Making the Switch

How to Know if Your Long-Term Treatment is Right for You

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[00:00:00] **Dr. Eoin Flanagan:** Hello everyone. My name is Owen Flanagan. I'm a neurologist at the Mayo Clinic in Rochester, Minnesota. I work in the field of neuroimmunology, work in the immunology lab and also the clinic where I see patients with multiple sclerosis and autoimmune neurological disorders. It's a great pleasure to be with you and thank you GG and the SRNA, and Chitra for inviting me.

[00:00:26] It's a real pleasure to talk to you again. Today the topic of my talk is making the switch, how to know if your long-term treatment is right for you. These are a few disclosures I do have. I work with some of the companies who are developing some of these treatments, both in their clinical trials where we've participated in some of those.

[00:00:45] But today will be more of a general talk just about the overall approach to treatment and treatment switches. Some people do remain on their medications for these autoimmune disorders in the long term. And the question people might ask is this the best fit for me? Knowing a little bit about the medication is important.

[00:01:08] Is the medication effective? Is it preventing relapses? Is it preventing the disease from being active? And are you tolerating the medication? Okay? Is it something that leaves you, in some people it can leave them very miserable, where they have a lot of side effects and then it's impacting their quality of life.

[00:01:26] And we need to consider that if the treatment is really, the benefits are outweighing the risks or the side effects. Is it safe in the long term? Some of these medications have risks, particularly those that drop the immune system. There are potential risks of infection. So, we'll talk a little bit about that.

[00:01:42] And then if you are going to switch medication, what are the other options, and do they make sense for you? And what are some of the factors that we consider in that? So, these are some of the things we will cover today. I just wanted to briefly mention a bit of a success story in terms of treatment and how that developed and how it can be a bit of a benchmark for us for many of these other conditions.

[00:02:04] Aquaporin-4 antibody positive neuromyelitis optica spectrum disorder was first really recognized actually in the late 1800s by a person called Devic. But really it was taught to be a subset of MS initially in

the 1900s. And then in 1999, Dr. Dean Wingerchuk and Brian Weinshenker wrote an article highlighting the clinical course of neuromyelitis optica and how it was different from multiple sclerosis with longer lesions in the spinal cord and some other differences.

[00:02:34] And around the same time, Dr. Claudia Lucchinetti in neurology at the Mayo Clinic looked under the microscope and looked at the biopsies and autopsies of these patients and found that there was prominent antibody deposition and also something called complement. A part of the immune system seemed to be deposited there, suggesting that both antibodies and complement were playing a role in this disease.

[00:02:56] And then Dr. Lennon discovered the aquaporin-4 antibody, or what we term the NMO antibody. And this was discovered in 2004 and five. And then what the researchers did, everybody went back to their labs and they, with this knowledge of this antibody, they went back to the labs and tried to discover what are the mechanisms involved in the process of this condition.

[00:03:17] And they found that, for example, interleukin six IL six seemed to be important. Complement seemed to be important. CD 19 positive plasmablasts CD 20 positive B cells all seem to be important in the disease. In the meantime, many investigators, including Dr. Wingerchuk and Weinshenker, were working on determining what the clinical features were and how to better get a better assay, better test for the aquaporin-4.

[00:03:46] And now we can pick up, up to 90% of cases on our testing. So, this was all going on. Then diagnostic criteria. International consensus diagnostic criteria were developed by Dr. Wingerchuk and Weinshenker. And then in 2019 and 2020 to 2023, based on the laboratory studies many treatments came out that were proven to work for this condition.

[00:04:13] Probably between around mid 2015 or so onward to 2019, these clinical trials were taking place of these conditions. Then we developed these proven treatments targeting complement Eculizumab and Ravulizumab, targeting IL6a medication called satralizumab, targeting CD 19 a medication called inebilizumab, and targeting CD 20 a medication called Rituximab.

[00:04:40] And all of these medications, you'll look at these lines here, were extremely effective at preventing relapses. So, we got, we went from a disease that had no proven treatments, where MS treatments used to make things worse, and patients who are misdiagnosed as MS tended to do worse. And these new treatments tend to really be effective at preventing relapses.

[00:04:58] This highlights how we can be really successful in developing treatments. Some of these treatments are not without problems because some of them are very expensive. We will need to work on that into the future. Overall, the great news is we have many different options for NMO patients compared to previously.

