris approval for aquaporin-4 NMOSD and the cost of it being so high, what are your expectations or their expectations for the cost of this?

27:24

Michael Levy: They never share that with me. It's always a fear of mine that a drug that I'm helping to get approved is going to be priced out of range of my patients and I'm not happy about that. But I already know that these companies will not share that type of information with me so even if I ask they're not going to say. And most of them don't even know. So, the team that's helping me to develop this at UCB, they're not even going to be involved in the pricing. It's going to be a whole different team of commercial people who price this out and figure out how to make a return on investment and still be within guidelines of payers, insurance companies and medicare and things like that so I'm worried that it will be priced high, and I'm always going to continue to put pressure on these companies to just make it accessible to our patients so if they're underinsured or uninsured, to have a free drug program at least for those patients.

28:26

Julia Lefelar: Oh, that's good to know. Thank you. So, we've heard and read about other studies and new upcoming research with satralizumab and tocilizumab being used for MOGAD. Are these the drugs for upcoming clinical trials and something you are familiar with, and if so, how do they help with MOGAD?

28:50

Michael Levy: So, these are studies - I'm under a confidentiality agreement to not talk about them until they're public because these companies don't want stocks being traded around on data that's not publicly available to everyone and so I can't say too much about satralizumab, but tocilizumab which is the parent compound, the older version of satralizumab has been studied in academic centers and we contributed our tocilizumab patients to a larger study group where we found that whether it's injected under the skin or infused intravenously tocilizumab does seem to help in MOG antibody disease. And so, it wouldn't be surprising that a company like Genentec, which manufactures both of those drugs, that they may take notice of that and they may want to investigate that further.

29:48

Julia Lefelar: Oh, I see. So, are either of these drugs that you know being used in any pediatric patients or is it just still only being used in adults?

30:00

Michael Levy: I don't think there's any reason why we couldn't use them in pediatric patients. Tocilizumab has pharmacokinetic data in children in the rheumatology literature. It's in fact approved for a juvenile rheumatoid arthritis in the United States so we do know what its pharmacokinetics are. So, if we wanted to dose it in children we could. I wouldn't say it's among the most popular options. I would say that IVIG is still the most available and widely used followed by a combination of prednisone steroid, prednisolone, with azothioprine or mycophenolate. And then there's still some people who are on b-cell therapies like rituximab that have some benefit from that. And so tocilizumab is probably right after that number - three or four on the list.

31:00

Julia Lefelar: I see. So, we have a community question and just to verify they are asking if this - you know - clinical trial for Rozimab is in reference to the trial that was discussed at the SRNA symposium a few weeks ago.

Michael Levy: I can't remember what I had for breakfast. I really don't remember what I talked about a few weeks ago but it is it is the only trial that's been launched in MOG so if we talked about a trial that was just recently launched at the SRNA that would probably be this one.

31:37

Julia Lefelar: Yeah I believe you're correct on that thank you. So, I kind of want to switch the conversation up a little bit just to talk about other progress made in the MOGAD world. So, as you know, proposals have been put into the World Health Organization and the CDC by The MOG Project with help of Dr. Jon Santoro and UCB, and you know we wanted to change the classification of MOGAD to be regarded as a separate disorder. This is going to allow doctors to give patients a specific diagnosis code for insurance purposes at least in the US. Can you talk a little bit about how, if and when this is approved, that your research especially in the MOG initiative will be affected and why would this be a good thing?

32:37

Michael Levy: Those diagnosis codes are mostly used by insurance companies and so if we have a diagnosis code for MOG, then an insurance company could say, "Okay if that's the diagnosis code here are the drugs that we'll pay for", and we're hoping that any new drug that's approved by the FDA will make it onto the insurance list and it should be matched to that diagnosis code. Currently for MOG people are given codes of MS, they're giving codes for neuromyelitis optical or acute disseminate encephalomyelitis or transverse myelitis and so MOG patients have all kinds of billing codes, none of which will probably be tagged to any new drug. So, when these companies are developing drugs, they really want to know that there's going to be a diagnosis code for them so that insurance companies know how to - how to match the drug to the diagnosis code. So that should come out, I would guess probably in the next year or so and I hope it will be widely adopted. It takes some time to transition our thinking. For example, I know the MS code is g35.0 and you know there was the diagnosis code before that and so these things take a little bit of time to transition but the electronic software should make that easier for us. And I think as soon as there is a diagnosis code for MOG most people will adopt it.

