Track MS Progress: Key Biomarkers Explained Transcript

(Transcripts are generated by AI and may contain errors)

Introduction and speaker background

Welcome to another really great interview. I'm your host for the MS and Neuroimmune Summit I'm here with Angela Sanchez. Now, Angela is an advanced Nurse Practitioner who has, a lot of Multiple Sclerosis, expertise.

And she is the medical science liaison with Octave Bioscience. She has over 20 years of experience with Multiple Sclerosis. And we're going to, get into a really interesting conversation about some new blood biomarkers that I personally am very excited about.

as a researcher in, as a clinician. now, Angela, is there anything that I've left out of your bio that we should be sure to include? No, that was perfect.

And thank you for that kind introduction, Dr. Wahls. Okay. So, again, for everyone who's listening, if you have multiple sclerosis or a autoimmune condition, you've probably had MRI's.

I bet you've had spinal taps. and we're trying to figure out what is the activity with a disease to guide what we're going to recommend, either as a conventional, neurologist specialist or as a functional medicine, integrative medicine, practitioner, because we want to help our patients have less disease activity.

So let's, talk a little bit about, biomarkers. you know, we have MRI's, we have spinal tap, you know, spinal fluid, and we have blood biomarkers. What's the difference between those three biomarkers?

Yeah, that's a great question. So as you know, biomarkers are an important tool for clinicians to use to again assess disease activity, and see how patients are progressing or not progressing, etc..

And each of those biomarkers are a little bit different. So imaging biomarkers or MRI, those give us kind of that, peek into what is happening structurally in the brain as well as, you know what, we can see where the lesions are located.

We can see the burden of lesions. So look how many lesions are present. you know, new and enlarging lesions and all of that. So with imaging, we can kind of longitudinally track over time changes, shifts, improvement and, worsening of disease with spinal tap.

It's really, important in the diagnostic process for MS. And it is included in the McDonald criteria in order to, you know, make sure that we're getting that accuracy in diagnosis for for patients with MS.

MRI, spinal tap, and blood biomarker basics

But what's really, interesting is that it tells us about the presence of proteins in the spinal fluid, and it tells us, you know, is there something that's occurred, and something, to guide that diagnostic process.

So dissemination and space and time are important criteria that can help fulfill that criteria. it's not generally used outside of research for monitoring patients and response to do any of activity.

And that's just because logistically, for many patients who've had to have this done, they know the the pain and the difficulty. Of getting a post spinal headache.

It was miserable. So, yeah. As a matter of fact, I've had one as well and had the same. I had to have a blood patch. So I have that personal experience as well as seeing that my in my patients.

So it's not feasible to monitor patients with with spinal taps with CSF. And so the other biomarkers that I want to

point out are also our clinical assessment.

So we can, you know, we think about when patients come in even just for blood pressure and other things. So those are also biomarkers they're telling us about, you know, where where the patient is at that point in time.

So we can do that with our clinical assessments when the patients come into the office. And as well as kind of subjectively, what the patients are reporting to us when we see them in the office, and trying to collect that in a way that is, has that methodology and, systemic, you know, accuracy and reliability.

There's a lot of variability there. So and I think even with imaging, we see a lot of variability in that biomarker. And that's because we're relying on the, you know, radiologists to do the assessment, to do the read, to do the comparison.

And so I think there's a lot of room for, you know, improvement in that variability as well. So that's a primer into imaging and CSF biomarkers. But let's talk about blood biomarkers because it's way easier for me to stick up my arm and have a blood draw.

And it has to curl up and have a spinal tap or to go, take a gadolinium enhancing MRI. So. Right. And what what are the advantages and disadvantages, to the biomarker.

So people are excited about serum neuro filaments which is somewhat helpful right. Yeah. So I think what is really unique about blood based biomarkers is that they give an objective assessment of disease activity, and they give an additional tool to help guide and inform mis management decisions.

But to your point, what makes them really unique is their accessibility for patients. And it's that they can go in. They can have a blood test done. They can it's noninvasive.