[00:05:16] And for many of the other conditions like MOG antibody disease or seronegative conditions, we're hopefully gonna be able to find treatments into the future. So that's just a historical background. So now focusing in on the treatment, what is the long-term goal of treatment? I like to think about the three "M"s.

[00:05:34] In terms of our goal of the medications, this is something Dr. Sean Pittock at Mayo Clinic had come up with, which is one, maximize reversibility. Sometimes we'll start these medications after an acute attack and we don't know, but the medications might help in some of that recovery. You maximize the reversibility.

[00:05:52] But the main goal of the medications is to maintain remission and prevent attacks that you may have or relapses, and to prevent the disease from being active and causing damage within your central nervous system, your brain, your spinal cord, or your optic nerve. And then the third M is to minimize side effects.

[00:06:11] We want to use these treatments, but we also wanna reduce the burden or prevent any side effects from happening. We try to balance all of these things when we're using these treatments. How do we choose about the initial treatment in terms of if we're going to go on one of these attack prevention medications?

[00:06:31] We want to know how effective this medication is. What I showed you for NMO, we have many highly effective medications and for some of the other conditions we have to rely on less high-quality data. So the, we don't have the clinical trial data, but we have data from our experience, and we tend to know what works and then we tend to use it.

[00:06:51] There can be lifestyle factors. Some people prefer to give the medication to themselves at home while others are happy to drive to an infusion center if that's close by. Then it might depend on the frequency of the dosing, et cetera. Sometimes if the patient has another medical condition, for example, if you have rheumatoid arthritis, if you have lupus, there may be a medication that works for both of those conditions.

[00:07:14] So rather than put you on two separate medications for those different diseases, you have one medication that covers both diseases. So that can be a rationale for choosing the medication. There can also be a concern about can the medication worsen other conditions. For example, if you have diabetes and you go on steroids, that can certainly worsen your blood sugar.

[00:07:33] So there are sometimes considerations about medications worsening other conditions. And then patient preference. Some patients have a preference in terms of which medication they've heard about or they have interest in. And then the physician will also be involved in this shared decision-making to help make that choice about the medication.

[00:07:54] So when might be a situation where your medication is not working or not right for you? One situation would be if you're having breakthrough relapses. So, we usually confirm these relapses with an MRI. So, we have to be careful about pseudo relapses, which means if you have an infection, for example, if you get COVID-19 or the flu, sometimes some of the old symptoms that you had from a previous attack come back and you can have a pseudo relapse.

[00:08:20] But we use MRIs and if we see new active inflammation, we can confirm a relapse. And if you're having a relapse on your current treatment or you're on no treatment and you're having a relapse, that's a situation where you might want to consider starting a treatment or switching your medication.

[00:08:36] Sometimes we'll do MRI and we'll see active inflammation that suggests that the medication might not be working even if you're not having symptoms. And that might be another situation where we see lots of new lesions. We say the medication is not working even though you're not having too many symptoms.

[00:08:51] If we do a repeat spinal tap, for example, when we see inflammation, that might be a reason to stop the medication. You have to be a careful because some of the medications can cause a inflammation in the spinal fluid. Example, IVIG can sometimes cause aseptic meningitis and some inflammation in the spinal fluid.

[00:09:10] So sometimes that can cloud your judgment on the spinal fluid results. Other reasons why the medication might not be working for you, if you're having side effects, for example, I know many people who are listening here will have been on steroids and steroids have a lot of side effects. They can cause weight gain, difficulty sleeping, skin changes, body habitus changes, osteoporosis, et cetera.

[00:09:35] And some of these side effects can be really intolerable where our patients tell us we wanna come off, I wanna come off my steroid medication. And in the case of steroids, we have to do that slowly because your adrenal glands sometimes go to sleep while you're on steroids and we need that to wake them up slowly.

[00:09:50] There can be serious complications. For example, if you have a serious infection like sepsis, that might be a reason why you might wanna switch off of the medication. As many of you know, we'll often monitor blood tests to look for abnormalities and some of the medications can cause lower immune system.

[00:10:07] So it might affect your white blood cell count and that might be a reason why we'd have to stop the medications. Or sometimes the medications can cause some liver enzyme elevation, or it can cause some other blood test abnormalities. That might be a reason where we have to either lower the dose or switch to a different type of medication that doesn't cause those abnormalities.