34:14

Julia Lefelar: That sounds great I think that a lot of people are looking forward to that. So, switching it up a little bit - Could you please tell us a little bit about any plans to create a MOGAD biorepository? Why would this be different than say blood collections made at various research laboratories like the Mayo Clinic or Johns Hopkins where many of us have donated tubes of blood - you know - probably yearly?

34:44

Michael Levy: Yeah, these biorepositories are so important because for a disease like MOG we can really try to understand what parts of the immune system are active or disrupted and we really can't do that without these biosamples. Every center has their own. We have a biorepository at our center, and I know Johns Hopkins has one and as you said Mayo. And Mayo also has the advantage that they are - they keep extra serum that we send them for clinical testing and so that really helps them in their research as well. Now the best case scenario is when we all contribute together in a systematic way so that the serum or cells that I'm studying are drawn and collected and preserved the same way at Mayo and at Hopkins and other places so that when we share data or compare data we're comparing apples to apples now that kind of cooperation is not super easy it is somewhat expensive as well. But some companies have stepped up. Guthy Jackson for example is a foundation in an NMO space that put together this huge biorepository and it's yielded dozens of papers in different studies already so it really enables good research that can only be done in the team setting rather than Mayo having to collect 50 samples over 10 years and us having to collect 50 samples over 10 years. By combining our resources and standardizing it across different centers we can really make progress a lot faster.

36:37

Julia Lefelar: Excellent. So, if you are planning on putting this together when would you expect to have it up and running?

36:49

Michael Levy: We don't have a funding source yet. We don't have a sponsor. We don't have a company that's really invested in this yet. We're applying for government grants to host a collaboration initially. Me and my colleague at the Mayo Clinic - Eoin Flanagan - we're going to put in for a small grant - small - it's a 2 million dollar grant funded by the FDA who's currently evaluating all these different trials for MOG and they must have a lot of questions as do we about: How long do people need to be treated? What is the current standard of care? What is this monophasic form of MOG? All these questions that can be answered if we're collecting data in the data and samples in a systematic way together. So, we're hoping the FDA approves our grant and that'll be just the start. It's just two centers but then we can expand from there and it is expensive. If you ask the Guthy Jackson Foundation how much they spent on their biorepository, I know the numbers. I don't want to embarrass anyone - it was a lot of money, so these things just are very expensive. So, we're going to have to do it probably in piecemeal.

38:04

Julia Lefelar: I see that does sound like a big endeavor. So, you know if somebody wanted to participate in that biorepository how would that work and would you be collecting samples just from adults or pediatric patients?

38:22

Michael Levy: In the proposal we submitted to the FDA we're trying to recruit patients from all over the United States to allow for remote recruitment, again over zoom, where we would send a kit for blood draws and other samples saliva and whatever else we need and then we would try to conduct an examination through zoom in a standardized way and in addition to that try to collect more clinical data using things like your phone, which is usually on you or a wearable device so that we can collect things like vital signs and how much movement you make and things like that so that we can really keep track of our patients daily function even when they're far away from Boston or Rochester, Minnesota. So, you know we haven't been approved. I don't want anyone to start asking me to enroll anybody because this is not even yet on the FDA's radar. This is still in the grant preparation process.

39:24

Julia Lefelar: Okay, I see. We'll make sure that we put that on hold in our minds for a little bit. So, just a quick question about - I guess - Does research in the area of MOGAD impact research in MS, and if so, how or what other demyelinating diseases does this research help?