It allows for regular monitoring. gives that again, that snapshot. And also I just want to point out that by the time we have imaging or clinical changes or symptoms present, the damage has occurred.

And it's like looking in a rearview mirror. And so what we really want to see is if we're trending in the right direction and therefore if we can, we can change tack a little bit earlier in advance as opposed to after the fact.

So I think that's, you know, obviously another huge benefit of of blood based biomarkers. Now I'm going to shift the order here a little bit because I want people to have hope to have a sense clinically how these can be useful.

So do you have a patient story, a case that you could share where the active biomarker helped guide, decision making. Yeah, absolutely. Well, we have some really great patient advocates that have told their stories.

and but first I kind of want to highlight, you know, an example case of, you know, a case study for a patient. And in this case, it was a patient who, was on a treatment and was, you know, had been doing fairly stable on the treatment and the imaging showed stability over time.

but, you know, the patient was noting at a certain point in time that, hey, I'm having a lot more symptoms. I'm feeling worse. and I'm curious what's happening.

And the patient had the MSDA test done, and it did show, change. So this is the Octave biomarker test, and we'll come back and we'll explain what that is. Yeah, yeah. And your your bio test.

Right. You had your bio test and it's showing that the disease activity has increased. And according to the MSDA score which the MS disease activity test will, we will go and highlight what that is exactly.

But in this case, it allowed for the clinician and the patient to kind of come together in a shared decision making model and say, hey, the track that we're on right now is, you know, we're seeing some changes and shifts we need to change to change the direction of what we're doing.

And the patient, did a couple of things as, along with changing their DMT, but making some lifestyle interventions as well, and, seeing, you know, over time and retesting.

Then again, at the six month mark, that score went from a high score to a low, low score category. And I think that was very reassuring for both the patient and the clinician that we are headed in the right direction, that this longitudinal tracking of the score is really showing us this picture, this snapshot of, of improvement in a in a tangible way.

And so this could be a motivation ahead of waiting for the new lesions on my brain that I need to do a better job of my self-care routine, my lifestyle factors.

And I should maybe think about changing my disease modifying treatment of my DMT to a more aggressive treatment, to prevent, worsening. So. Right. why don't we explain what MSDA stands for and how is that different from the blood marker serum neuro filament that people may have heard about?

Absolutely. So what the MSDA test is. So MSDA stands for MS Disease Activity. And it is again a serum blood test. But it actually measures a panel of 18 different protein biomarkers.

And so these are proteins that show up in the blood. And what we do is we take those 18 individual biomarkers. And we don't just provide a readout of the level of those biomarkers.

So the clinician and the patient can can see those individual biomarker results.

Why blood biomarkers are useful in MS

But what we do and what's really special about MSDA is we take those 18 individual biomarkers into an algorithm. And this this algorithm was specially developed in order to produce an overall disease activity score that tells the patients and the clinicians at that point in time how active the disease is.

So it's not just relying on a single protein biomarker, such as NFL or GFP in the blood. It's actually taking this kind of symphony of proteins. And, and then what's also very unique about it is you also get pathway scores that are four pathways, and that helps to.

Understand what of the four. Driving. Yeah, the four pathways that are immuno modulation neuroinflammation myelin biology and neuro axonal integrity. And we've arranged these proteins into these pathways to help understand what's driving disease activity at that moment in time.

So, I think it's it's kind of a unique way of approaching the problem. to your point, we have NFL, GFP and that they provide us single protein, but what they don't tell the clinician is, you know, how to interpret that clinically. What does this mean clinically for my patient.

How do I make that actionable? And so, Mr.. And the report that's provided gives that, in the clinical Associations of disease activity. So let me see if I'm going to recap this for our, our listeners.

So I'll get a score that says things are low. So that's a good number. You want to be low. Yeah. Medium or high. High is a bad number. Yeah. Medium is is cautionary.

And so I'm getting some feedback that my brain inflammation markers are going up. So I'm going to be at higher risk for having new lesions or a relapse probably in the next six months to a year.