[00:10:26] There can be lifetime lifestyle issues, which we'll talk about. Frequency of dosing, the way the medication is given. Some people prefer to take an oral medication; some people like to get an infusion and then travel to get the treatment. Are you near somewhere where you can get that treatment or is it difficult for you to travel?

[00:10:44] Do you live in a very rural area where traveling to an infusion center, particularly if it's a frequent treatment that you need, frequent dosing, that can be a challenge. And then the cost, sometimes neither the physician nor the patient will be able to make the decision because the insurance company says this is the only medication we will allow for you.

[00:11:02] And that can be an issue. Or sometimes patients switch insurance or the insurance company changes the requirements and then there could be a high out-of-pocket cost. And then patients will want to switch over on their medication. But don't forget to ask about patient assistance programs. Many of these companies have patient assistance programs that will help and you can appeal and your doctor can help you with these appeal letters.

[00:11:25] I tend to write extremely strong appeal letters for these insurance companies because these diseases are very rare and it takes a long time for us to get all the data, but in the meantime, we can't leave patients hung out to dry. So, we really have to fight hard. And sometimes that's a big fight that involves a phone call,

[00:11:41] it involves very strong letters arguing for treatment for our patients. Because we really have to advocate. Patients have to advocate for themselves and we as the physician community have to really advocate for our patients to help them out. So, partner with your doctor because you sometimes have to really fight to get that medication that you need.

[00:12:02] When you're with your doctor, how can you communicate about a potential switch? So, it's important when you're with your physician you should be asking your doctor, is the medication working for my disease? Is it controlling my disease? Are any symptoms that you're having, are these side effects from the medications?

[00:12:19] If you're fatigued, could that be a side effect of medication? But sometimes the disease itself can cause some of these symptoms. Or if you're having infections with COVID-19 for example, many people got infected. That doesn't mean that the medication caused the infection because many people in the world got COVID-19 infection.

[00:12:39] So there is a background rate of infections, but you wanna see is that above what would be expected. It's important to ask about, are the blood tests okay? If they're abnormal, sometimes that's the reason why you might need to reduce the dose or switch the medication. Some of these medications in the long term can increase the risk even of some blood cell cancers.

[00:12:57] Some of the oral immunosuppressants like mycophenolate and azathioprine. And that can be a risk where we don't want to use the medications for too long and we want to switch. It's also important to know if I am going to switch, what are the alternatives and do they work for me? And I think there's always a fear.

[00:13:13] If you've been stable in your disease, there's always a fear of patients about, and rightfully so, about if I switch off of this medication, am I gonna be at risk of a relapse? So as we get new data, sometimes we get newer medications that look better, but for a patient who's been stable on their old medication, they may be somewhat reluctant to switch, but sometimes there can be risks staying on those medications in the long term, even if your disease is stable, risks of cancer, et cetera, that we have to keep in mind.

[00:13:43] So how the medication is given can be important. Some of these medications are available orally and orally can be a good option because you can take it at home. Some of these medications are twice daily dosing, so you have to remember to take the medication and sometimes that can be a challenge, remembering to take it twice a day and getting that into your routine.

[00:14:01] And if you're not taking the full medication, then you may not be getting the full benefits. Oral medications can have a bit of a higher risk of gastrointestinal side effects, so you can get a heartburn or sometimes some of the medications can be hard on the stomach like mycophenolate sometimes will cause some diarrhea or GI upset.

[00:14:19] And subcutaneous medications can be a good option. This is where you inject the medication under the skin, like people inject insulin and these medications, an example of this would be satralizumab or Enspryng or subcutaneous immunoglobulin. The benefit of these is they can often be given at home, but it does require either that you have some dexterity, so some patients who have vision issues or if you have challenges using those injections,

[00:14:44] that can be a challenge. And sometimes family members are available to do that, but if not, then sometimes the subcutaneous might not be the option for you. And then sometimes if you inject under the skin, there can be skin reactions. So, you can get a little bit of redness there. And then we usually have people will alternate the sites where they inject, for example.

[00:15:04] Or sometimes with larger volume medications, you can have a bit of a pouch in your abdomen where you inject a lot of fluid and there's a bit of a temporary pouch for a few days. And then that will go down, and some patients don't like that or don't want that. And that's a reason why they might switch to an intravenous formulation,

[00:15:20] for example. Intravenous medications, for example rituximab, is one that's given every six months. Ravulizumab is one that's given every eight weeks. IVIG is sometimes given up to weekly, and these are usually often given at an infusion center, although sometimes they can be given by an infusion therapy company at your home.