39:48

Michael Levy: Well it's - it - from the start MOG has always thought - been thought to be a variant of multiple sclerosis. The MOG mouse model that was developed in the 80s and 90s was thought to be MS and a lot of MS drugs that worked in the MOG mouse failed in human trials with an MS because MS is not MOG and MOG is its own thing now. MOG in a mouse is not exactly the same it's MOG in the person, so you can't just immediately translate that. But there is a lot of interest in MOG because there is an immunological target. We don't know the target in MS. We think there's one. We don't know if there is one and we don't know what it is. But if there is one in MS then we can take everything we're doing in MOG in terms of trying to calm the immune system down and even to re-educate it and then we can apply it to MS. So it's what we call a proof-of-concept disease model where we know the target in MOG we're going to try to target the exact problem and then if we can fix it in MOG and we can fix it in aquaporin-4 NMO, then when we find the target in MS and maybe we'd be able to fix it in MS and other autoimmune diseases. Myasthenia gravis we know the target but in lupus we don't. Sjogren's we don't. Lots of other autoimmune diseases we don't but these are proof of concept studies that we could then apply when those targets are discovered.

41:25

Julia Lefelar: Ah, interesting. I do have a clarification from the community they're asking for - going back to the clinical trial. Does this pertain to NMO, they ask, and does this include ADEM? And so, just give a quick clarification there.

41:44

Michael Levy: It does include a dem if it's MOG positive. Somewhere between 40 and 50 percent of ADEM cases are MOG antibody positive and so that would - it would include those cases as well. And NMO you asked about an NMO. If NMO is MOG positive it would be included. So, it doesn't necessarily matter so much whether you have optic neuritis, transverse myelitis or both or ADEM, it doesn't - the clinical - the attacks that occur are less important than the underlying immunological process that we're targeting and if there is a MOG antibody component to your attacks that's really the important part.

42:23

Julia Lefelar: I see. That's good, that's a good clarification. So, we have about a little over 10 minutes left. So I wanted to switch over and just discuss the future of your research for the MOG initiative. And, you know, really what's going on now. Could you tell us what research has been happening at the NMO Clinic and Research Laboratory concerning MOGAD and what areas of research do you consider the most potentially impactful?

43:00

Michael Levy: We're really excited about identifying the precise problem in MOG - to identify which cells are reacting to MOG and why they're reacting that way and then to see if we could re-educate those cells so that they don't attack for whatever reason. In MOG patients, their immune system is treating MOG like a foreign protein they're mounting an immunity to it as if it's a foreign protein like the viral protein or something like that. But it's not. It's a self-protein and what we

need - what we're really trying to do in the lab is to re-educate the immune system to take it from a foreign protein to us back to a self-protein to just switch that response off. And we're doing that in mice first and we're hoping to translate it to people. And the MOG disease has caught the attention of companies so there are companies - at least three out there - that are also excited about this approach and they're all working in these mouse models of MOG to re-educate the mouse immune system. Now it's not - as I said - it's not that easy to just translate that into a human study you then you need to understand the basis of the MOG response in mice and how that works in people and so we're kind of doing both we have a mouse group and we have a human group and then eventually we're hoping to synthesize the two and I'll say that we're working with all three companies to do this we - I don't have a horse in this race, I just want to solve this problem. I don't care who makes all the money at the end. I just, I really believe that this approach is really the one that's going to fix the underlying problem so that's why we're excited about it.

44:52

Julia Lefelar: Oh believe me we all are! That would be incredible. So, I want to ask - Are there any greater hopes of regenerating the spinal cord brain lesions or optic nerve and would this help all types of demyelinating these diseases including MS?

45:14

Michael Levy: well you know MOG is one of those really interesting conditions. Early on after people have even a severe attack early in the course of the disease most MOG lesions heal fairly well. There's some residual problems and I know several patients who have persistent problems but compared to almost every other demyelinating condition like multiple sclerosis or neuromyelitis optica, MOG patients heal the best and they routinely have the better outcome compared to MS and certainly compared to NMO. So, there's something about MOG that allows remyelination even of long horrible looking lesions in the brain and the spinal cord and sometimes in the optic nerve and we're wondering if we can learn from that. What if we could take the MOG healing process and apply that to MS? Would MS patients then do better? Or to NMO? So, I know it sounds a little odd right that we're - you're asking about remyelinating MOG patients, but I'm actually thinking about taking the - learning the biological process that allows MOG patients to heal so well and then applying it to the diseases that don't heal so well. For all of these diseases, we're also working on a stem cell approach. We've partnered with a company called Blue Rock. They're based in Boston. They have a stem cell product that we're testing in optic neuritis. So, these rats get optic neuritis. We use rats because they have big optic nerves. They get optic neuritis and then we surgically transplant without cutting any bone we can get directly to the optic nerve and transplant these stem cells and we're really hoping to regenerate the optic nerve after optic neuritis. And so that's - that could potentially be applied to any condition whether it's MOG or NMO or MS or optic neuritis from any other cause.