So I haven't shown up on my MRI, but I should be changing something so they don't show up on the next MRI. I might also be getting a score that suggests I'm at risk for degeneration in probably at risk to see, fixed disability develop.

And the interesting thing about, oh, yeah, go ahead and And then, if I get a score that would give me some clue

about the microglia activity in myelin biology.

So I have an environment that is helpful for my own repair or an environment that is harmful to myelin repair is is that correct? Yeah. So the this particular test was really developed to measure disease activity in the moment and not so much to predict progression but what the pathways do show us.

So if you think of immuno modulation as one pathway score, those are a lot of the proteins that signal the immune system to become more active.

Patient case: using MSDA to guide treatment changes

So you have this immuno modulation this early activation of the immune system. Then you have the pathway that's neuroinflammation. So once there's started, the kind of breakdown of that blood brain barrier has started and you start to see these proteins that are, neuro inflammatory.

And then we have the myelin biology, which is, one of the primary proteins in that pathway is Mog. Mog protein, which, you know, is kind of telling us, again, to your point about myelin biology and the the, potential for, you know, where are we at in that process of myelination?

And then later in the neuron auto integrity, we have NFL, GFP and other neurodegenerative, markers. So we do get kind of this picture of it by looking at the pathways of maybe where the patient is, and within that disease cycle.

and potentially, yeah, if we're in a, in a position of, you know, and with microglia, it's, there's not a straight shot to understanding, microglial biology, but we do include.

Yes, we're working on it. Yeah. You know. and again, for all the listeners, I think we we agree and I certainly tell my patients and I encourage all of you, the goal is no new enhancing lesions, no new relapses, because I want you to have your brain cells as healthy and as protected as possible. and, this is just another tool that your clinicians can use to help you achieve that goal.

the hopefully you have for yourself. No new lesions, no new relapses, and that your medical team has for you, no new enhancing lesions, no new relapses.

So it's another tool to help know, are you shifting the biology that's happening in your brain towards a less and less disease activity? Right. And I mean, you know, that there's a lot of with this iceberg effect and mass, there's so much that's happening beneath the surface that we can't really see.

And that's why, you know, blood biomarkers have that potential to highlight, like what is happening beneath the surface to a greater degree than has been possible before.

I think so. and this is new stuff. I mean, we're very excited. I know the last couple of years at the Ms. scientific meetings, we've been going to we've been hearing about these individual biomarkers.

and we've been, you know, I've been very excited to hear about these individual biomarkers and their role in, Parkinson's, in Alzheimer's, in multiple sclerosis and other neuro immune conditions.

What I think is unique, that active, is doing is combining all of this so we can have, if I get a report and I've seen this in my functional medicine integrative clinics, we get these reports with, hundreds of data points, and it overwhelms the patient, the like.

Oh, my gosh, I just don't know how to deal with this. And it can overwhelm the clinicians. So if we can use, our algorithms, our statistical analyzes to simplify it so I can just get a score of low, medium, high, it's easier for me to interpret and it's easier for my patients to then to know, like, okay, everything's looking good.

I can I can feel good about my program or there is activity that is worrisome and I would benefit from making some

changes. Right. And that, I think, is why what is so important is what is the actionability from and not just doing the tests and having it available, but how do you make it actionable?

And I think looking at the utility of the tests and how clinicians are using it to inform decision making is really valuable and important as well. when we validated the MSD test and what that means is we looked at the tests association to specific disease endpoints for patients with Ms..

And in this case we did look at gadolinium enhancing lesions.

What MSDA measures and how it differs from single biomarkers

We looked at new and enlarging T2 lesions as well as active versus C. So hang. On people don't know what new enlarging T2. Yes. Helps translate that. That's translate.

So first gadolinium enhancing lesions. Those are lesions that are active. That means that it's taking up contrast when you give the patient the contrast.

The there's a breakdown in the blood brain barrier that is allowing that contrast to cross, the blood brain barrier and go into these lesions where there's active demyelination so that those are areas with active demyelination or active disease activity.