[00:15:40] The things you have to monitor for here is allergic reactions. Sometimes when you get these infusions you can get a bit of an allergic reaction where we need to give you medications like Benadryl or antihistamines. You also might need; you'll need an IV line for some of these. And I know many of our patients tell us that they have hard veins from just all of the sticks that they've gotten over the years and getting multiple IV lines, particularly if it's frequent dosing, can be a reason why they might not want to do this or might want to do more of a longer term, like every six month-type medications.

[00:16:11] So some of these aspects play a role in our decision making about the treatments. How frequently the medication is given is also important in addition to how it's given. So, if it's once or twice daily dosing, are you going to be able to remember to take that? If you take a medication every morning, maybe that's okay, but if you're not taking medication in the evening, then maybe twice daily dosing may not work as well for you, for example.

[00:16:37] And we have had situations where new medications became approved. For example, with Eculizumab for neuromyelitis optica spectrum disorder, that was every two-week medication. And then the company developed every eight-week medication, which is identically pretty much identical to the other medication, but it allows you to take it every eight weeks.

[00:16:55] And then when this came out, then we switch many of our patients from every two-week to every eight-week dosing. But again, that can be a concern for patients who've been very stable on every two weeks, they say I don't want to take the chance of switching to every eight weeks. So, we have to discuss the risks and benefits of that when these newer medications become available.

[00:17:13] But sometimes having every eight-week treatment is a little bit easier. You only have to travel to the infusion therapy center every 8 weeks. You only have to disrupt your life every eight weeks. So, it can be a little bit easier. Injection site reactions can be an issue in finding injection sites.

[00:17:30] We often will inject in the stomach area, but sometimes you can inject in the thigh or even in in certain areas of the buttock. Oftentimes you'll have to rotate injection sites, but if you're giving your injections frequently, like once a week or a few times a week, it can be more challenging to find enough injection sites.

[00:17:50] And that can be a bit of a challenge. And then some of the medications are given every six months. Some patients like this, that they just have to go every six months, and then they're happy to make that trip to an infusion center, even if it's a far place away because it's only every six months. And sometimes that can be more convenient for people.

[00:18:07] Other times people say, I can take the medication at home. I prefer to do it that way. So certainly, patient preference comes into all of this. What about side effects? IVIG, subcutaneous immunoglobulin, these are nice medications in that they don't lower your immune system. And if anything, they boost the immune system a little bit and sometimes they can help.

[00:18:27] If your immunoglobulins are low with rituximab or inebilizumab sometimes your production, your B cells are targeted, and they're reduced and you make less antibodies. So, in that situation, if you're starting to get infections, we will give you back IVIG to boost up your immune system. So, the IVIG, subcutaneous immunoglobulin doesn't lower the immune system and that way have a nice benefit there.

[00:18:51] And they can be used in conjunction with other medications if those medications lower your IgG. Sometimes to reduce the risk of infections, you may want to try and be on one medication rather than multiple immunosuppressants. So that may be an option. Or sometimes we'll adjust the dose, we'll put you on a lower dose or we'll adjust the interval.

[00:19:10] Sometimes instead of giving the medication every six months, we might give it once a year or adjust it in that way to try and reduce the risk of side effects. Sometimes we'll have patients go on other medications to prevent infections. With some of the complement inhibitors like Eculizumab, ravulizumab, Soliris, Ultomiris, there is a risk of meningitis, a specialist type of bacteria called meningococcus that can cause a bacterial meningitis, which can be a serious infection.

[00:19:38] So in that situation, we will put people on preventative antibiotics, sometimes like with penicillin, and they'll take that daily to prevent side effects or with steroids. If you're on a high dose of steroids, we often need to use a medication called Bactrim, which is an antibiotic that will help prevent against a special type of infection in the lungs.

[00:19:59] It's important also to be up to date with vaccines. For our patients with autoimmune diseases on immunosuppressants, we avoid live vaccines, but we do recommend keeping up to date with many of those other vaccines like the influenza vaccine. The injectable one is an inactivated vaccine. The COVID-19 vaccine is not a live vaccine.