47:17

Julia Lefelar: Wow that would be amazing. Because you know there's some people that even with MOG that have just two attacks and have devastating results and some people that have multiple attacks like myself and recover almost completely. So, you know it would - it might even be a mystery solved there just to capture that. So, are there any potential for targeting the MOG antibody specifically in treatments?

47:53

Michael Levy: You know we don't know if the MOG antibodies should be targeted. We know - we don't know that it's that harmful. Maybe it's just a product of the immune response and really, it's the immune response that's harmful. So, we're not quite sure what to make of the MOG antibody. There's a lot of interest in that area. If you take the mag antibody in the mouse model and you transfer it by itself it doesn't cause any harm. So, but that again doesn't always translate to a human person and we're not going to do a human study like that. So we just don't know the answer completely yet but it's something that we're looking at trying to understand better.

48:39

Julia Lefelar: Interesting. So, I want to kind of have you comment on your recent study in nutrition. Did you come to any conclusions about the link between any nutritional changes you might want to do and MOGAD.

48:58

Michael Levy: The conclusion we came to is that diet studies are difficult. They're difficult to do. You have to remember what you've ate - what you've eaten in the past two weeks and I can't remember what I had for breakfast, for example. So, it's a really hard type of study to do and we did not find any really strong associations, no. One of our experts is thinking about doing an elimination study where we pick one thing that we want to eliminate from the diet and then follow that pros...those group of patients prospectively to see if it makes a difference either in their activity - disease activity, like how many relapses they have in the future or in their daily function. Those are also - those are just really hard to do. There's a lot of gluten, for example, in foods that you don't even know have gluten and it's really hard to ask people to make sure that every single thing that they eat, even in restaurants, is gluten free. So, diet studies are just notoriously difficult to do, not just in MOG, but everywhere. But we have people interested in doing it so I'm going to continue to support them and we'll see where we can get with them.

50:13

Julia Lefelar: Okay thank you. I want to grab a community question, and they, this person says, "So, those that get on the trial and have success, will they have to stop the medication until it gets cleared by FDA or would they be able to continue the drug until FDA cleared?" That's assuming - I assume that's if they - the drug seems to be helping them.

50:38

Michael Levy: If the drug proves helpful, patients get to stay on it until the FDA approves and they have a chance to transition to insurance care insurance covered drug.

50:50

Julia Lefelar: Oh wow!

Michael Levy: That is a promise from the company for participating.

50:56

Julia Lefelar: Wow that's actually a very good thing! That was a great question. It's good thing to know. I want to ask another question that - we kind of have - we kind of have a couple minutes here - that seems to be asked all the time. How can patients get away from using steroids for their MOGAD especially in the acute stage? Is there any research besides - you know - in this acute stage - going on to replace those medicines or I guess the steroids used for the acute attack?

51:30

Michael Levy: Steroids work. That's just the truth about it. In MOG patients with the relapse, you start treating them with high dose steroids and the relapse starts to go away. So, it's really hard to minimize that fact because steroids are widely available. They're easy to get. Almost every emergency room has them, people aren't allergic to it, I mean it's just - it's really very effective. The problem with steroids is of course coming off of them. You can't. If you could just stay on high dose steroids every day your MOG would disappear. But steroids have many other metabolic effects so many side effects I can't even name them including weight gain, blood pressure, just hormonal effects, everything else. And so, the challenge is treating them with steroids - if you're going to do that the challenge is then taking them off of the steroids. If you do it too quickly it'll trigger a relapse of MOG so you can't do it quickly you have to do it slowly over a period of - we don't know - two or three months, maybe sometimes slower, sometimes maybe a little faster. Because of this steroid problem, this biological dependence on steroids and all the side effects from it, I've transitioned to using IVIG as much as I can even in the acute stage. It's hard to get IVIG in any setting including inpatient but it's something I've been pushing for because of that benefit - that ability to defer having to use steroids. That's what I've been doing. But what we really need are better trials in the acute stage. We know plasma exchange works, we think IVIG works and we know steroids work.