New and enlarging T two lesions are actually when we are looking comparatively between two MRI studies. So one from the past and one from the current we're looking at are there new areas of disease activity.

This doesn't require contrast to be given. It just requires a comparison. So we're able to see, you know, in each area and section of the brain. Are there new areas, new lesions.

So that would be new T2 lesions. And T2 is just the sequence of MRI that we're using to look, look at the lesions. So are there new lesions or are existing lesions.

Have they enlarged from previous. So what that tells us is at some point between those two time points of imaging, there has been new disease activity.

It doesn't tell us if there's current disease activity. It tells us if there has been. And so that helps us understand again, are there changes that indicate that, the disease has continued, the disease activity has persisted.

And so go ahead. Yeah. No. Yeah. So and then active versus stable side as we looked at that that was a composite score of clinical disease activity and radiographic disease activity.

And so what we wanted to see was what is the association of the Mr.. To those specific endpoints. And that's important because we want to know that the test that we're doing is actually, you know, associated with the specific things that we're describing.

So in this case radiographic disease activity. And and that was part of our clinical validation for the test. And so and that's how we also looked at the score categories.

So when I said low, moderate or high we looked at the association of low for example, to know Catalonian and have seen lesions moderate to one and high to two or more.

And so we we wanted to capture those groups. and, and to the best of our ability in those categories. So does that make sense. Yes. Yes. And I think this could be also helpful as people age village of 50 over the age of 60.

and now the question may be talking to you like, you're older. The risk of the disease modifying drugs continue to climb as we get older, and the benefits maybe are diminishing because there won't be as many new enhancing lesions because your older your immune cells are less active.

But the patient's nervous about stopping the DMT. The clinician is nervous about stopping the DMT. and are there any clinicians that have turned to active to help them navigate what to do with the older patient?

I'm curious what's happening there. Yeah, I think that's one of the really important, use cases that is looking as, patients come off of disease modifying therapies because as to our prior point, about by the time you have new symptoms, our new radio, imaging changes on MRI, the the damage has already occurred.

And so if patients are coming off of therapy, if we can utilize this as a tool to monitor longitudinally, if we see shifts and changes in that baseline score, we can then say, oh, we're trending in a great direction.

You look fantastic. We've your office therapy now and you're looking you know, the scores is stable, right? Things are looking good. And conversely, we can much more quickly identify if we've taken patients off of therapy and, we're monitoring them.

If, if we see a spike in one of one of our, important cases was actually a patient who had been, was in his late 60s and had been on therapy for 20 years, and, came off of therapy and, had been doing, doing, pretty stable off of therapy.

But had Mr. Score that came back very high and that was followed by a clinical and, clinical disease activity. And so he was actually in this case, you know, a patient that needed to go back on therapy.

And conversely, we have had patients that, you know, are in their 70s and doing well off of therapy. And and their MSK score is stable. So it provides that additional like data point for the patient to feel confident.

And and that can apply not just in older adults, but when we think about any of the interventions that we're doing, throughout the patient journey with Ms.

is, you know, making that decision early on, like what level of therapy do I need to go on? You know, how active is my disease? Can I tolerate a lower efficacy therapy?

And for the time being, do I need to go on something that's more, that's more, more aggressive or highly effective? Right. So we just talked about, the older patient sensitive that since I'm now, in my late 60s.

So, yes.

Validating MSDA against MRI and clinical disease activity

I think that's an important question, but we also had young women who who maybe want to have kids, and they're trying to navigate, what to do about their disease modifying treatment.

given the fact I'd like to, work on getting pregnant, and, that complicates which DMT should I use? Is there a role for the active testing for that person who, you know, thinking like, you know, doc, I really would like to have kids.

how do I navigate this? Right. And I think that, you know, with where we're at in the current, landscape of DMT and what's out there, what's available, you know, there's a lot of different options now.

And I think thinking through childbearing and planning in that process with your clinician, your clinician is really important. And the way that a blood biomarker test might be helpful is if you do decide you maybe need to switch to a DMT, that's more that is, more conducive with, you know, getting pregnant and breastfeeding in the interim and having some reassurance with that switch that you, you know, your disease activity is remaining relatively stable throughout that process.