[00:20:20] The pneumonia vaccine is not a live vaccine. The shingles Shingrix vaccine is not a live vaccine. There is a live shingles vaccine. We would recommend that one be avoided. And then if you are sick, if you do develop an illness, make sure you go see your doctor or your provider when you're sick to make sure that any illnesses don't get out of hand and that you can be treated rapidly because your, if your immune system is lower, then you wanna get into the doctor quickly and get it treated quickly, more so than if you're not on an immunosuppressant.

[00:20:49] There are other side effects. We talked a bit about steroids. Steroids can impact the mood, diabetes, weight gain, lots and lots of side effects with steroids. So, we often talk about steroids sparing agents, because we really want to get, you use the steroids to get the inflammation down very quickly. They are super helpful in an attack of these conditions, but then we want to try and get you off of them and get you onto other medications that have lower risk of side effects.

[00:21:13] We talked earlier about antihistamines, like Benadryl for infusion reactions or sometimes you can slow the speed of giving the infusion, which means unfortunately you have to hang out in the infusion therapy center maybe for six, eight hours or it's a longer infusion at home. But that way we can help reduce those reactions.

[00:21:30] And then for injection site reactions, as mentioned, we'll often rotate the sites. And then fatigue. Remember that can be from the disease itself, so it might not necessarily be from the medication. There are special populations to think about, children, particularly with MOG antibody disease.

[00:21:43] Acute flaccid myelitis. Children can be affected by this and some of the medications can impact their growth, like steroids, you have to be a little bit careful about steroid use in children. And there can be an impact on schooling. So, for example traveling to an infusion therapy center you may have to miss days of school and that can be a challenge with children.

[00:22:05] So we got to think about that as we're making our choices about medication. Family planning and pregnancy. It's important in young females to think about this. Many of these medications can be problematic for pregnancy and in general, we would like to plan ahead if we're thinking about pregnancy.

[00:22:22] So discussing this with your provider, seeing if there's a dosing schedule that you could use. For example, with some of the six-monthly medications, sometimes physicians will recommend taking the medication and then a month later trying to become pregnant and the medication will be out of your system.

[00:22:37] But the effect of the medication may remain all the way through pregnancy, and that can help get you through pregnancy and prevent relapses. Other times the risk of relapses is so high that we will just continue the medication because that's the safest approach. But the bottom line is we wanna avoid any medications that are harmful for a baby.

[00:22:55] There can be religious considerations. Certain medications may have blood products or other things that can interfere for Jehovah Witness populations and things that we have to consider as we make our treatment decisions. And it's important that if any of these are pertinent to you, that you bring them up at your doctor and we're happy to work with patients to help get the treatment that's right for you, that fits with their beliefs and so forth.

[00:23:19] And for older adults, we have to be a little bit more careful. The risk of side effects is a little bit higher. Some of those people have other medical conditions that increase the risk of infection. So, we have to be a bit more cautious as we're trying to choose a medication for our older adults to make sure that we're not giving them too much risk of serious infections.

[00:23:39] Other things that might be a consideration for you? For example, with MOG antibody associated disease, we don't have any proven treatments, so we often encourage people to enroll in a clinical trial because that can help get us those proven treatments. Like I mentioned with the NMOSD earlier on, there are great benefits to being in a trial.

[00:23:57] You may have access to a medication that's not otherwise available. For many of our MOGAD patients, for example, they will not be able to get approval, insurance approval for any of these medications. And then we're stuck. We're not able to have access to any medications and getting into the trial may be a way to have access to some of those medications.

[00:24:15] For the trial, the pharmaceutical companies will usually cover the costs, and they may give some money to help cover your travel to and from the center. So, these should be cost neutral and should not cost you anything. So that can be a benefit of being in the trial. There can be, some of these trials use medications where we've experience for their use in other diseases.

[00:24:38] Some of these were used in, for example, myasthenia gravis or in neuromyelitis optica that I mentioned earlier, and that now these are being repurposed to other conditions. So, we have experience with their use and that can give us, be more reassuring in terms of risk of side effects, et cetera. When you're within the trial, you really get expert care.

[00:24:59] There's very close monitoring of all the blood tests. There's very close monitoring if you have a relapse, those tend to be identified very quickly and treated very quickly. And then once you have one relapse in many of these trials, then you'll go into the open label, and everyone will get the medication.

[00:25:14] And in general, if you're in a clinical trial, you may be helping future patients and the whole community where if you're a participant in the trial then and that medication works, then that medication may be available to a whole range of people around the world. So, you could really be helping a whole group of patients.