53:18

Julia Lefelar: That's great to hear that it is being looked at. It seems to be a problem for a lot of people. One more question about MRIs. We wanted to know if a patient has - thinks they are having an acute attack in there. They have a negative MRI - you know - and yet they have seemed to have clinical findings. Is there any research going on on better imaging to detect disease activity?

53:49

Michael Levy: Oh, that's a great question. You know there's a lot of disease activity that just doesn't show up on MRI because it's not an anatomical activity so MRI just shows you a picture of what the brain and optic nerve, and spinal cord look like. But you can't see anything moving and happening on an MRI. Same with an optical coherence tomography picture of the back of the eye the retina. It's a snapshot. It's a one-time view but you can't see anything happening. There are other studies, other modalities to look at activity but within the central nervous system it's hard to access that activity. For example, if there's something going on in the spinal fluid you don't have to do a lumbar puncture just to get that and then you're only getting a snapshot in time of when you got the lumbar puncture. It's a very difficult thing to do. So, we don't have any great modalities at this moment but I can tell you that in mice, for example, in MOG mouse models, in mice, there is a lot of disease activity that occurs outside of attacks so even in between attacks in mice there's a lot of stuff going on. For example, in the spinal fluid, that may explain some of their odd behaviors that could be - are considered more psychological like anxiety and shivering and things like not being social. And if you translate that to people, maybe that translates to anxiety, depression and other behavioral things that are going on in people. But those are big stretches and I don't want to make any major conclusions like that. But it is something that we think could be going on even between attacks.

55:36

Julia Lefelar: Yes, wow. Well that is really - I'm sure it's very difficult but we hope that there's some, you know, more progress made in that area. I just have one question because we've run out of time and it's been a wonderful discussion. So, this community question is asked: How can I participate in the clinical trial when it starts? Just so everybody knows.

56:04

Michael Levy: You just go to [clinicaltrials.gov](http://clinicaltrials.gov), you look up Rozimab - rozanolixizumab. You can even look up MOG and it should be listed there and when you click on that link all of the sites, all the actively participating sites, will be at the bottom and ours would be first because I'm proud to be the first site and if you don't see anything near you can just email me. My email will be on that [clinicaltrials.gov](http://clinicaltrials.gov) site and I'll be able to tell you where to go. If there is a site opening up in the near future for example.

Julia Lefelar: Okay, and we will post in the event page that link as well as some other links especially to your MOG Initiative. You know I just want to stress how, you know, everything we talked about - donations from the community are so important so we'll make sure that people can send money directly to the MOG Initiative either through our website, we have a special link there, or it'll be directly on the on the event page there. So...

57:07

Michael Levy: Much appreciated.

57:09

Julia Lefelar: Thank you for everything you do. So, you know I'd like everyone to just give a round of applause at home for Dr. Levy and we'd like to thank him for his time and commitment to the MOG community. So, if you'd like to check out the page on our website dedicated to the work that's being done for MOGAD at the NMO Clinic and Research Laboratory at Mass General Hospital, please visit our website at [mogproject.org](http://mogproject.org) and look under the "From Our Medical Advisors" menu option then select "The MOG Initiative" and so there's a nice page there with some videos that Dr. Levy so graciously made. So, if you scroll to the bottom of the page there are suggestions on how to participate in the MOG Initiative including a link to directly donate to research. So, you can also go directly to the page for the MOG Initiative at [mogresearch.org](http://mogresearch.org) and like I said, we'll have some of these links in the event page after. So, Dr. Levy, thanks for this great discussion. I hope you have a really good afternoon and we'll look forward to following you. Take care! Bye-bye, bye-bye

Michael Levy: Take care

[Music]