And also we are still and there's so much room for research in and postpartum women as well and timing when to go back onto therapy. And I think, you know, being able to understand that is really invaluable as well.

and I want to take a moment for, all of you young women who are considering, conceiving if you are successful getting pregnant. I want to encourage you to breastfeed because there's really some wonderful, data that points of women who breastfeed have lower rates of relapses and lower rates of new enhancing lesions.

So part of what I'm visualizing and Angela, I want you to weigh in here. So we have someone who, made her adjustments to her DMT, had a successful pregnancy.

She's talking to her for, family physician, obstetrician, pediatrician. I really want to breastfeed. So she breastfeed? She's, made whatever decision she did about her DMT.

She's, And what's would you see doing the Mr.. And how frequently might this breastfeeding mom, and her clinician look at that. Mr.. To figure out how to manage, her disease modifying treatments.

Yeah, that's a really great question. And I think there's, again, there's so much that we need to further understand about how hormones impact the, Ms..

Disease activity. We know that pregnant women seem to have a lower risk of relapse during pregnancy, but pretty, in the postpartum period, that risk kind of goes up.

But to your point, there's good evidence now for breastfeeding as well. And it'd be great to understand more about how biomarkers changed during that that time period.

But I think if you're monitoring patients in that postpartum period, what we looked at for our validation was really plus or -60 days. So ideally in that acute scenario, you'd want to test probably more frequently over every three months.

you know, for, for the most part for longitudinal testing, most clinicians are seeing patients back every six months or once a year. And so the cadence of MSD can kind of be in line with the, follow up time periods that they're having with their clinician.

And I think women in that postpartum period do need closer monitoring by, by their clinicians. Yeah. Yeah. I mean, I think that's definitely true. You we monitor pregnant people a lot, during their pregnancy and certainly, breastfeeding, women.

I'd like them to get monitored a lot. Yeah. And I, I have to be a huge champion. Breastfeeding is great for the kiddos. it looks like it's really good for, ladies with Ms..

And, of course, talk to your neurologist, talk to your primary care, person, and talk to whoever's, looking after your youngster as well. but I think that would be a huge, boost, to the confidence that everyone has if we include, the active testing.

Now, people who are listening are probably like, wow, this sounds like a pretty interesting way to get more information about my disease activity, how happy my brain is, happy my spinal cord is happy, my nerves are, so can I just call the lab up and say, hey, I want that because it sounds really cool.

That's a great question. Yeah, it is really cool. But I think, the best route right now is for patients to go and talk with their neurologist about it or their Ms.

clinician, and their clinician can get in touch with octave so that we can get them set up to order the test.

Using biomarkers in older adults and pregnancy planning

This is unique in the sense that we have, a clear and cap approved lab where all of these tests are run in one place. And so when patients do get their blood test done, it's drawn with the typical two, but it's shipped overnight to our lab to be processed.

And the clinician usually gets the results in about 5 to 7 days. and then they can review it with, with their patient. So is this limited to only, the, the United States or is this, available outside the United States right now?

We are just available in the US. But we're hoping, you know, of course, we're working on to be able to offer it. Yeah, yeah. Okay. this is super, super exciting.

And then I want everyone to know that I'm so excited about this. And we are, as we are developing new research ideas and proposals, one of the areas that we'd like to investigate.

And we we keep writing grants that we're going to get funded for this. I'm sure at some point, where what we'd like to do is, a stopping study, bring people in, put them on, diet and lifestyle, for three months, randomize them to either go after DMT or stay on their DMT.

and then, see what happens over the next 18 months. Now, we'd have to have the more mature individuals, in that one. They'll do that for youngsters. And so, you know, they, probably age 55 and older, because the current stopping studies, you just get randomized to stay or stop.

And, you know, we think you could do so much better if you would fix the diet and lifestyle first and then stop, and including active in those research proposals would be such a, very useful biomarker.