[00:25:33] There are potential downsides though, to clinical trials. Some of these will have a placebo arm, and that's a big concern for patients. If you enroll in the trial, you may be getting placebo and not getting a medication at that time. Sometimes they'll allow a background immunotherapy, so that might be an option for you.

[00:25:49] So there are aspects of the trials that sometimes can be a challenge. But many of them have designs that help prevent against being in a placebo for too long. For example, you're only allowed to have one relapse and then everybody will go into the open label arm or in some of the trials will be a three to one ratio, where three times as many people get the treatment as get the placebo, et cetera.

[00:26:12] So there's some ways around that. When you're in a clinical trial, you need to be available and make frequent visits often to the center, which can be challenging sometimes for people to make those time commitments. And then the possibility of side effects. Some of these medications we have a little bit less experience with.

[00:26:28] So there may be side effects that we, that turn up in the medication trials that we weren't fully aware of. So, there's some of the challenges. But overall, I think clinical trials, particularly for treatments where there's no proven treatment available, it's hard to get access to medications.

[00:26:44] If there's clinical trials in your area, certainly look into them and consider those as potential options. What about when you do decide to switch and what happens when you switch? The transition process, it's important to check that you have insurance approval before you stop the medication that you're on.

[00:27:02] It may, it's all well and good, the doctor will say, or the provider will say, let's switch to this medication. But if that doesn't get approved, then we may need to remain on the medication that we're already on. Now, you may need updated blood tests and MRIs at the time of the switch.

[00:27:16] It's usually a time where we'll re-baseline everything to see where everything is at, and then that'll give us a new baseline on the new medication. And then there's some safety considerations. For example, if you were on rituximab or inebilizumab where it has a long duration of effect where the effect of that medication, even if we're not dosing it any more may last six months or a year.

[00:27:37] And that may overlap with your new medication. So, you may be at particular risk of infection at that time, or it may take some of that medication some time to take effect and there may be a risk of rebound when you come off of the old medication, et cetera. So sometimes we have to think about some of these things as we transition medications. When we switch, sometimes people ask me, what should I switch to?

[00:28:00] And in general, one consideration is to switch to a different immune pathway. So, if you're on a treatment, sometimes the doctor will say you're on a B-cell targeted treatment like the rituximab, inebilizumab for NMO. Then you might wanna switch to a different mechanism, like a complement inhibitor or an interleukin six blockade to try and get a different treatment that may work better for you.

[00:28:22] So that's one component we think about. And then we'll look at the data. It's important to look at what has the clinical trial shown as best, what does our retrospective data show. How have these conditions, these medications worked for other diseases, and you can work with your provider to make your choice.

[00:28:39] After considering all of this data and the data changes, so each time you visit with your doctor, it's always good to ask are there any updates? Are there any new treatments that are coming out? Will those be options for me? And next question that people will ask is, can I ever stop my medication?

[00:28:53] For aquaporin-4 antibody positive, neuromyelitis optic spectrum disorder. This is the condition where I'm always concerned about the risk of stopping the medication. We have done it in rare occasions, but you have to be very cautious here because the risk of a severe attack, these attacks with the NMO can be more severe than some of those other conditions and can lead to permanent disability.

[00:29:14] For example, blindness in one eye, difficulty with walking. So, you have to be very cautious in this situation about dropping the medication even if your antibody goes negative. We'll talk a little bit about that. On the other hand, with MOG antibody associated disease, the first attack tends to be the worst.

[00:29:29] And then with other attacks, they tend to be less severe. And some people will just have one attack that we call monophasic. So, in some of those patients, we don't need to start them on a long-term treatment, or we can do it temporarily and then potentially remove it off. And attacks tend to be most frequent in the first five years and then reduce.

[00:29:48] At about five years' time, that may be a time when you would reduce and stop the medication. And there's less risk than risk with NMO because they, people tend to recover fairly well from the attacks. And most of the time, if you give steroids, people will get back most of any vision that they lost,

[00:30:05] for example. What about if your antibody titer level goes negative or your titer level goes down? That might be a situation where your doctor thinks about reducing your medication. If that happens, that does decrease the risk of future relapse, but it doesn't, sometimes it just falls below the cutoff, but the antibody is still there and then it will come back.

[00:30:24] Or some people will even continue to relapse while the antibody is just below the cutoff. So, you have to be a little bit careful about this, particularly with the NMO. I think you've got to be most careful even if the antibody is negative, many of these patients will continue with them on treatments.