So, we plan on, on, reaching out to octave and including them, in future proposals that we're writing, for stopping study. And so if we have any one who's listening, who has, exceptional resources, who could help fund such a study, please reach out to us, because, so far, I've not been able to get the NIH willing to fund a stopping study like this.

I crazy, I think they should be, we will keep writing the grants. But if you believe that Dutton lifestyle matter and would like to see a stopping study like this happen, please reach out to us.

and we can help, work with you to get that kind of, funding going. It would. Yeah, it would be. And I think biomarkers are so unique and in this, in Mr..

In this case, because I think we want to be able to show how much of an impact diet and lifestyle have. And I think this is a very objective way to to just show that right to to kind of prove that point.

Yes, yes, yes. You know, and that will be a very powerful addition to our studies to look at changes in the media as people implement, you know, better diet, meditative practice, exercise.

this because, patient reported outcomes, they're useful, you know, for te quality of life. The reviewers, when they review our papers, they want to know what happened to the, biomarkers.

They would like to know the mechanisms by which diet and lifestyle matter. And so I could see, I'm seeing in the papers that we could write together where we could talk about here are the mechanisms by which diet and lifestyle is influencing the markers of degeneration, influencing the markers of inflammation, influencing these.

and what were the other two domains? I sort of I've sort of blew past the. Yeah, the the immune modulation neuroinflammation, myelin biology and neuro axonal integrity.

And, and that that will be very exciting. papers for our postdocs to write about in terms of, how lifestyle factors can influence the biology, that's happening in our bodies, in our brain.

Yeah. Absolutely. Agree. Yeah, yeah. Okay. So, one more question. you were a clinician and now you're into active. I'm sure there's a story there. What what how did this happen?

Yes. Thank you for that question. so many years ago, as you know, I've been involved in taking care of MS patients for many years. And I went to Rems, which is a, it's a committee.

It's a meeting that happens every year. It's very focused on, you know, research and advancement in MS. Care.

Accessing the test, research plans, and closing remarks

And I saw in 2021 a poster, presentation by Octave just on the early development of this, blood based biomarker test for MS Disease Activity. And I was just captured.

And I think what really captured me about it in that moment was, you know, as you know, in the field and manages these patients, we always would love to have additional tools and measures that really can bring us closer to precision care.

And it's very MS is complex. It is has a wide variability. It's very diverse. And how it presents and progresses and, how it responds to different interventions and therapies.

And because each patient is so unique, when I saw this, I was like, this is this could be really you know, life changing for patients. And so I think for me, when I saw that poster, I reached out to octave and I actually, got in touch with some members of the team, and I stayed in touch with them, over a couple of years, actually, and watched as they progressed.

And, so when the opportunity came, to join the team and be able, I think, to have, impact on patients from a bigger perspective, I still love my individual patients.

And, you know, I have a big passion for clinical care, but in this way, I think I and have getting to have that bigger impact, and kind of changing the field of MS for the better.

Okay. Well, I can I can appreciate that shared passion. Now For everyone who's listening, if you're a clinician, or you're a patient, how could they learn more about Octave?

so they could either add it to their clinical practice or, you know, to learn more, to ask their medical team to consider. Yeah. Yeah, absolutely. Thank you for that question.

So the patients and, clinicians can go to octavebio.com. we actually also. Do that a little slower. For sure. Yes of course. So they can go and we have a custom URL for, for everybody.

that's listening in today. They can actually go to octavebio.com/patients/drtalks all one word octavebio.com/patients/drtalks so they can go there and find more information.

There's also information for patients. in order to empower them to talk to their clinicians. So there's actually some resources for them as they're preparing to have a conversation with their doctor about the test, in order to kind of have that, open discussion about what their interest is and having the test done that's available on there and additional educational materials.

And we have one of our great patient advocates, heard a little bit of her story is on that website as well. Okay. Marvelous. Well, Angela, thank you so much.

I really enjoyed this conversation, and I am optimistic that at some point we will be able to do that stopping study and include, Octave in those biomarkers.

Me too. I'm looking forward to it. Dr. Wahls, thank you again for having me.