[00:30:39] And then there's other conditions where you're seronegative all the way, for example, seronegative neuromyelitis, optica spectrum disorder, recurrent transverse myelitis or single transverse myelitis, acute flaccid myelitis, optic neuritis, autoimmune encephalitis. And these are situations where you'll wanna talk to your doctor about how long do I need to use the medication?

[00:30:56] Is this long term for me? And it really depends on the patient situation, how severe the attacks have been, how many attacks there has been, is the medication working for you? Is it causing complications, et cetera. What about stem cells? People often ask about this, should I switch to stem cells? I would have a word of caution here.

[00:31:14] There is a high risk upfront with these treatments up to zero to 1% risk of severe complication or even death. So, you got to be very careful. It may be okay in a reputable center in the USA; there are some clinical trials where you may be able to enroll in clinical trials. Some of these are open for multiple sclerosis, and they may be open for some of the other autoimmune conditions, but I would be very careful here doing this outside of a trial, there's often a lot of promise made, but they often don't deliver in my experience.

[00:31:44] And we'll see many patients who this treatment has not worked for them. We've had people go to other countries where they've undertaken some of these procedures and it's been very dangerous and led to severe complications. You wanna be very careful about this issue of stem cells, some of these things as clinical trials going on, and we'll get more data.

[00:32:02] And if the data starts to look good, then maybe it'll be an option in the future. It's important to have shared decision making. This is the patient and the family discussing, along with the physician or the advanced practice provider team and neurologists, neuro-ophthalmologist, rheumatologists may be involved in some of these decisions, helping to decide which medication is best for you and should I make a switch or not.

[00:32:28] What about the future? We may get into a situation where we have ways now where we can look in a patient's blood and see if they have active complement, for example. And then if they did, we would say, okay, a complement inhibitor is for you. On the other hand, in some patients' macrophages or microglia might be quite involved, and these are immune cells within the brain.

[00:32:51] We say, okay, for you we need to use something that targets microglia, like BTK inhibitors or something. On the other hand, the natural killer cells might be a big component and then we would target that for treatment. In other patients, we might see elevations in this IL six or other cytokines and we say, okay, we'll target interleukin six in you with some of these interleukin six blocking medications.

[00:33:14] In other people there is or in research there is a goal of trying to remove specific antibodies. So right now, with many of our treatments, for example, we use plasma exchange, we try and take away all of people's antibodies. But if we had a way where we could remove just the MOG antibody or just the aquaporin-4 antibody or just the antibody of interest for you, these are called seldegs or selective removal of antibodies.

[00:33:40] Others we have right now remove all your antibodies like the FcRn blockers, ravulizumab as an example of one of those. And then the FC gamma receptor signaling. There are ways that we can measure the signaling in patients and then see if that might be the option for you. So, there may be individualized where we have many different approved medications, but this one will work better for you and that might be a way we move in the future to get to these more targeted treatments that have less side effects.

[00:34:09] So the key takeaways of my talk, don't be afraid to ask your provider, is the treatment best for you? Does it remain best for you? As you see your provider back work in partnership with the physician, your family, what works best for you, it's not always the best medication in terms of effectiveness.

[00:34:27] Many of these medications are very effective in different ways. And the best decision for you might be that I can take the medication at home where that's easiest for me because it's very difficult for me to travel. So that might be the decision for you. On the other hand, for another patient, it might be that I want to do an infusion once every six months and then not worry about the treatment after that.

[00:34:48] So make sure you take into account some of those lifestyle factors because they're important. You may wanna explore before switching a medication. You may wanna explore ways of mitigating the challenges with the current medication. For example, if you're having a side effect and infusion reaction, maybe you can slow the infusion medication, take some additional Benadryl and deal with it that way, rather than switching medications.

[00:35:11] Make sure that you bring your goals and your values into the decision. The patient will always make the decision. So, it's important you bring your goals and values to the table. And make sure that you're asking your doctor about the latest research. Sometimes new medications have become available that work much better, that have less side effects, that are a better option for you, and that might be a time when you wanna switch medications.

[00:35:35] So I'm gonna stop there. I'd like to thank you all for your time and hopefully I addressed some of those questions about when to switch, when to stay, what are the things you need to know about your medication. Thank you all for your attention and I look forward to seeing you all in the future and thanks again to the SRNA for the opportunity.